

Research Article

## Serum Lipid Profile in Pregnancy and Postpartum Severe Preeclampsia

### Profil Lipid Serum pada Preeklamsia Berat dalam Kehamilan dan Postpartum

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#### Abstract

**Objective:** To investigate the association between serum lipid profile (total cholesterol, triglyceride, HDL, LDL, VLDL) and pregnancy as well as postpartum severe preeclampsia.

**Methods :** This is a cross-sectional comparative analytic study

**Results:** From 28 preeclampsia subject were found, mean value of systole 165.36 mmHg and 105.71 diastole. Serum lipid profile in pregnancy and postpartum has a significant differences and correlated with preeclampsia, total cholesterol 234.5 mg/dl and 192.71 mg/dl,  $p=0.000$ ; medium positive in pregnancy with systole  $r=0.461$ ;  $p=0.013$ , weak positive with diastole  $r=0.380$ ;  $p=0.046$ ; postpartum with systole medium positive  $r=0.615$ ;  $p=0.001$ , and weak positive with diastole  $r=0.317$ ;  $p=0.100$ . LDL 140.5 mg/dl and 102.5 mg/dl,  $p=0.000$ ; pregnancy and systole  $r=0.446$ ;  $p=0.017$ ; and postpartum were medium positive  $r=0.546$ ;  $p=0.003$ . HDL 51.5 mg/dl and 43.5 mg/dl,  $p=0.003$ ; not correlated with BP. Triglyceride 268.89 mg/dl and 208.96 mg/dl,  $p=0.000$ ; pregnancy  $r=0.516$ ;  $p=0.005$ ; postpartum  $r=0.515$ ;  $p=0.005$  has medium correlation with systole. VLDL 53.78 mg/dl and 41.79,  $p=0.000$ ; pregnancy  $r=0.461$ ;  $p=0.013$  systole medium positive;  $r=0.380$ ;  $p=0.046$  diastole weak positive; postpartum  $r=0.615$ ;  $p=0.001$  systole strong positive.

**Conclusions:** All parameter of serum lipid profile in pregnancy and postpartum had significant differences and related with severe preeclampsia. Total cholesterol, LDL, triglyceride, and VLDL correlated with BP in severe preeclampsia.

**Keywords:** endothelial dysfunction, lipid profile, preeclampsia.

#### Abstrak

**Tujuan:** Untuk mengetahui hubungan profil lipid serum (kolesterol total, trigliserida, HDL, LDL, VLDL) dengan preeklamsia dalam kehamilan dan postpartum.

**Metode:** Penelitian ini merupakan studi potong lintang analitik komparatif.

**Hasil:** Dari 28 subjek dengan preeklamsia, ditemukan rerata systole 165,36 mmHg dan 105,71 diastole. Profil lipid serum dalam kehamilan dan postpartum ditemukan berbeda bermakna dan berhubungan dengan preeklamsia berat, kolesterol total 234,5 mg/dl dan 192,71 mg/dl,  $p=0,000$ ; kehamilan dengan sistole positif sedang  $r=0,461$ ;  $p=0,013$ , diastole positif lemah  $r=0,380$ ;  $p=0,046$ ; postpartum dengan sistole positif sedang  $r=0,615$ ;  $p=0,001$ , dan diastole positif lemah  $r=0,317$ ;  $p=0,100$ . LDL 140,5 mg/dl dan 102,5 mg/dl,  $p=0,000$ ; dalam kehamilan dengan sistole  $r=0,446$ ;  $p=0,017$ ; dan postpartum positif sedang  $r=0,546$ ;  $p=0,003$ . HDL 51,5 mg/dl dan 43,5 mg/dl,  $p=0,003$ ; tidak berkorelasi dengan TD. Trigliserida 268,89 mg/dl dan 208,96 mg/dl,  $p=0,000$ ; kehamilan  $r=0,516$ ;  $p=0,005$ ; postpartum  $r=0,515$ ;  $p=0,005$  korelasi positif sedang dengan sistole. VLDL 53,78 mg/dl dan 41,79,  $p=0,000$ ; kehamilan  $r=0,461$ ;  $p=0,013$  positif sedang dengan sistole;  $r=0,380$ ;  $p=0,046$  positif lemah dengan diastole; postpartum  $r=0,615$ ;  $p=0,001$  positif kuat dengan sistole.

**Kesimpulan:** Seluruh parameter profil lipid serum kehamilan dan postpartum ditemukan memiliki perbedaan bermakna dan berhubungan dengan preeklamsia berat. Kolesterol total, LDL, trigliserida, dan VLDL ditemukan berhubungan dengan TD pada PEB.

**Kata kunci :** disfungsi endotel, lipid, preeklamsia.

## INTRODUCTION

Maternal death in Indonesia is dominated by top three causes which are bleeding, hypertension in pregnancy, and infection.<sup>1</sup> But the proportion has experienced changes, with bleeding and infection has been declining while hypertension in pregnancy is arising. More than 25% of maternal death in Indonesia 2013 associated with hypertension in pregnancy.

Endothelial dysfunction can be caused by lipid metabolism changes.<sup>2</sup> Lipid serum has a direct effect in endothelial dysfunction.<sup>2</sup> Preeclampsia were characterized with lipid concentration changes e.g. hypertriglyceridemia, relative elevation of LDL-C, while both are associated with endothelial injury and dysfunction.<sup>3</sup> HDL-C concentration decline were associated with preeclampsia.<sup>3</sup> With rich information on serum lipid, American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy 2013 doesn't include serum lipid profile as their diagnosis criteria.<sup>4,5</sup>

Several previous studies has found the relation within serum lipid changes with preeclampsia.<sup>2,3,6-18</sup>

Generally, the study that being performed is focused on "peak" condition before labour, while postpartum concentration still very few explored.<sup>14</sup> Study that documented the differences of serum lipid in preeclamptic subject still scarce.<sup>6,9,14</sup> The lack of data on this matter is what the base of this study.

## METHOD

This was a cross-sectional analytic comparative study to investigating the differences of serum lipid concentration on preeclamptic subjects in pregnancy and postpartum. The study was performed in Prof. Dr. R.D. Kandou General Hospital Manado, and its affiliated hospital. Since October 2016<sup>th</sup> till January 2017<sup>th</sup>.

The population is all preeclamptic patient that has come for labour and or pregnancy termination. Samples are patients that fulfilled the inclusion criteria and signed the informed consent.

Inclusion criteria were all preeclamptic women that going to delivered and or pregnancy termination, that is willing to participate in this study and signed the informed consent form, and willing to fasting in <sup>6-8</sup> hours before blood sample collection.

Sample collection were performed in the delivery room and obstetrics ward. The sample was 5cc of venous blood, while the subject has been debriefed and signed the informed consent form. All data collected were analysed using SPSS 16.0.

## RESULT

A total of 28 subjects were recruited for this study. Samples were collected from 28 severe preeclampsia subjects.

## DISCUSSION

The characteristic of the subjects are presented in Table 1. A total of 16 subjects (57.1%) belonged to the age group of 20-35 years old. Subject occupation with majority stay home mother 25 (89.2%) subject. Parity were found 13 primigravida (46,4%) and 15 (53.6%) multigravida. Based on mode of delivery were found majority cesarean section 22 (78.6%), and 6 (21.4%) vaginally.

Statistical analysis in table 2 found that mean total cholesterol value increased in pregnancy with 234.5 mg/dl, and within a normal value in postpartum with 192.71 mg/dl. We found a significant difference with between pregnancy and postpartum preeclampsia ( $p=0.000$ ). Using Spearman correlation test, were found medium positive correlation between total cholesterol and systole BP in pregnancy ( $r=0.461$ ,  $p=0.013$ ), weak positive with diastole BP ( $r=0.380$ ,  $p=0.046$ ). In postpartum condition were found medium positive correlation ( $r=0.615$ ,  $p=0.001$ ) with systole BP, and weak positive correlation ( $r=0.317$ ,  $p=0.100$ ) with diastole BP. Interpreted with higher total cholesterol concentration in severe preeclampsia on pregnancy and postpartum, higher the systole and diastole BP.

Increase in total cholesterol value also found in other studies,<sup>2,3,7,9,11-13,16</sup> while only few study that



found significant differences that strongly related with preeclampsia ( $p=0.000$ ). Correlation analysis using Spearman test found medium positive correlation ( $r=0.516$ ,  $p=0.005$ ) in pregnancy, and medium positive correlation ( $r=0.515$ ,  $p=0.005$ ) in postpartum with systole BP. Interpreted by higher triglyceride value in pregnancy and postpartum, higher the systole BP.

Increases in triglyceride value were consistently documented in studies.<sup>2,3,6-9,11-18</sup> Preeclampsia risk documented doubles in pregnancy on triglyceride elevation.<sup>20</sup> Positive correlation with diastole were found in study by Winkler et al.<sup>2</sup>

In our study we found mean value of VLDL 53.78 mg/dl in pregnancy and 41.79 mg/dl in postpartum, where both increases compared to normal value (3-40 mg/dl). Using t-test analysis significant difference and strong relation with preeclampsia ( $p=0.000$ ). In correlation analysis there is medium positive correlation ( $r=0.461$ ,  $p=0.013$ ) with systole in pregnancy, and weak positive correlation ( $r=0.380$ ,  $p=0.046$ ) with diastole in pregnancy. In postpartum there were strong positive correlation ( $r=0.615$ ,  $p=0.001$ ) with systole. Interpreted by higher VLDL value on severe preeclampsia in pregnancy and postpartum, higher the systole BP. While diastole found higher in pregnancy period.

VLDL value increases significantly in several studies.<sup>2,7-9,12,16</sup> VLDL elevation in preeclampsia cases were associated with endothelial injury.<sup>8</sup> Triglyceride value increase were reported consistently in other preeclampsia studies and also our study, it is said that hypertriglyceridemia associated with twice more risk of preeclampsia in pregnancy.<sup>20</sup> Although causative relationship haven't been reported, it is widely known that higher triglyceride concentration increases the risk of placental blood vessel impairment, which spark endothelial dysfunction, atherosclerosis and thrombosis, and atherosclerosis formation in placental spiral arteries on women with preeclampsia.<sup>21,22</sup> Triglyceride and VLDL increase in this study is an dyslipidemia marker, and were associated with endothelial injury that spark atherosclerosis.<sup>6,8,9,11,15-18</sup>

Women with preeclampsia having greater changes in lipid metabolism compared with normotensive pregnancy.<sup>11</sup> Dyslipidemia

in women with preeclampsia related with characteristics that were found in insulin resistance, which can be found in women with hyperglycemia in metabolic syndrome with hypertension characteristic. Insulin resistance in pregnancy with preeclampsia were thought to increases free fatty acid sum in visceral adiposity, that increases VLDL production in liver, and suppressed lipoprotein lipase activity, that causes serum triglyceride increased, which then increasing the risk of preeclampsia.<sup>6,8,9,11</sup>

Bellamy et al in their systematic review, reported that women with preeclampsia history will experienced increased risk of cardiovascular disease (relative risk,  $RR=3.7$ ), hypertension ( $RR=2.16$ ), ischemic heart attack ( $RR=1.81$ ), vein thromboembolism ( $RR=1.79$ ), and death ( $RR=1.49$ ).<sup>23</sup> This findings concluded there is connection between hypertension while pregnant and cardiovascular disease in the future.<sup>23</sup>

Multifactorial disorders that causes maternal and fetal mortality is a preeclampsia characteristic, which makes it difficult to be prevented.<sup>8</sup> LDL/HDL ratio increase, as stated previously in this study were related with endothelial dysfunction. This can causes thrombocyte aggregation and free fatty acid formation in the blood vessel, which in turn causes endothelial injury and dysfunction, then clinically manifested as hypertension and proteinuria in preeclampsia.<sup>8</sup>

Clinically, although relation of serum lipid profile with preeclampsia, the use of anti-hyperlipidemia in pregnancy especially associated with preeclampsia still scarcely documented and still haven't been recommended.<sup>24</sup> Even in most studies of anti-hyperlipidemia pregnancy is an exclusion criteria.<sup>24,25</sup> Omega-3 fatty acid can be used safely in pregnancy for decreasing maternal triglyceride concentration.<sup>24-26</sup> Nicotinic acid (niacin) reported to increases HDL concentration, but only documented in case reports, so still not being recommended.<sup>24-27</sup>

Fibrates that can decreases TG concentration, increases LDL clearance, and increases HDL level also not being properly studied in pregnant women, hence the usage still not recommended.<sup>24-27</sup> HMG-CoA reductase inhibitor studies, or widely known as statins, in pregnancy has a controversial reports associated with

teratogenicity and congenital malformation, generally not recommended.<sup>24,26</sup>

Our study limitation, is the absence of control in normotensive pregnancy and postpartum, lipid concentration increase also found in normal pregnancy,<sup>2,5,6,8,9,11,13-18</sup> so the increase of all lipid parameter in our study cannot properly confirmed against normotensive pregnancy. The association of all lipid parameter with preeclampsia were not found in other studies, though the relation of single or other parameter can be confirmed.<sup>2,3,6-18</sup> This finding is thought to be associated with majority of cesarean section delivery in subjects 22(78.6%), but with our small number of sample, chi-square statistical analysis cannot properly performed to verify this notion.

### CONCLUSION

There is significant differences in total cholesterol, triglyceride, HDL, LDL, and VLDL value on severe preeclamptic subjects in pregnancy and postpartum that strongly related with preeclampsia. Higher total cholesterol in preeclamptic pregnancy and postpartum, higher systole and diastole BP. Higher LDL and triglyceride in preeclamptic pregnancy and postpartum, higher systole BP. There haven't been found correlation between HDL and BP in preeclampsia. Higher VLDL in severe preeclampsia in pregnancy and postpartum, higher systole and diastole BP; while in postpartum higher VLDL, higher diastole BP.

### SUGGESTION

Further study needed with bigger sample size and control group usage. There could be further study in researching the relation between triglyceride and preeclampsia.

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