



Original Article

## To Study Serum Lipid Profile as predictor of Gestational hypertension and Preeclampsia in early Second trimester of pregnancy

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### ABSTRACT

**Context:** -Hypertensive disorders of pregnancy affects up to 8% of all gestations.<sup>1,2</sup> Plasma lipids are significantly increase during pregnancy. Various studies suggesting that abnormal lipid metabolism in early pregnancy could be one of the factors for subsequent development of PIH.<sup>9,10</sup> The present study was planned to estimate serum lipid profile during 14-20 weeks of pregnancy with the aim to investigate the role as predictors of gestational hypertension and preeclampsia.

**Objectives:** To investigate the role of serum lipid profile at 14-20 weeks of gestation as predictors for the development of gestational hypertension and preeclampsia.

**Material & Methods:** A prospective cohort study was conducted in Tertiary care hospital in New Delhi. The study group included 150 pregnant women attending the ANC OPD; the sample size was calculated assuming alpha to be 0.05 and power of study to be 90%. For the analysis, the study group (n=150) was divided into 2 groups on the basis of the subsequent development of hypertension (with and without proteinuria). Cases (n=20): Women who subsequently developed gestational hypertension or preeclampsia were included in the case group and were labelled as the hypertensive group. Controls (n=130): Women who remained normotensive till delivery were included in the control group and were labelled as normotensive group. The obstetrical examination was done at every visit to note fetal growth and wellbeing. Besides routine antenatal investigations, Lipid profile: 2ml of overnight fasting blood sample was collected in plain vial for lipid profile and was analysed by Automated chemistry analyzer Hitachi 912 using fully automated analyzer kit as per kit procedure, on the same day. All the women were monitored for the development of gestational hypertension /preeclampsia and were followed up till delivery.

**Results & Conclusion:** Out of all the components of lipid profile, TC is the only component which is significantly associated with the development of hypertension. There is no significant association of other components of lipid profile Viz. triglycerides (TG), high density lipoprotein (HDL) and low-density lipoprotein (LDL). At an acceptable sensitivity of 85%, a value of TC obtained from ROC curve is 171 mg/dl. The accuracy of this value in predicting hypertension is only 36.67%. Hence it is not a good predictor.

**Keywords:** Serum Lipids, Gestational hypertension, pre-eclampsia.

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### INTRODUCTION

Preeclampsia is one of life-threatening systemic disease of pregnancy associated with endothelial injury. Although sign and symptoms of illness appears in the third trimester of pregnancy but there are multiple indicators that shows the disease process begins early in pregnancy. Second trimester changes in several maternal serum factors are among the frequent precursors of clinical symptoms.<sup>3-6</sup> Hypertension and proteinuria are the simplest clinical criteria for the diagnosis of preeclampsia but the pathophysiological mechanism that leads to this disorder are by all very complex.<sup>7</sup>

Increase in plasma lipids are normal physiological process in pregnancy but it is not atherogenic and it is believed to be under hormonal control. However, in pregnancy complicated by hypertension, there is a possible defect in the mechanism coping with physiological hyperlipidemia.<sup>8</sup>

Maternal plasma lipids are significantly elevated during pregnancy. There are evidences suggesting that abnormal lipid metabolism in early pregnancy could be one of the factors for subsequent development of gestational hypertension and preeclampsia.<sup>9</sup> Elevated plasma lipid and lipoprotein may trigger endothelial injury secondary to oxidative stress and dyslipidemia may impair trophoblast invasion thus contributing to the development of preeclampsia as result of pathophysiological process.<sup>11</sup>

Lipid profile includes total cholesterol, triglycerides, HDL, VLDL, LDL. Abnormal lipid metabolism in early pregnancy could be one of the factors leads to development of PIH.<sup>9,10</sup> Studies reported that high serum cholesterol, TG, LDL, HDL were associated with preeclampsia on the other hand other studies reported that low serum cholesterol or no difference in serum cholesterol, TG, LDL, HDL in preeclampsia compared to normal pregnancy. Various mechanisms of dyslipidemia in association with preeclampsia described in literature are 1) Elevated plasma lipid and lipoprotein may trigger endothelial injury secondary to oxidative stress.<sup>11</sup> They also noted that dyslipidemia may impair trophoblast invasion thus contributing to the development of pre-eclampsia as normal Patho-physiological process in body. 2) Dysregulation of enzyme lipoprotein lipase resulting in a dyslipidemic lipid profile.<sup>12</sup> In preeclamptic women increased uptake of free fatty acids, which are further esterified to triglycerides.<sup>13</sup> 3) The metabolic syndrome. Insulin resistance syndrome, hyperinsulinemia and hyperuricaemia are also present in pre-eclampsia.<sup>14</sup>

The present study is planned to estimate serum lipid profile during 14-20 weeks of pregnancy with the aim to investigate the role as predictors of gestational hypertension and preeclampsia.

### **AIMS AND OBJECTIVES**

To investigate the role of serum lipid profile at 14-20 weeks of gestation as predictors for the development of gestational hypertension and preeclampsia.

### **MATERIAL AND METHODS**

A prospective cohort study was conducted in Tertiary care hospital in New Delhi. Permission of study was taken from the ethical committee of the hospital. The study group included 150 pregnant women attending the ANC OPD; the sample size was calculated assuming alpha to be 0.05 and power of study to be 90%. A total of 150 pregnant women who give written consent to participate in study and who planned to deliver at Hospital were included in the study. The women were recruited as per the inclusion and exclusion criteria and were followed till delivery.

#### **Inclusion criteria**

1. Singleton pregnancy
2. Gestational age between 14-20 weeks
3. Women sure of last menstrual period (LMP)
4. History of previous regular menstrual cycles

#### **Exclusion criteria:**

1. Gestational age less than 14 weeks and more than 20 weeks
2. Multiple pregnancy
3. Women not sure of Last Menstrual Period
4. History of previous irregular cycles
5. Any gross congenital abnormality in fetus
6. Women with chronic medical disease like hypertension, diabetes, thyroid disease, heart disease and collagen disorders

For the analysis, the study group (n=150) was divided into 2 groups on the basis of the subsequent development of hypertension (with and without proteinuria).

**Cases (n=20):** Women who subsequently developed gestational hypertension or preeclampsia were included in the case group and were labelled as the hypertensive group.

**Controls (n=130):** Women who remained normotensive till delivery were included in the control group and were labelled as normotensive group.

Informed consent was obtained from all the women who participated in study. A detailed history regarding age, parity, menstrual cycles and period of gestation, pre-pregnancy weight, any chronic medical and surgical history and family history was taken at first visit. Complete physical examination including height, weight, blood pressure, pedal oedema and systemic examination was done. The obstetrical examination was done at every visit to note fetal growth and wellbeing. All the women were monitored for the development of gestational hypertension /preeclampsia and were followed up till delivery.

### Case definition:

Gestational hypertension refers to BP equal to or more than 140/90 mmHg for the first time in pregnancy without proteinuria, after 20 weeks of gestation.<sup>15</sup>

Preeclampsia is medical condition characterized by BP equal to or more than 140/90 mmHg and proteinuria equal to or more than 300mg / 24 hour or equal to or more than 1+ dipstick that develop after 20 weeks of gestation.<sup>15</sup>

### Sample collection and procedure

Lipid profile: 2ml of overnight fasting blood sample was collected in plain vial for lipid profile and was analysed by Automated chemistry analyzer Hitachi 912 using fully automated analyzer kit as per kit procedure, on the same day.

### STATISTICAL ANALYSIS

Mean, S.D., Range of all the parameters of interest was calculated for hypertensive and for normotensive groups separately. p value <0.05 was set as statically significant. The difference of various parameters between the two groups was tested by applying chi square test. To choose the cut off value of lipid profile The Receiver Operating Characteristic Curve (ROC) curve was used. The logistic regression model was used for causal effect relationship. The effects of these predictors were measured in terms of odds ratio (OR) and its confidence limits (C.I.).

### RESULTS AND DISCUSSION

In the present study, out of 150 antenatal women, 20 women developed hypertension (with or without proteinuria) till delivery and 130 remained normotensive. Among 20 hypertensive women, 13 developed preeclampsia while 7 developed gestational hypertension. In our study, 50% of the hypertensive women had normal BMI (18.5-24.99) and 50% had BMI between 25-29.99. In the normotensive group, most (89.2%) women had normal BMI. The mean BMI in hypertensive and normotensive women was 25.1 and 19.7 respectively; the difference was statistically significant. Punthumapol C also observed a significantly higher mean BMI in hypertensive women as compared to normotensive control; however mean BMI of hypertensive women observed in their study was much higher (33.95) as compared to the present study.<sup>16</sup> Other studies have reported that the risk of preeclampsia increases with increasing maternal weight; it increases from 4.3 % for women with BMI < 21 kg/m<sup>2</sup> to 13.3% in those with a BMI > 35 kg/m<sup>2</sup>.<sup>1</sup> In contrast to results shown by our study, other studies reported no significant difference in BMI in normotensive and hypertensive.<sup>17,18</sup>

The Mean  $\pm$  SD of SBP in the hypertensive group at delivery was 148.00  $\pm$  13.88 and in normotensive group, it was 118.96  $\pm$  7.59 mm Hg. The difference was statistically significant (p-value <0.001). In the study by Vidyabati et al, the mean SBP was 165.52 mm Hg and DBP 98.66 mmHg, at delivery among hypertensive women.<sup>12</sup> In the hypertensive group, the Mean  $\pm$  SD of DBP at delivery was 96.95  $\pm$  8.80, while in normotensive group, it was 78.82  $\pm$  3.65 mm Hg. The difference was statistically significant.

**Table 1: Comparison of Mean  $\pm$  SD serum lipid profile between hypertensive and normotensive group.**

| Variable          | HYPERTENSIVE (PE/GH) (n = 20)<br>Mean $\pm$ SD | NORMOTENSIVE (n=130)<br>Mean $\pm$ SD | p -value |
|-------------------|--|---------------------------------------|----------|
| Total Cholesterol | 203.80 $\pm$ 30.45                             | 186.22 $\pm$ 28.11                    | 0.011    |
| Triglycerides     | 151.20 $\pm$ 41.36                             | 140.25 $\pm$ 43.67                    | 0.295    |
| HDL               | 49.35 $\pm$ 8.59                               | 49.39 $\pm$ 11.05                     | 0.990    |
| LDL               | 129.7 $\pm$ 32.39                              | 121.37 $\pm$ 25.21                    | 0.188    |

**Table 2: Distribution of total cholesterol between hypertensive and normotensive group.**

| Total cholesterol (mg/dl) | HYPERTENSIVE (n = 20) |            | NORMOTENSIVE (n=130) |            |
|---------------------------|-----------------------|------------|----------------------|------------|
|                           | No.                   | percentage | No.                  | percentage |
| 120-160                   | 1                     | 5%         | 18                   | 13.8%      |
| 161-200                   | 9                     | 45%        | 86                   | 66.2%      |
| 201-240                   | 6                     | 30%        | 18                   | 13.8%      |
| 241-280                   | 4                     | 20%        | 8                    | 6.2%       |

**Table 3: Accuracy of Total Cholesterol in predicting hypertension**

| Total cholesterol (mg/dl) | Sensitivity (%) | Specificity (%) | Positive Predictive Value (%) | Negative Predictive Value (%) | Accuracy (%) |
|---------------------------|-----------------|-----------------|-------------------------------|-------------------------------|--------------|
| 171                       | 85.00           | 29.23           | 15.60                         | 92.68                         | 36.67        |
| 185.5                     | 70.00           | 58.46           | 20.59                         | 92.68                         | 60.00        |

**Table 4: Crude Odd's Ratio independently for each variable**

| variable    | Cut off | p value | OR     | 95% C. I.     |
|-------------|---------|---------|--------|---------------|
| Age (years) | 28      | 0.009   | 3.895  | 1.407- 10.783 |
| Weight (Kg) | 55      | < 0.001 | 19.333 | 6.4- 58.401   |
| TC (mg/dl)  | 171     | 0.194   | 2.341  | 0.648-8.454   |

**Table 5: Findings of Multiple Logistic Regression Model**

| variable | OR    | p value | 95% C. I.      |
|----------|-------|---------|----------------|
| Age      | 3.970 | 0.184   | 0.520- 30.312  |
| Weight   | 4.691 | 0.128   | 0.640- 34.397  |
| TC       | 8.799 | 0.124   | 0.549- 140.973 |

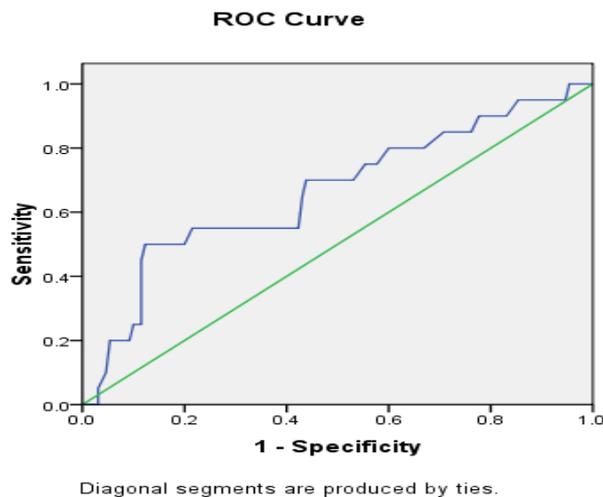
The present study observed that the mean of TC in hypertensive women was 203.80mg/dl, while in normotensive women it was 186.22 mg/dl. The difference between the two groups was statistically significant.(Table 1). This is similar to the observations made by Vidyabati et al which reported significant increase of TC in the hypertensive group .<sup>19</sup>Another study also reported an increase in mean of TC in hypertensives ; however it was not statistically significant.<sup>20</sup> In contrast to our study , Aziz et al and Punthumapol C et al reported an nonsignificant decrease of TC in hypertensive women as compared to controls, while Setareh et al reported significant decrease in TC.<sup>17-18</sup>

In our study, the mean of TG in hypertensives was higher than that of normotensive women, but the difference was not statistically significant.Vidyabati et al and Punthumapol C et al also reported similar observations.<sup>16,19</sup> However, other studies have reported statistically significant increase of TG in hypertensive women.<sup>20,17,18</sup>

No statistically significant difference was observed in the mean HDL of both hypertensive and normotensive groups in our study.Similar results were reported in other studies.<sup>19,16</sup> Studies showed significant decrease of HDL in hypertensive as compared to normotensive women.<sup>20,17,18</sup> The present study observed an insignificantly higher LDL levels in hypertensive women as compared to controls.Similar observations were made by other studies.<sup>20,17</sup> However, other studies reported significant increase of LDL in hypertensive as compared to normotensive women.<sup>19,18</sup>

In the hypertensive group, 50% of the women had TC more than 200 mg/dl, but in the normotensive group only 20% of women had TC more than 200 mg/dl. Majority of normotensives had TC in range of 161-200 mg/dl. The association of hypertension with TC was statistically significant (p-value 0.026).(Table 2).

Almost equal percentage of hypertensive and normotensive women were having similar triglycerides up to 180mg/dl. A higher percentage (35%) of hypertensive women were having triglycerides in the range of 181-220 mg/dl as compared to normotensives (19.2%). The association of triglycerides with blood pressure was statistically not significant (p-value 0.389). The association of HDL with blood pressure was statistically not significant (p-value 0.390). The accuracy of TC was compared by taking cut off values from ROC curve at 85% sensitivity. (Table 3).



**Figure 1: ROC Curve of Total Cholesterol**

**Area Under the Curve**

Test Result Variable(s):TC

| Area | Asymptotic 95% Confidence Interval |                              |             |             |
|------|------------------------------------|------------------------------|-------------|-------------|
|      | Std. Error <sup>a</sup>            | Asymptotic Sig. <sup>b</sup> | Lower Bound | Upper Bound |
| .664 | .070                               | .019                         | .527        | .800        |

The test result variable(s): TC has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

- a. Under the nonparametric assumption
- b. Null hypothesis: true area = 0.5

The cut off value for prediction of hypertension was taken from ROC curve. From the ROC curve shown as figure 1, the cut off value of 171 mg/dl of TC was chosen. This value had 85% sensitivity, the specificity was 29.23%, PPV was 15.6%, NPV was 92.68%. The accuracy of this value in predicting the development of hypertension was 36.67%. When the cut off value of TC was chosen at 185.5mg/dl, the sensitivity was 70%, specificity was 58.46%, PPV was 20.59%, NPV was 92.68% and accuracy was 60%. The accuracy of this value in predicting development of hypertension was 60%. (Table 3). On calculating Odd's Ratio, no significance association of TC with development of hypertension was observed. The accuracy of TC at 171 mg/dl was 36.67%. In the women with age >28 years there was 3.895 times chances of developing hypertension. In the women with weight >55 kg, there was 19.333 chances of developing hypertension. In TC, the p value was not significant. There was no association of TC with development of hypertension. (Table 4). By applying Multiple Logistic Regression, none from age, weight and total cholesterol came out to be a significant predictor for developing hypertension.

## CONCLUSION

Out of all the components of lipid profile, TC is the only component which is significantly associated with the development of hypertension. There is no significant association of other components of lipid profile (TG, HDL and LDL). At an acceptable sensitivity of 85%, a value of TC obtained from ROC curve is 171 mg/dl. The accuracy of this value in predicting hypertension is only 36.67%. Hence it is not a good predictor.

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