

## Research Article

**Hypertriglyceridemia is Associated with the Incidence of Preeclampsia*****Hipertrigliseridemia Berkaitan dengan Insidensi Preeklamsia***

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**Abstract**

**Objective:** To investigate the correlation between lipid profile during the second trimester II pregnancy and the incidence of preeclampsia.

**Methods:** This Universitas prospective study was conducted at the Woman's Health Clinic of Hasanuddin Teaching Hospital, Department of Obstetrics and Gynecology of the Faculty of Medicine, and its affiliated hospital in Makassar city from March 2015 to March 2016.

**Results:** The examination of the lipid levels of 115 pregnant mothers, aged 24-28 weeks. The mothers were then observed whether they experienced preeclampsia up to the time they gave birth or not. In the end, eight subjects (6.9%) experienced preeclampsia, and 107 subjects (93.1%) have no preeclampsia. The statistical analyses used Fisher's Exact test and Mann Whitney test. The research results indicated that the mean value of the total cholesterol and Low-Density Lipoprotein (LDL) was higher in the preeclampsia group compared to the non-preeclampsia group:  $267.37 \pm 64.12$  vs  $238 \pm 37.98$ ;  $177.38 \pm 55.38$  vs  $157.24 \pm 35.08$  ( $p > 0.05$ ). The mean value of High-Density Lipoprotein (HDL) was lower in the preeclampsia group compared to the non-preeclampsia group:  $64.75 \pm 14.64$  vs  $67.86 \pm 16.72$  ( $p > 0.05$ ). The mean value of triglyceride in preeclampsia group was significantly higher (19.5%) compared to the non-preeclamptic group:  $260.12 \pm 58.86$  vs  $209.14 \pm 65.10$  ( $p = 0.027$ ).

**Conclusion:** The hypertriglyceridemia was correlated with the preeclampsia incidence.

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**Keywords:** lipid profile, preeclampsia, trimester II of pregnancy

**Abstrak**

**Tujuan:** Mengetahui hubungan antara profil lipid kehamilan trimester II dengan kejadian preeklamsia.

**Metode:** Studi prospektif ini dilaksanakan di Poliklinik RS jejaring pendidikan Departemen Obstetri dan Ginekologi Fakultas Kedokteran Universitas Hasanuddin dan Poliklinik Kesehatan Ibu dan Anak di beberapa Puskesmas Kota Makassar selama Maret 2015 sampai dengan Maret 2016.

**Hasil:** Dari 115 ibu hamil dilakukan pemeriksaan kadar lipid, 115 ibu hamil pada usia kehamilan 24 - 28 minggu, kemudian diamati apakah subjek mengalami preeklamsia hingga proses persalinan. Terdapat delapan subjek (6,9%) berkembang menjadi preeklamsia dan 107 subjek tidak preeklamsia. Data dianalisis secara statistik dengan menggunakan uji Fisher's Exact dan uji Mann Whitney. Hasil penelitian menunjukkan bahwa nilai mean kolesterol total dan Low Density Lipoprotein (LDL) lebih tinggi pada kelompok preeklamsia dibandingkan kelompok tidak preeklamsia, yaitu  $267,37 \pm 64,12$  :  $238,01 \pm 37,98$ ;  $177,38 \pm 55,38$  :  $157,24 \pm 35,08$  ( $p > 0,05$ ). Nilai mean High Density Lipoprotein (HDL) lebih rendah pada kelompok preeklamsia dibandingkan tidak preeklamsia yaitu  $64,75 \pm 14,64$  :  $67,86 \pm 16,72$  ( $p > 0,05$ ). Nilai mean trigliserid daripada kelompok preeklamsia secara signifikan lebih tinggi 19,5% dibandingkan kelompok tidak preeklamsia, yaitu  $260,12 \pm 58,86$  :  $209,14 \pm 65,10$  ( $p = 0,027$ ).

**Kesimpulan:** Hipertrigliseridemia berhubungan dengan kejadian preeklamsia.

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**Kata kunci:** kehamilan trimester II, preeklamsia, profil lipid

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**INTRODUCTION**

Hypertension in pregnancy plays a major role not only in improving maternal morbidity and mortality during pregnancy and childbirth but cause problems after delivery which cause the risk of cardiometabolic disease in the future. World Health Organization (WHO) estimates that cases of preeclampsia occurs seven times higher in developing countries than in developed countries and contribute maternal deaths due to its complications during pregnancy. The prevalence of

preeclampsia in developed countries is 1.3% - 6%, while in developing countries is 1.8% - 18%. The incidence of preeclampsia in Indonesia itself is 128 273 / year (5.3%) and became one of the three causes of maternal mortality include haemorrhage (30%), eclampsia (25%) and infections (12%).<sup>1</sup>

Abnormal lipid metabolism had a significant impact on the pregnancy-induced pathogenesis of preeclampsia and associated with increased lipid peroxidation products that act as oxidative stress dysfunction endothelial.<sup>2</sup>

Results of a meta-analysis conducted by Gallos against 24 case-control studies and five cohort studies suggest a link between preeclampsia with triglyceridemia levels that precedes the occurrence of preeclampsia. In the study mentioned further research will be needed to define the prognostic accuracy test to identify women at risk, as well as whether the treatment lowers triglycerides can provide beneficial effects during pregnancy.<sup>3</sup>

Examination of biomarkers to predict preeclampsia developed at this time in addition to expensive, limited examination carried out on laboratory and specific regions. This research will conduct a cohort study that will look at the relationship between lipid profile in the second trimester and pregnant women with preeclampsia.

### METHODS

This study is a prospective cohort study, consecutive random sampling. This research was conducted at the Dr. Wahidin Sudirohusodo teaching Hospital Department of Obstetrics and Gynecology, Universitas Hasanuddin Makassar and its network.

The inclusion criteria of this study were pregnant women who do the antenatal care in the second trimester of pregnancy (24-28 weeks), with a complete identity, has a phone number that can be contacted, volunteered to follow the research and planned deliveries in Makassar. Subjects will be excluded if she had a history of metabolic diseases such as diabetes mellitus, vascular disease and coronary heart disease, a blood sample lysis

and the data is incomplete and does not follow the entire procedure. While the subject is considered to drop out if the pregnant women moved from Makassar or cannot be contacted or subject decided to stop participating in the study. Of the 115 subjects, obtained 8 (6.9%) of people who become preeclampsia serve as study groups, and 107 non-preeclampsia was used as a control group.

Three millilitres of venous blood of pregnant women who agreed to be the subject of research was taken and stored in tubes serum separator tube (SST), then the serum was examined on the same day. Serum lipid profile has been checked were total cholesterol, HDL, LDL and triglyceride using colourimetric, enzymatic through ROCHE / Hitachi system COBAS c. The concentration of lipid profile using milligrams per deciliter (mg/dl). Furthermore, the subjects were observed until delivery or until preeclampsia. Data analysis using the Fisher exact test and Mann Whitney's.

### RESULTS

During the period of one year (March 2015 - March 2016), we obtained 128 second trimester pregnant women, gestational age range 24-28 weeks who were willing to be the subject of research. Of the 128 subjects, there were 13 subjects who lost through observation and only 115 subjects were followed until childbirth. Of the 115 subjects, we obtained 8 (6.9%) of people who become preeclampsia serve as the study group and 107 people who did not preeclampsia used as a control group.

**Table 1.** Characteristics of the Sample

Characteristics	Preeclamptic Group n=8 (%)	Non-Preeclamptic Group n=107 (%)	p-value
<b>Age (years)</b>			
< 20 and > 35	2 (25)	30 (28)	0.608
20-35	6 (75)	77 (72)	
<b>Body Mass Index</b>			
< 25	2 (25)	49 (45.8)	0.223
≥ 25	6 (75)	58 (54.2)	
<b>Parity</b>			
Primi / nulliparous	2 (25)	45 (42.1)	0.290
Multipara	6 (75)	62 (57.9)	

Fisher's Exact Test

**Table 2.** Lipid Levels in Pregnancy

Lipid levels (mg/dl)	Preeclamptic Group n=8	Non-Preeclamptic Group n=107	p-value
Total cholesterol	267.37 ± 64.12	238.01 ± 37.98	0.218
LDL	177.38 ± 55.38	157.24 ± 35.08	0.353
HDL	64.75 ± 14.64	67.86 ± 16.72	0.704
Triglycerides	260.12 ± 58.86	209.14 ± 65.10	0.027

*Mann-Whitney Test*

In table 1 we can see the tendency of preeclampsia occurs in the age group 20-35 years, body mass index greater than 25 kg/m<sup>2</sup> and multiparous. Characteristics of age, body mass index and parity ( $p > 0.05$ ) were not statistically significant. The data showed homogeneous between groups of pre-eclampsia and non-preeclampsia group.

Table 2 shows the mean of each lipid in the preeclampsia and its counterpart. The increased levels of total cholesterol, LDL and HDL did not achieve a significant relationship between preeclampsia and non-preeclampsia group. There is a significant association between elevated levels of triglycerides of preeclampsia compared to the non-preeclampsia group with  $p = 0.027$ . The mean triglyceride levels of preeclampsia group 19.5% higher than its counterpart, whereas the mean value of total cholesterol and LDL respectively 12.3% and 11.3% higher, and the mean HDL levels 4.5% lower in the preeclampsia compared to the non-preeclamptic group. Compared with normal triglyceride levels in non-pregnant women (high levels of triglycerides <150 mg/dl) an increase of 42.3% was obtained among pregnant women.

## DISCUSSION

This study shows an association between high levels of triglycerides in the second trimester of pregnancy and preeclampsia. The participation rate of the subjects in this study amounted to 89.8% with a total of 115 subjects. Of the 115 subjects who obtained 6.9% of subjects in the course of her pregnancy developed preeclampsia. It is concluded that there were 3.9% of cases the diagnosis of preeclampsia enforced of all pregnancies and is half of the cases are found in gestational hypertension.<sup>4</sup>

The incidence of preeclampsia is affected by parity, race/ethnicity, genetic predisposition,

environment, socioeconomic and other factors. It is said the incidence of preeclampsia in nulliparous population ranged from 3 to 10%. In this study, two (4.3%) of 48 subjects nulliparous become preeclampsia.

Extremes of maternal age under 20 years and above 35 years increases the risk of preeclampsia.<sup>5</sup> In this study, 32 subjects are at the extreme age groups, and two of them suffered from preeclampsia, which is obtained statistically not significant results. Duckitt reported that the increase in preeclampsia increased almost two-fold in pregnant women aged 40 years or higher in primiparous and multiparous, while young age does not increase the risk of preeclampsia.<sup>1,6</sup>

Pregnancy causes changes in lipid profiles of different levels each trimester. Okojie et al. conducted a study involving 120 pregnant women, and they measured the total serum cholesterol, HDL, LDL and triglycerides in the first, second and third trimester compared with healthy women who were not pregnant. The result is an increase in total cholesterol, HDL, LDL and triglycerides were not significant in the first trimester but becomes significant in the second and third trimester compared to controls. Levels of lipid profile in second trimester described in Table 2, which found elevated levels of total cholesterol, LDL, HDL and triglycerides as much as 236.72 mg / dl, 156.64 mg / dl, 66.93 mg / dl and 207.93 mg / dl compared to the levels of healthy adult women who are not pregnant as much as <200 mg / dl, <100 mg / dl, 40-60 mg / dl and <150 mg / dl. It happens due to the increase of maternal fat metabolism is needed as an alternative to the energy needs of fetal development. In addition, lipids also caused hormonal changes among pregnant women (insulin resistance, progesterone, 17- $\beta$  estradiol, Human Placental Lactogen), maternal factors that include the body mass index, weight gain during pregnancy, the nutritional

status of the mother, lipid levels before pregnancy and other medical problems having a significant effect on the metabolism of lipids and levels in plasma. It does not only have an impact on the pregnancy itself but a risk factor for atherosclerosis and cardiovascular disease in the future.<sup>4,7,8</sup>

Moningkey on nested control study involving 82 non-preeclamptic and 84 preeclamptic women were divided into 31 and 53 cases of early-onset and late-onset, respectively. Triglyceride level as risk factors that most contribute to the early and late onset of preeclampsia. The same results were obtained on systemic reviews conducted by Ray and Gallos, investigating the risk of preeclampsia with triglyceride levels of maternal included 24 case-control studies involving 2720 women and five prospective cohort studies involving 3147 women second trimester before the onset of preeclampsia, showed hypertriglyceridemia precede the onset of preeclampsia.<sup>3,9,10</sup> In this study, of 115 subjects of second-trimester pregnant women (gestational age 24-28 weeks), 8 (6.9%) subjects whose pregnancy develops into preeclampsia and its triglycerides were elevated significantly before the onset of preeclampsia ( $p = 0.027$ ).

Pregnancy with hypertension and preeclampsia have a relationship with the occurrence of chronic hypertension and increased risk of cardiovascular disease in the future. This is because the metabolic abnormalities in pregnancies that include obesity, insulin resistance and abnormal lipid levels cause endothelial dysfunction and eventually preeclampsia. The underlying mechanisms are still further research. Early detection, control and handling is expected to positively affect the outcome of the pregnancy itself and lifestyle modifications for future cardiovascular health.<sup>11</sup>

## CONCLUSIONS AND SUGGESTIONS

High levels of triglycerides in the second trimester of pregnancy is associated with the incidence preeclampsia. Examination of triglycerides can be considered as a basis of examination in the second trimester in order to see the likelihood of preeclampsia.

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