



## ASSOCIATION OF SERUM LIPID LEVELS, THYROID DYSFUNCTION, AND PROTEINURIA WITH PREECLAMPSIA - A CASE CONTROL STUDY

## Obstetrics &amp; Gynaecology

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## ABSTRACT

**Background:** Preeclampsia remains an established risk factor for adverse maternal and perinatal outcome. Many concepts have been put forward regarding its etiology, pathogenesis, and complications but commendable success has not so far been achieved to prevent this age-old disorder. Also, the changes in thyroid function in normal pregnancy are well-documented but in complicated pregnancy like preeclampsia, very little is known. Studies have shown evidences of hypothyroidism in preeclampsia necessitating thyroid function tests to be done in preeclampsia. The present study was conducted to find association between lipid profile, thyroid dysfunction, and preeclampsia. **Methods:** This is a case-control study of 101 pregnant (after 34 weeks of gestation) women each (matched for maternal age) with preeclampsia and healthy controls. Lipid profile, TSH and proteinuria status were determined to study its association. **Results:** The baseline characteristics (maternal age, BMI, gestational age, parity, history of smoking / alcohol / tobacco chewing) were comparable at baseline among cases and controls. The serum total cholesterol, triglycerides, LDL values (cases) were significantly higher than controls ( $p < 0.001$ ). There was a significant difference seen in the mean of total cholesterol, triglycerides, and LDL in the three levels of proteinuria with higher levels showing increase in lipid profile parameters among cases;  $p = 0.003$ . The median TSH levels were statistically increased in hypertensive pregnant women than controls;  $p = 0.012$ , but there was no correlation between TSH and lipid profile. **Conclusions:** This study showed a dyslipidemic profile (LDL, total cholesterol and triglycerides were elevated, decrease in HDL), hypothyroidism and significant proteinuria among preeclamptic pregnant women. These patients need early referral to mitigate risk of adverse outcomes. Future studies should focus on the status of these abnormalities post-pregnancy and their role in long-term health outcomes.

## KEYWORDS

dyslipidemia, preeclampsia, proteinuria, hypothyroidism

## INTRODUCTION

Preeclampsia (PE), which is defined as new onset hypertension after 20 weeks of pregnancy accompanied by proteinuria, is characterized by inadequate placentation, oxidative stress, inflammation, and widespread endothelial dysfunction.<sup>1</sup> During pregnancy physiological changes occur in the lipid metabolism due to changing hormonal conditions: the LDL cholesterol (LDL-C), triglycerides (TG) and lipoprotein(a) [Lp(a)] increase throughout pregnancy. Common lipoprotein disorders are associated in pregnancy with two major clinical disorders: severe hypertriglyceridemia (SHTG) is a potent risk factor for development of acute pancreatitis and elevated cholesterol due to greater concentrations of LDL and remnant lipoproteins and reduced levels of HDL promote atherosclerosis.<sup>2</sup>

Proteinuria is one of the cardinal features of preeclampsia, a common and potentially severe complication of pregnancy. Proteinuria in pregnancy can also indicate primary kidney disease or kidney disease secondary to systemic disorders, such as diabetes mellitus or primary hypertension. Adding to the complexity, 20 to 25 percent of pregnant people with chronic hypertension, diabetes mellitus, or chronic kidney disease develop superimposed preeclampsia.<sup>3</sup>

It is well recognized that thyroid function can influence lipid synthesis, mobilization, and degradation. Thyroid hormones are crucial for the regulation of lipids, which play an essential role in fetal development and health maintenance in pregnant women. Since the fetal thyroid gland does not functionally mature until 20 weeks of pregnancy, the fetal demand for thyroid hormones depends on maternal supply in the first half of the pregnancy.<sup>4</sup> As a result, women with thyroid dysfunction have an increased risk of maternal-fetal complications, including stillbirths, preeclampsia (PE), and neonatal morbidity.<sup>5</sup>

So, this study aims to study the association between dyslipidemia, thyroid dysfunction, and proteinuria in pregnant women with preeclampsia.

## MATERIALS AND METHODS

The present case-control study was carried out at the Tertiary Care Institution, Central India over a period of 18 months between June 2021 to November 2022 to determine the association among dyslipidemia and proteinuria in pregnant patients of severe preeclampsia and to determine the association between thyroid dysfunction and development of preeclampsia in pregnant patient after

34 weeks of gestation. A total of 202 pregnant women - 101 with preeclampsia (cases) and 101 with normal pregnancy (controls) were selected consecutively for purpose of study. All the women admitted in hospital aged  $\geq 18$  years and beyond 34 weeks of gestational age were included in this study. Pregnant women with blood pressure of  $\geq 140/90$  mmHg beyond 20 weeks of gestation and proteinuria of  $\geq +1$  by dipstick method were enrollment criteria for the cases while pregnant women with normal blood pressure without any evidence of proteinuria were selected as controls. Pregnancy with other complications, gestational hypertension, chronic hypertension, diabetes, history of thyroid disorder before pregnancy, multifetal pregnancy and known case of dyslipidemia were excluded from the study. Data were processed and analyzed using Statistical Package for the Social Sciences (SPSS) Statistics for Windows [version 24.0, Professional]. The test statistics used to analyse the data were descriptive statistics, chi square probability test and odds ratio. Results were graphically represented where deemed necessary. All statistical tests were two tailed. A p-value of  $< 0.05$  was considered statistically significant.

## OBSERVATION AND RESULTS

This study involved 101 women with preeclampsia and 101 healthy pregnant women as controls after 34 weeks of gestation who were matched for maternal age. The baseline characteristics (maternal age, BMI, gestational age, parity, history of smoking / alcohol / tobacco chewing) were comparable among cases and controls.

The serum total cholesterol, triglycerides, LDL values from the women with preeclampsia (cases) were significantly higher than those of the healthy women (controls) ( $p < 0.001$ ). The serum HDL values from cases were significantly lower than controls ( $p < 0.001$ ). There was a positive association seen between increased proteinuria levels and higher LDL, triglyceride, and total cholesterol levels among cases. The median TSH levels were statistically increased in hypertensive pregnant women than controls;  $p = 0.012$ . There appeared to be no correlation between TSH and lipid profile parameters.

**Table 1: Distribution of study population according to dyslipidemia**

| Variables               |         | Lipid profile |      | P-value |
|-------------------------|---------|---------------|------|---------|
|                         |         | Mean          | SD   |         |
| Total Cholesterol mg/dl | Case    | 231.4         | 62.2 | <0.001  |
|                         | Control | 176.8         | 27.6 |         |

|                        |         |       |      |        |
|------------------------|---------|-------|------|--------|
| Triglycerides<br>mg/dl | Case    | 307.5 | 92.1 | <0.001 |
|                        | Control | 167.4 | 44.9 |        |
| LDL<br>mg/dl           | Case    | 140.9 | 34.9 | <0.001 |
|                        | Control | 120.7 | 20.1 |        |
| HDL<br>mg/dl           | Case    | 47.8  | 11.4 | <0.001 |
|                        | Control | 66.3  | 21.8 |        |

The serum total cholesterol was higher among cases with a mean±SD of 231.4±62.2 mg/dl and 176.8±27.6 mg/dl in controls and this difference was statistically significant;  $p<0.001$ .

The serum triglyceride levels were higher among cases with a mean±SD of 307.5±92.1 mg/dl and 167.4±44.9 mg/dl in controls and this difference was statistically significant;  $p<0.001$ .

The serum LDL levels were higher among cases with a mean±SD of 140.9±34.9 mg/dl and 120.7±20.1 mg/dl in controls and this difference was statistically significant;  $p<0.001$ .

The serum HDL levels were lower among cases with a mean±SD of 47.8±11.4 mg/dl and 66.3±21.8 mg/dl in controls and this difference was statistically significant;  $p<0.001$ .

**Table 2. Association of dyslipidemia among preeclamptic pregnant patients with the severity of proteinuria among cases**

| Lipid profile     | Proteinuria levels |            |            | P value |
|-------------------|--------------------|------------|------------|---------|
|                   | 1+                 | 2+         | 3+         |         |
| Total Cholesterol | 210.6±54.3         | 261.1±50.6 | 302±50.6   | <0.001  |
| Triglycerides     | 278.7±78.9         | 348.9±87.4 | 413.4±37.1 | <0.001  |
| LDL               | 134.5±17.9         | 153.3±38.5 | 166.4±61.9 | 0.003   |
| HDL               | 46.2±12            | 50.5±10.3  | 46.4±11.2  | 0.252   |

One way ANOVA was used to determine whether there are any statistically significant differences between the means of three levels of Proteinuria. There was a significant difference seen in the mean of total cholesterol, triglycerides, and LDL in the three levels of proteinuria with higher levels showing increase in lipid profile parameters. But there was no significant difference seen in HDL levels across the three proteinuria levels.

**Table 3. Association of thyroid dysfunction among cases and controls**

| Variables | Thyroid status             |                            | P-value |
|-----------|----------------------------|----------------------------|---------|
|           | Normal<br>(0.3 to 3 mIU/L) | Hypothyroid<br>(> 3 mIU/L) |         |
| Cases     | 53(52.5%)                  | 48(47.5%)                  | 0.001   |
| Control   | 75(74.2%)                  | 26(25.8%)                  |         |

There was a significant association seen in thyroid dysfunction in preeclamptic pregnant patients, more so among cases than controls and this difference in numbers was statistically significant;  $p=0.001$ .

## DISCUSSION

Pregnancy induced hypertensive disorders are one of the commonest complications of pregnancy which accounts for 12% of the maternal and perinatal mortality and morbidity. Dyslipidemias are associated with endothelial dysfunction that may result in proteinuria and hypertension which is a clinical hallmark of PIH. It affects both maternal health as well as fetal growth. Thyroid function in early pregnancy is also associated with dyslipidemia, hence this study was done to study association of serum lipid levels, thyroid dysfunction, and proteinuria with Preeclampsia. Many studies have been conducted on the status of different lipids in the serum during pregnancy. Several of them have documented association of preeclampsia with dyslipidaemia. Specifically, hypertriglyceridemia, is common in women with preeclampsia. Nidhi D et al (2019)<sup>6</sup> studied the mean level of TC in preeclampsia as 224.36±43.68mg/dl. This was significantly higher as compared to normotensive group 180.77±36.58mg/dl. Our study findings are concordant to the studies conducted across the world and have shown that dyslipidemia is evident among pregnant women with preeclampsia.

Proteinuria generally increases as preeclampsia progresses, but increased urinary protein excretion may be a late finding.<sup>8</sup> The degree of maternal hypertension and proteinuria, as well as the presence/absence of other clinical manifestations of the disease that represent the severe end of the disease spectrum (alarm findings), are highly variable.<sup>9</sup> In our study there was a significant difference seen in the mean of total cholesterol, triglycerides, and LDL in the three levels

of proteinuria with higher levels showing increase in lipid profile parameters. But there was no significant difference seen in HDL levels across the three proteinuria levels. Which suggests that there is significant correlation between proteinuria and dyslipidemia.

Also, the association of hypothyroidism and preeclampsia is not surprising, hypothyroidism being an accepted cause of reversible hypertension in the pregnant women. Some studies have shown that 29.3% of pregnant women with preeclampsia had hypothyroidism, 71.42% had subclinical hypothyroidism and the rest had overt hypothyroidism.<sup>10</sup> Other studies showed that 16.7 and 43.7% of preeclamptic women had subclinical and overt hypothyroidism, respectively.<sup>11</sup> Subclinical hypothyroidism is defined by an increase in TSH concentration and normal FT4 concentration, and overt hypothyroidism is defined by an increase of TSH level and decrease free thyroxine.<sup>12</sup> Hajifoghaha M et al (2022)<sup>13</sup> findings revealed that TSH was significantly higher in preeclamptic women. Findings of this meta-analysis indicated preeclamptic women were more at risk of changes in thyroid function tests.

In our study, the median (IQR) TSH levels were increased in hypertensive pregnant women [3(2, 6.8)] (cases), [2.3(1.9, 3.1)] (controls) and the difference in medians between the two groups was statistically significant;  $p=0.012$ .

Estimation of maternal lipid profile in early second trimester may bring about early recognition of patients at risk of preeclampsia before the clinical symptoms and complications of preeclampsia appear for a better fetomaternal outcome. The findings from this study continue to support a role for dyslipidemia in preeclampsia. Prospective studies measuring lipid profiles throughout pregnancy and the postpartum period are needed to further our understanding of the importance of dyslipidemia in preeclampsia and its long-term impact on the cardiovascular health of women.

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