# Alteration of various lipids in pregnancies complicated by hypertensive disorders

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## ABSTRACT

**Background:** Preeclampsia is a common medical problem associated with pregnancy with substantial risk to the mother and fetus. Abnormal lipid metabolism seems important in the pathogenesis of pregnancy-induced hypertension. **Objective:** The objective was to study the alteration of various lipids in pregnancies complicated by hypertensive disorders. **Materials and Methods:** This prospective study was conducted among 150 pregnant women in the department of obstetrics and gynecology, from September 2009 to May 2011. The subjects were divided into two groups of normotensive women and women with complicated pregnancy by hypertensive disorder with 75 patients each. Serum lipid profile including total cholesterol, triglyceride (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) was determined and compared between the two groups. The data were analyzed using the Chi-square test and analysis of variance test. $p<0.05$ was considered statistically significant. **Results:** The mean TG level in the normotensive women was 121.5±25.0, while in the preeclamptic women were 311.4±79.5 ($p<0.001$). The mean cholesterol level was 181.7±27.8 in the normotensive and 259.4±40.6 in the hypertensive arm ($p<0.001$). Mean LDL was 122.6±24.6 in the normotensive group whereas 255.3±41.9 in the hypertensive pregnant women ($p<0.001$). HDL was 49.4±5.6 in the normotensive and 49.7±5.5 in the hypertensive arm ($p=0.69$). **Conclusion:** The endothelial dysfunction in preeclampsia could be due to an altered lipid profile. This association of hyperlipidemia may be significant in understanding the pathogenesis of preeclampsia and may help in developing strategies for early diagnosis and prevention of preeclampsia.

**Key words:** *High-density lipoprotein, Lipid profile, Low-density lipoprotein, Preeclampsia, Total cholesterol, Triglyceride*

The hypertensive disorder is still the most common medical disorder complicating pregnancies leading to maternal and perinatal morbidity and mortality. Preeclampsia is a multisystem disorder characterized by blood pressure (BP) more than or equal to 140/90 mmHg, proteinuria (>/=300 mg/day), and edema induced by pregnancy after 20 weeks of gestation [1]. The global burden of preeclampsia is 2–5%, whereas, in India, the incidence ranges between 5% and 15% contributing to 16% of maternal mortality and 20% of perinatal mortality [2]. Although the pathogenesis of preeclampsia is unknown, some studies have identified trophoblastic cells and an accelerated maternal systemic response to trophoblastic tissue [3]. Dyslipidemia is also known to have a direct effect on endothelial dysfunction which leads to vasospastic effect on the kidney, uterus, placenta, and brain [4]. The altered lipid synthesis has a direct effect on the endothelial dysfunction leading to decreased prostacyclin:thromboxane A2 (PGI2:TXA2) ratio which further leads to fibrinoid necrosis at uteroplacental implantation site [5]. The severity of renal disease due to altered lipid profile is reflected by proteinuria. In view of the above facts and hypothesis, the present study was designed to compare the lipid profile in women with complicated pregnancies secondary to hypertensive disorder with that of normal pregnancies.

## MATERIALS AND METHODS

This prospective study was conducted among 150 pregnant women in the department of obstetrics and gynecology, from September 2009 to May 2011. The study was approved by the Institutional Ethics Committee. Women with pregnancies beyond 20 weeks of gestation but not in labor were included in the study. The study population was divided into two groups, with 75 patients each. Women with pregnancies complicated by hypertensive disorder having gestational hypertension (BP ≥140/90 mmHg) or preeclampsia were considered in one group. The control group included normotensive healthy pregnant women. Women with chronic hypertension, preeclampsia superimposed on chronic hypertension, eclampsia, ruptured membranes, antepartum hemorrhage, chorioamnionitis, or any other medical illness were excluded from the study. A detailed history and examination were conducted, and a proper pro forma was maintained. Verbal consent was taken from all the patients and fasting blood sample was sent for the evaluation of the lipid level.

BP was recorded in the sitting position with cuff that is large enough for the subjects arm on at least two occasions 6 h apart. Elevated BP, equal to or more than 140/90 mmHg in combination with proteinuria after 20 weeks gestation in the

previously normotensive non-proteinuric patient, was diagnosed as preeclampsia. BP between 140/90 and 159/109 mm Hg was considered mild preeclampsia, whereas BP >160/110 mm Hg was considered as severe preeclampsia. Blood samples were drawn from all the subjects following 8–10 h of fasting. Blood samples were subjected to ultracentrifuge to separate serum and lipoprotein. The densest classes were settled at the bottom and the least dense toward the top. Following centrifugation, the quantity of each lipoprotein class was determined based on its movement in an electrical field and analyzed for serum triglycerides (TG), total cholesterol (TC), and high-density lipoprotein (HDL). Serum low-density lipoprotein (LDL) was calculated by Fredrickson Fredwalds formula. According to which: LDL cholesterol=TC–(HDL+VLDL), very LDL was calculated as 1/5 of TG.

The data recorded were analyzed using SPSS software. The results were expressed as mean±Standard deviation. The qualitative and quantitative data were analyzed by Chi-square and analysis of variance, respectively. $p<0.05$ was considered as statistically significant when the probability of the null hypothesis was less than at least 5%, and highly significant if <0.001.

## RESULTS

The present study comprised 150 pregnant women who were further divided into control and case groups on the basis of BP evaluation, each arm comprising 75 women each. Normotensive pregnant women represented control and those with pregnancy-induced hypertension (PIH) represented the case group. The age of the patients ranged between 18 and 37 years, with no statistically significant difference between the two groups, where the mean age of pregnancy-induced hypertensive case group was 26.8 years and that of normotensive control group was 27.0 years. Similarly, there was no statistically significant difference seen between the body mass index ($p=0.08$) and period of gestation ($p=0.18$), between the two groups (Table 1).

The systolic and diastolic BP between the two groups showed statistically significant difference, where the mean systolic BP of the normotensive and PIH patients was 118.2 mm Hg and 152.02 mmHg, respectively ($p<0.001$), while the mean diastolic BP for the control and case was 76.9mm Hg and 94.7 mm Hg (<0.001), respectively. While comparing various lipids between the control and cases, we observed that the level of TG ($p<0.001$), LDL ($p<0.001$), and cholesterol ($p<0.001$) was significantly higher in the patients with hypertension complicating pregnancy (Table 1). Our study did not find a significant difference in various lipid parameters in mild or severe hypertensive arms (Table 2).

## DISCUSSION

Preeclampsia is a challenging medical disorder to be dealt with cautiously and promptly during pregnancy, as it can endanger the life of both mother and fetus. During normal pregnancy, adaptive alteration occurs to deal with the increasing demands of the growing fetus, but in preeclampsia, the normal physiological alteration is exaggerated, including insulin resistance, hyperlipidemia, and upregulation of inflammatory markers. The exaggerated insulin resistance causing hyperinsulinism may lead to hypertriglyceridemia, which leads to the accumulation of TG in the endothelium of the predisposed uterine spiral vessels leading to endothelial dysfunction either directly or indirectly through the generation of small, dense LDL. The hypertriglyceridemia may also be related to hypercoagulability [4].

In a normal pregnancy, there are increased hepatic lipase and decreased lipoprotein lipase activity. The increased hepatic lipase leads to increased TG at the hepatic level, while the decreased lipoprotein lipase causes decreased catabolism at the adipose tissue level. The estrogen level in late pregnancy causes increased VLDL production and decreased lipolysis. The upregulated placental VLDL receptor causes direct maternal TG toward the fetoplacental unit for increasing fetal nutritional demands. In preeclampsia, reduced maternal lipolysis and decreased TG uptake by fetoplacental unit cause accumulation of TG in maternal circulation [4]. In the present study, alike the findings of Mweu *et al.* [5], the TG level was significantly higher ($p<0.001$). The mean TG level in the normotensive women was 121.5±25.0, while that of hypertensive women was 311.4±79.5.

It has been seen that the oxidized LDL increases the sensitivity to vasopressive agents and inhibits epithelial dependent vasodilatation. In preeclampsia, there is increased lipid fraction and activation of plasma lipid peroxidase and free radicals [3]. We observed a significantly elevated LDL level in hypertensive women ($p<0.001$) with a mean of 255.3±41.9, while the mean LDL value of normotensive women was 122.6±24.6. Our finding was in accordance with the observation of Reddy *et al*. [2]. The association between TC and preeclampsia can be explained by hypercholesterolemia promoting the formation of free radicals [3]. In our study, there was a significant elevation of TG and LDL, the TC levels ($p<0.001$) which were in accordance with the study by Kumari *et al*. [6]. Past studies have observed no significant difference in the level of HDL between hypertensive pregnant and normal pregnant women; similarly, we observed no statistically significant difference in the value of HDL between the two arms [6,7]. The low level of HDL in preeclampsia is not only due to hypoestrogenemia but also due to insulin resistance [8]. We did not observe any significant difference between the various lipids and the severity of preeclampsia.

The strength of our study is its prospective nature. Many other retrospective reports assessing lipid profile during pregnancy could not avoid the individual bias with respect to lipid profile during pregnancy. Our study was conducted at a single center with a limited number of patients, which constitutes the limitation of the study. In the present study, we analyzed a single measurement of lipid profile; hence, we lack the baseline lipid parameters in the second and third trimester. A study conducted by Pusukuru *et al*. [9] evaluated lipid profile in the second and third trimester of pregnancy, where they observed an increase in cholesterol, TG, LDL, and VLDL in

**Table 1: Comparison between clinical characteristics and lipid profile**

| Parameters | Normotensive (Mean±SD) | Pregnancy-induced hypertension (Mean±SD) | p-value |
|---|---|---|---|
| Age (in years) | 27.0±4.7 | 26.8±5.0 | 0.828 |
| Body mass index | 23.11±2.69 | 22.44±1.87 | 0.08 |
| Period of gestation (in weeks) | 31.59±2.90 | 31.01±2.32 | 0.183 |
| Systolic blood pressure (in mm Hg) | 118.26±5.77 | 152.02±9.91 | <0.001 |
| Diastolic blood pressure (in mm Hg) | 76.96±5.61 | 94.72±4.74 | <0.001 |
| Triglyceride (mg/dl) | 121.5±25.0 | 311.4±79.5 | <0.001 |
| Low-density lipoprotein (mg/dl) | 122.6±24.6 | 255.3±41.9 | <0.001 |
| Cholesterol (mg/dl) | 181.7±27.8 | 259.4±40.6 | <0.001 |
| High-density lipoprotein (mg/dl) | 49.4±5.6 | 49.7±5.5 | 0.694 |

**Table 2: Comparison of lipid profile according to the severity of hypertension**

| Severity of hypertension | Triglyceride | Cholesterol | Low-density lipoprotein | High-density lipoprotein |
|---|---|---|---|---|
| Mild (n=6) Mean±SD | 310.07±79.06 | 254.46±39.10 | 255.98±44.93 | 50.37±5.14 |
| Severe (n=19) Mean±SD | 315.47±83.04 | 273.94±41.10 | 253.36±32.64 | 47.94±6.42 |
| p-value | 0.80 | 0.07 | 0.81 | 0.10 |

both the second and third trimesters. The increase was more in the third trimester than the second. The level of HDL was found to be decreased in the third trimester when compared to the second trimester.

At present, the investigations done for the diagnosis of preeclampsia reflect the already established disease process. The role of other novel methods for diagnosis of the early phase of the disease is warranted. The role of angiogenic biomarkers in the diagnosis of preeclampsia is emerging and promising. In preeclampsia, soluble fms-like tyrosine kinase-1, which is an antiangiogenic protein made by placenta, is increased, and the placental growth factor (PlGF) levels are decreased causing vasoconstriction and endothelial damage leading to fatal growth restriction and preeclampsia [10]. In normal pregnancy, the PlGF concentration increases with gestation, with the peak concentration at 26–30 weeks; thereafter, declining toward term but in preeclampsia, the PlGF concentration is abnormally low [11]. Despite the cost of the novel, biomarkers authors suggest that the benefits exceed the additional cost, and it has the potential to provide substantial cost saving by reducing unnecessary resource use [12-14]. Other biochemical markers such as pregnancy-associated plasma protein-A, a disintegrin and metalloproteinase-12, placental protein 13, angiopoietin 1 and 2, inhibin A, activin A, soluble endoglin, and human chorionic gonadotropin are under investigation for prediction of preeclampsia [15].

## CONCLUSION

There is no specific test formulated so far for the early prediction of preeclampsia. Hence, with the understanding of the pathogenesis of preeclampsia, if there is any tool to predict the development of the disease early and measure its severity, then the maternal and perinatal morbidity and mortality can be substantially reduced. Hence, there is a need for further research for the formulation of specific tests to predict preeclampsia. The study of alteration in blood lipid profile not only helps in early detection and prevention of obstetric complications such as PIH but also increases the scope of correction of dyslipidemia causing preeclampsia which is also the need for the hour.

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