STUDY OF LIPID PROFILE IN PREECLAMPSIA

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Abstract:  
Background: Hypertensive disorder may complicate in about 3-10% of all pregnancies with variable incidence among different hospitals and countries. It is one of the important member of deadly triad, along with hemorrhage and infection which contributes for the maternal morbidity and mortality rates. Long term health implications in women who develop hypertensive disorders of pregnancy (HDP) include an increased risk of developing cardiovascular diseases (CVD) later in life.

Aim: So based on this the present study was undertaken to investigate the lipid profile in normal pregnant and preeclamptic women.

Materials and Methods: After Ethical committee Approval, serum fasting lipid profile were estimated in 100 normal pregnant women (controls) and 100 pregnant women with preeclampsia (cases) and comparison between cases and age matched controls of age group 18-35 years done ‘z’ test. All statistical analyses were performed using GRAPH PAD PRISM version 5.00 software.

Results: Serum Triglyceride (TG), very low density lipoprotein (VLDL), low density lipoprotein (LDL) were significantly elevated (p < 0.0001) while high density lipoprotein (HDL) was significantly decreased (p < 0.0001) in preeclamptic group than in control group. No significant difference found in total cholesterol level in either group. Lipid ratios (TC/HDL C, LDL/HDL C and TG/HDL C) were also significantly elevated (p < 0.0001) in cases compare to controls.

Conclusion: This study concluded that dyslipidemia contributed for developing preeclampsia.

Keywords: Preeclampsia, Lipid profile, Dyslipidemia

Introduction

Hypertensive disorders accounts for 5-10% of all pregnancies, and considering their complications, they are among the major causes of maternal morbidity and mortality.\textsuperscript{1,2} Preeclampsia, the most prevalent hypertensive disorders of pregnancy, is defined as a systolic blood pressure level of 140 mm Hg or higher or a diastolic blood pressure level of 90 mm Hg or higher that occurs after 20 weeks of gestation with proteinuria (≥300 mg/24 hrs).

Studies have already shown alterations in serum lipid profile in pre-eclampsia. Dyslipidemia has a direct effect on endothelial dysfunction. The most important feature in preeclampsia is hypertension which is supposed to be due to vasospastis phenomenon in kidney, uterus, placenta and brain. Altered lipid synthesis leading to decrease in PGI\textsubscript{2}: TXA\textsubscript{2} ratio. It has also
role in pathogenesis of preeclampsia. In this way abnormal lipid metabolism has important role in the pathogenesis of preeclampsia.

The hormonal imbalance is major factor for the etiopathogenesis of preeclampsia and this endocrinal imbalance is well reflected in altered serum lipid profile. Early pregnancy dyslipidemia is associated with an increased risk of pre-eclampsia. Disorders of lipoprotein metabolism are major cause of hypertension and proteinuria in Preeclampsia. So that the present study was undertaken to investigate the alteration in lipid profile (Cholesterol, triglycerides, HDL-cholesterol, VLDL-cholesterol and LDL-cholesterol) in normal and pre-eclamptic women.

**Materials and Methods**

The present study has been carried out in Indira Gandhi Government Medical College & Mayo Hospital, Nagpur during the period of November 2011 - January 2013. The study protocol was approved by the Institutional Ethical Committee. Informed written consent was obtained from all the study subjects enrolled in the study. Study sample was included total of 200 individuals; 100 diagnosed preeclamptic patients (Cases) admitted in ANC ward in this institute and 100 age matched healthy and apparently normal pregnant women (controls) were also selected for study.

**Inclusion criteria for cases and controls:** The cases and controls were in the age group of 18-35 years.

**Exclusion criteria for cases and controls:** Pre-existing hypertension, IHD, CRF, DM, liver diseases, thyroid disorders, past and family history of hyperlipidemia, treatment with drugs may influence lipid profile.

**Serum lipid profile**

5 ml of fasting venous blood sample was withdrawn from the anti-cubital vein of each participant after taking all aseptic precautions using sterile needles and syringes without the aid of a tourniquet. Haemolysed samples were excluded from the study. For estimation of lipid profile, 5ml of the blood sample were then immediately transferred to a clean dry sterile plain bulb. The blood samples were analyzed immediately. Serum lipid profiles were estimated from fasting blood sample.

Total cholesterol (TC) and triglyceride (TG) estimated by enzymatic method, high density lipoprotein (HDL C) by precipitation method and very low density lipoprotein (VLDL) and low density lipoprotein (LDL) by Friedewald equation. The estimation was done on TRANSASIA ERBA CHEM-5 Plus Semi-Automatic Analyzer.

**Statistical Analysis**

Z test was used to assess the significance of the differences in values of the parameters in cases and controls and values were reported as the mean ± SD. Differences were considered statistically significant at a probability value p < 0.05. All statistical analyses were performed using GRAPH PAD PRISM version 5.00 software.

**Results**

In cases the mean age of distribution was 22.86 ± 2.63 years and gestational age was 34.85 ± 1.03 weeks while in controls the mean age of distribution was 22.95 ± 2.27 years and gestational age was 34.85 ± 1.03. (Table 1, Fig. - 1 & 2) On comparing mean age and gestational age of cases and controls by z test, p value was 0.79 and 0.97 respectively which was statistically non significant. Hence both the groups were comparable.

Total cholesterol, triglycerides, VLDL, HDL and LDL levels in cases were 230.5 ± 6.817, 209.0 ± 6.442, 41.84 ± 1.293, 34.02 ± 3.533 and 154.7± 8.940 respectively. In controls total cholesterol, triglycerides, VLDL-cholesterol and LDL-cholesterol were 229.0 ± 5.585, 169.0 ± 7.247, 33.80 ± 1.477, 73.86 ± 2.247 and 121.3 ± 4.661 respectively. (Table 2, Fig 3)

Triglycerides, VLDL and LDL were significantly (P < 0.0001) increased in cases than controls while total cholesterol was not significantly increased in cases than controls. HDL was significantly (P < 0.0001) decreased in cases than controls.

Lipid ratios- TC/HDL C, LDL/HDL C and TG/HDL C in cases were 6.9 ± 0.88, 4.6 ± 0.72 and 6.2 ± 0.83 respectively. In controls TC/HDL C, LDL/HDL C and TG/HDL C were 3.1 ± 0.11, 1.6 ± 0.09 and 2.3 ± 0.10 respectively. (Table...
2, Fig 4) All three lipid ratios- TC/HDL C, LDL/HDL C and TG/HDL C were significantly (P < 0.0001) increased in cases compared to controls.

**Discussion**

Preeclampsia continues to be a main obstetric problem in present day healthcare practice. It affects not only maternal health but also puts fetal development at risk. The high blood pressure problems of pregnancy are very frequent. During pregnancy and the puerperium it is accountable for 12% of maternal mortality worldwide.7

The relation between a disordered lipid profile, endothelium cell and oxidative stress is of major importance to the patho-physiology of pregnancy induced hypertension. Elevated plasma lipids are believed to be probable cause of endothelial cell activation. In normal pregnancy adaptive alteration occur in women’s physiology to setup needs for the rapidly developing fetus.8 This normal alteration exaggerated in preeclampsia includes insulin resistance, hyperlipidemia and up-regulation of inflammatory markers.7,9 Studies have revealed that patients having preeclampsia are more exposed to cardiovascular diseases, signifying that preeclampsia and cardiovascular disorders may share similar mechanisms.9,12

In the present study, no significant difference in total cholesterol level of cases and control could be observed which was consistent with the findings reported in studies conducted in other populations.3, 5, 9, 13-15 Some earlier studies3, 15-18 reported that the striking change in the lipid profile in preeclampsia was serum hypertriglyceridemia. In our study also this observation holds true and the rise in serum triglycerides was statistically significant (P<0.0001) in pregnancy induced hypertensive patients when compared to women with normal pregnancy

Hypertriglyceridemia may be modulated by hyperinsulinism established in pregnancy.19 Triglycerides, small dense LDL particles and free fatty acids levels increased in normal pregnancy are correlated with insulin resistance.20 In preeclampsia this insulin resistance is exaggerated and causing further increased in triglycerides levels.21 During gestation these interactions along with increased endothelial triglyceride accumulation may result in endothelial cell dysfunction.22 In preeclampsia increased triglyceride found8, is probably deposited in predisposed vessels, such as the uterine spiral arteries and contributes to the endothelial dysfunction, both directly and indirectly through generation of small, dense low density lipoprotein cholesterol. Moreover, this hypertriglyceridemia may be linked with hypercoagulability.23

In pregnancy hepatic lipase activity increased and lipoprotein lipase activity decreased. Hepatic lipase induces synthesis of the more triglycerides at the hepatic level, and low lipoprotein lipase activity causing decreased catabolism at the adipose tissue level. In late pregnancy estrogen increases VLDL production and decreases lipolysis. Upregulation of placental VLDL receptors causing a coordinated rerouting of TG-rich lipoproteins from the mother toward the fetoplacental unit to meet the nutritional demands of the growing fetus. But in preeclampsia nutrient uptake by fetus is affected resulting in fetal distress and retardation. So that reduced maternal lipolysis and the low uptake of TG-rich lipoproteins by the fetoplacental unit lead to the accumulation of TG-rich lipoproteins in the maternal circulation.24, 25

Another hypothesis is that hypertriglyceridemia is as a result of competition between chylomicrons and very low-density lipoprotein cholesterol for the lipoprotein lipase. Chylomicrons removal occurs in two sequential steps: (1) Hydrolysis of triglyceride by lipoprotein lipase (2) uptake of the remnant by the liver. Delay in the second step leads to accumulation of remnants in plasma and is generally thought to represent the atherogenic risk of hypertriglyceridemia.24

In present study, serum VLDL-C level rose significantly (P<0.0001) in the patient. This rose in VLDL cholesterol may be due to hypertriglyceridemia leading to increased entry of VLDL-C that carries endogenous triglyceride into circulation. VLDL-C level further elevates in preeclampsia as found in the present study in validation with those of other researchers.5, 9, 16, 26 Increased VLDL-C accumulate over the maternal vascular endothelium, mainly those of uterine and renal vessels.3 Further VLDL-C may cause injury to the endothelium, while a particular toxicity preventing- activity-protein protects against the VLDL-induced damage in the pathogenic process of toxaemia.27

In our study HDL cholesterol was significantly decreased (p<0.0001) in preeclamptic group than healthy control group. Decrease in HDL-C level in preeclampsia supported by other studies also.4, 14, 15, 17 Our finding of increased LDL-
cholesterol (p <0.0001) in preeclamptic group also proved by various studies.4,14,15,28

Oestrogen is responsible for induction of TG and HDL and suppression of serum LDL in pregnancy but oestrogen level falls in preeclampsia.3 Low level of HDL in pre-eclampsia is not only because of hypoestrogenaemia but also due to insulin resistance.21 So that low LDL-C level in normal pregnancy as observed in present study may be attributed to hyperoestrogenaemia and significantly higher LDL-C level in pre-eclampsia are due to low oestrogen level in preeclampsia.29 Low HDL C level in preeclampsia reduces prostacyclin level and antioxidative protection for the other lipoproteins.13

We had also calculated the ratios between different lipids like TC: HDL-C, LDL-C: HDL-C and TG: HDL-C for the patients and control groups. There was a significant increase (p < 0.0001) in TC: HDL-C, LDL-C: HDL-C and TG: HDL-C in pregnancy induced hypertensive women in contrast pregnant women with normal blood pressure. Similar finding was found in other studies.3,30,31 These ratios also indicates insulin resistance. Insulin resistance in preeclampsia was proved by various studies.32-34

Though the association of these ratios in pregnancy and preeclampsia is yet to be recognized, the significance of altered lipid profile ratios (TC: HDL-C, LDL-C: HDL-C and TG: HDL-C) cannot be ignored as they point toward more threats in preeclampsia.5

Dyslipidemia mediate activation of the endothelial cells to the placental derived endothelial disturbing factors like lipid peroxides and trophoblastic components or combination of placental derived factor with the lipoproteins could be considered as probable contributor for pathogenesis of pregnancy induced hypertension. High levels of triglycerides and low level of HDL along with hypertension are associated with metabolic syndrome. Association between preeclampsia and metabolic syndrome proved by various studies.36,37

Kawamoto R et al (2011)38 showed that lipid ratios of TC/HDL-C, LDL-C/HDL-C as well as TG and HDL-C were consistently associated with metabolic syndrome and insulin resistance. Lipid ratios may be used as reliable markers. Similar result was proved by Kimm H et al (2010).39 In our study also this finding was confirmed. Review article by Houston MC et al (2005)40 had mentioned TG: HDL-C ratio > 3 for diagnosis in expanded definition of metabolic syndrome and also as a metabolic marker of insulin resistance. McLaughlin T et al (2005) conclude that a plasma triglyceride/high-density lipoprotein cholesterol concentration ratio ≥ 3.5 provides a simple means of identifying insulin-resistant, dyslipidemic patients who are likely to be at increased risk of cardiovascular disease. In our study also TG: HDL-C ratio was significantly increased and shares one of the components of metabolic syndrome and insulin resistance. So it can be use as a simple and better metabolic marker of insulin resistance and metabolic syndrome in preeclampsia.

By appropriately recognizing the metabolically challenged pregnancy, we could have the opportunity to prevent or delay the onset of clinical disease and because of the increased risk of morbidity and mortality associated with the metabolic syndrome, an understanding of the presentations of this syndrome is vital especially among pregnant women.

### Table 1: Comparison of mean age and mean gestational age in cases and controls

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Cases (n=100) Mean ± SD</th>
<th>Controls (n=100) Mean ± SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age ± SD</td>
<td>22.86 ± 2.625</td>
<td>22.95 ± 2.271</td>
<td>0.79</td>
</tr>
<tr>
<td>Mean Gestational age ± SD</td>
<td>34.85 ± 1.030</td>
<td>34.85 ± 1.028</td>
<td>0.97</td>
</tr>
</tbody>
</table>

### Table 2: Comparison of serum lipid profile in cases and controls

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group A (n=100) Mean ± SD</th>
<th>Group B (n=100) Mean ± SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol (mg %)</td>
<td>230.5 ± 6.82</td>
<td>229.0 ± 5.59</td>
<td>0.086</td>
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<tr>
<td>Triglyceride (mg %)</td>
<td>209.0 ± 6.44</td>
<td>169.0 ± 7.25</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>VLDL (mg %)</td>
<td>41.84 ± 1.29</td>
<td>33.80 ± 1.48</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>HDL (mg %)</td>
<td>34.02 ± 3.53</td>
<td>73.86 ± 2.25</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>LDL (mg %)</td>
<td>154.7± 8.94</td>
<td>121.3 ± 4.66</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>TC/HDL-C</td>
<td>6.9 ± 0.88</td>
<td>3.1 ± 0.11</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>LDL-C/HDL-C</td>
<td>4.6 ± 0.72</td>
<td>1.6 ± 0.09</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>TG/HDL-C</td>
<td>6.2 ± 0.83</td>
<td>2.3 ± 0.10</td>
<td>P&lt;0.0001</td>
</tr>
</tbody>
</table>
Conclusion

Findings from this study support that dyslipidemia in pregnancy is contributed to preeclampsia. Altered lipid profile specially increased triglycerides, VLDL and low HDL level has role in pathogenesis of preeclampsia. Also, the results of this study have shown that women prone to preeclampsia are predisposed to developing metabolic syndrome. So that women with preeclampsia has future risk of developing cardiovascular diseases.

References


29. Islam NAF, Chowdhury MAR, Kibria GM, et al. Study of serum lipid profile in pre-eclampsia and...


