Section: Physiology

Original Research Article

SERUM BETA hCG AND LIPID LEVELS IN NORMOTENSIVE PREGNANT WOMEN, MILD PREECLAMPSIA AND SEVERE PREECLAMPSIA

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Received : 07/03/2025
Received in revised form : 20/04/2025
Accepted : 09/05/2025

Keywords:
Preeclampsia, Serum β-hCG, serum lipid profile, LDL, HDL, VLDL, triglyceride.

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DOI: 10.47009/jamp.2025.7.3.92

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2025; 7 (3); 485-490

ABSTRACT

Background: Preeclampsia, a hypertensive complication in pregnancy remains an important cause of increased maternal and neonatal morbidity and perinatal loss. Hypoxic placental damage caused by preeclampsia may result in increased secretion of β-hCG. Lipid alterations can mediate endothelial dysfunction and vasculopathy which may contribute to the pathophysiological mechanism of preeclampsia. **Aim:** To study the serum β-hCG and serum lipid levels in normotensive pregnancy, mild preeclampsia and severe preeclampsia. **Materials and Methods:** A case control study was performed in the Institute of maternal and child health, Government Medical College, Kozhikode after obtaining clearance from the Institutional Ethics Committee. 40 antenatal women with mild preeclampsia and 40 antenatal women with severe preeclampsia were selected as cases based on their blood pressure recording and urine protein estimation. 40 normal antenatal women were selected as controls. Serum β-hCG assay and fasting lipid profile were done in the cases and controls. The data was analyzed using Statistical Package for Social Sciences (SPSS) version 16. **Result:** The mean serum β-hCG, serum cholesterol, serum triglyceride, serum VLDL, serum LDL and serum Triglyceride / HDL ratio were higher in groups with mild and severe preeclampsia when compared with that in the normotensive pregnancy. The mean serum HDL levels were lower in groups with mild and severe preeclampsia when compared with that in normotensive pregnancy. There was a significant positive correlation between serum β-hCG and the mean systolic and diastolic blood pressures in preeclampsia cases. **Conclusion:** The study showed that Serum β-hCG and all lipid fractions except HDL were elevated in preeclampsia.

INTRODUCTION

Preeclampsia is a pregnancy specific disorder [1] and remains an important cause of increased maternal and neonatal morbidity and perinatal loss.[2] It can result in maternal complications like renal failure, abruptio placentae, antepartum hemorrhage, stroke, eclampsia and foetal complications like foetal growth retardation, low birth weight, premature birth and still birth. In India, the incidence of preeclampsia is about 10%.[3]

Preeclampsia is diagnosed by the new development of hypertension ≥ 140 / 90 mm of Hg after 20 weeks of gestation, significant proteinuria and remission of these signs after delivery.[4] Preeclampsia is primarily a disorder of endothelial function with associated vasospasm.[5,6,7] The genesis of preeclampsia is clearly related to deficient trophoblast invasion and failure of uterine artery remodeling.[8,9] Women with pregnancy induced hypertension have hyperplacentosis or an abnormal placentation.[10] It can decrease the uteroplacental blood flow about 30-50% compared to normal pregnancy.[11]

Human Chorionic Gonadotropin (hCG) is a glycoprotein synthesised by the syncytiotrophoblast cells of placenta. Its activity progressively increases from 1 IU/ml at 6 weeks of gestation to reach a peak of 100 IU/ml between 60 – 80 days and then declines progressively to reach a nadir by about 20 weeks. According to Zygmunt et al,[12] hCG could be involved in placental vasculogenesis and angiogenesis in early stages of placental development. Defective spiral artery remodeling in

ISSN (O): 2687-5365; ISSN (P): 2753-6556

preeclampsia is likely to result in decreased uteroplacental perfusion and foci of placental hypoxia or ischemia.[13,14,15] Shanti Yadav,[2] suggested that hypoxic placental damage caused by hypertensive disorders results in reactive hyperplasia of trophoblastic cells and thereby increases the secretion of hCG.

Preeclampsia and related disorders are known to affect function of various organs involved in lipid and lipoprotein metabolism. It may result from over production of lipoproteins by the liver or from impaired delipidation of plasma lipoprotein triglyceride by lipoprotein lipase present in peripheral tissue.[16] Raised plasma triglyceride may be a potential contributor to hyperlipidemia.[17,18] Triglyceride mediated endothelial dysfunction and vasculopathy may contribute to the pathophysiological mechanisms of preeclampsia. According to Pirzado et al,[19] there is a direct correlation between adipose tissue lipoprotein lipase activity and plasma HDL cholesterol. Studies by Jayanta De observed that in preeclampsia the levels of triglyceride, VLDL, LDL, total cholesterol: HDL ratio and Triglyceride: HDL ratio increased significantly whereas the levels of HDL decreased significantly.[20]

The present study has been undertaken to estimate the levels of β-hCG and lipids in normal pregnancy, mild preeclampsia and severe preeclampsia. Elevated β-hCG and lipid levels may prove to be an indicator of the severity of preeclampsia because of the possible role of β-hCG and lipids in the pathophysiology of preeclampsia. So, the estimation of β-hCG and lipids may help in developing strategies for prevention and early diagnosis of preeclampsia and necessary steps can be taken to prevent the complications of preeclampsia.

MATERIALS AND METHODS

After obtaining necessary clearance from the Institutional Ethics Committee, a case control study was conducted in the Institute of Maternal and Child Health, Medical College, Kozhikode.

Inclusion Criteria

Forty antenatal women with mild preeclampsia (Study group I) and another forty antenatal women with severe preeclampsia (Study group II) were selected as cases. Forty normotensive women as were included as controls. Mild preeclamptic women were diagnosed by BP ≥ 140/90 mmHg but < 160/110 mm of Hg on more than two occasions and persistent proteinuria < 2+ dip stick in random urine samples without clinical features of severe preeclampsia. Severe preeclamptic women diagnosed by BP > 160/110 mm of Hg on more than two occasions, persistent proteinuria > 2+ dipstick, rise in liver enzymes and with clinical features like headache, dizziness, convulsions, pulmonary oedema, thrombocytopenia or coagulation disorders. All antenatal women were in the third trimester, between 28 - 40 weeks of gestation.

Exclusion Criteria

Women with history of diabetes mellitus, chronic hypertension, renal or liver disease, history of thromboembolism and multiple pregnancy were excluded.

Method

After getting an informed consent, a detailed history was taken from all subjects which includes age, gravida, parity, history of hypertension, dyslipidemia, cardiac illness, renal diseases, hepatic dysfunction, details of previous pregnancies, or any other acute or chronic illness. Blood pressure recording along with a detailed physical examination was done. Urine protein was detected using the dipstick method. From the above three groups of subjects blood samples for β-hCG and lipid profile were collected after 8 to12 hours of fasting. Under aseptic precautions, 3 ml of blood was drawn from antecubital vein, of which 2ml was put into a clean dry bottle for doing lipid profile. Lipid profile was estimated using automated analyser (Erba). 1ml of blood was allowed to clot and the serum separated by centrifugation at 3000 rpm for 15 minutes. β-hCG was assayed in the serum using Chemiluminescent Microparticle Immunoassay (CMIA). Estimation of urine protein by dipstick method was done using magistik reagent strips. The data was analyzed using Statistical Package for Social Sciences (SPSS) version 16. The results were expressed as mean ± standard deviation. The mean differences between the groups were analyzed using ANOVA (Analysis of Variance). The P value of < 0.05 was taken as the level of significance. In order to find out whether there is a significant association or not between two variables, coefficient of correlation was calculated.

RESULTS

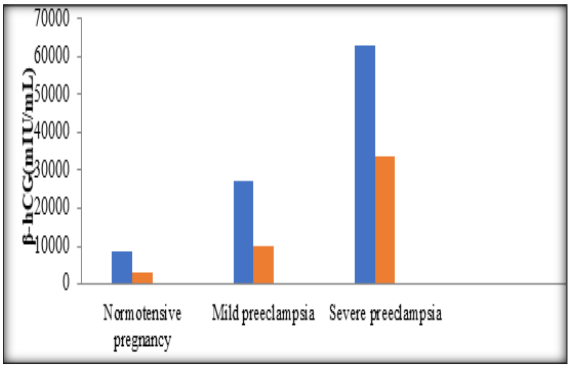

Figure 1: Comparison of serum β-hCG levels in severe and mild preeclampsia with normotensive pregnancy

The mean serum β-hCG values were higher in groups with mild and severe preeclampsia when compared with that in normotensive pregnancy. The differences were statistically significant in between the study groups.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

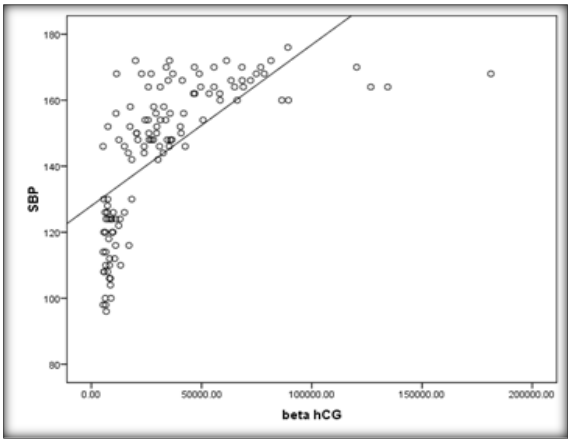

Figure 2: Scatter plot showing correlation between serum β-hCG and systolic blood pressure (SBP) in preeclampsia.

Positive correlation, Correlation coefficient r = 0.665, Significant (p = <0.000)

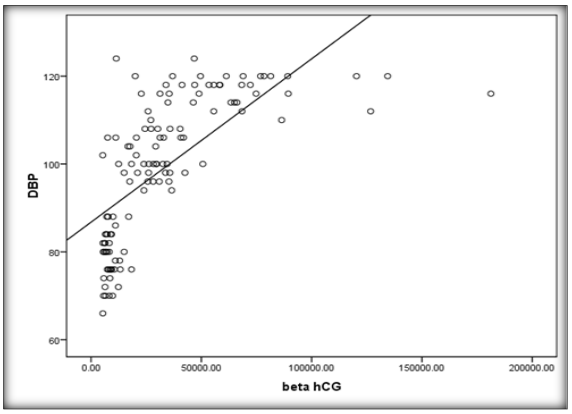

Figure 3: Scatter plot showing correlation between serum β-hCG and diastolic blood pressure (DBP) in preeclampsia

Positive correlation, Correlation coefficient r = 0.685, Significant (p = <0.000)

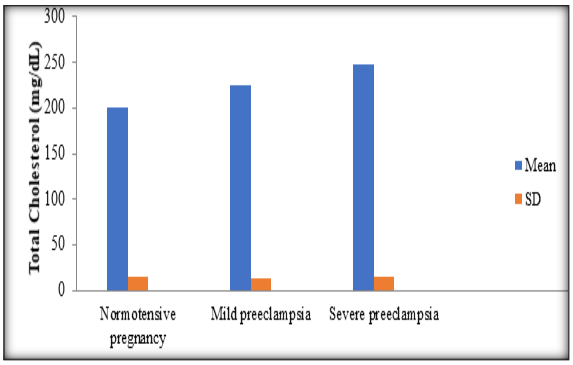

Figure 4: Comparison of total cholesterol levels in severe and mild preeclampsia with normotensive pregnancy

The mean serum cholesterol values were higher in groups with mild and severe preeclampsia when compared with that in normotensive pregnancy. The differences were statistically significant in between the study groups.

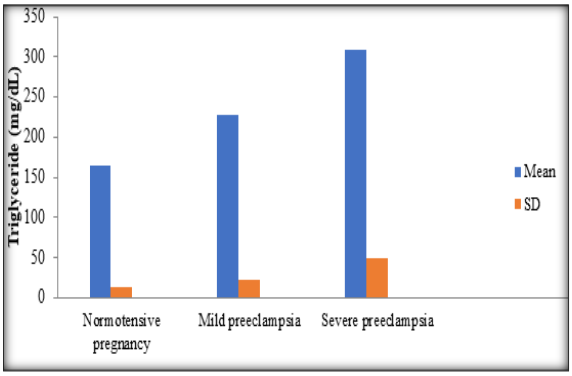

Figure 5: Comparison of serum triglyceride levels in severe and mild preeclampsia with normotensive pregnancy

The mean serum triglyceride values were higher in groups with mild and severe preeclampsia when compared with that in normotensive pregnancy. The differences were statistically significant in between the study groups.

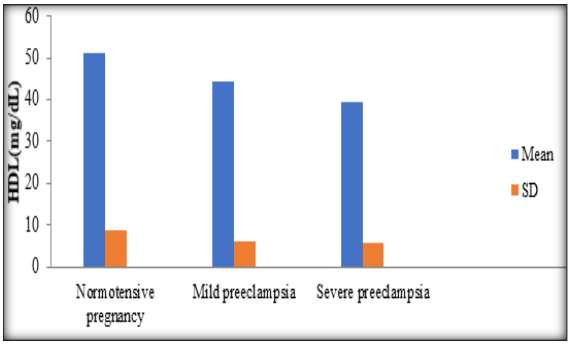

Figure 6: Comparison of serum HDL levels in severe and mild preeclampsia with normotensive pregnancy

The mean serum HDL levels were lower in groups with mild and severe preeclampsia when compared with that in normotensive pregnancy. The differences were statistically significant in between the study groups.

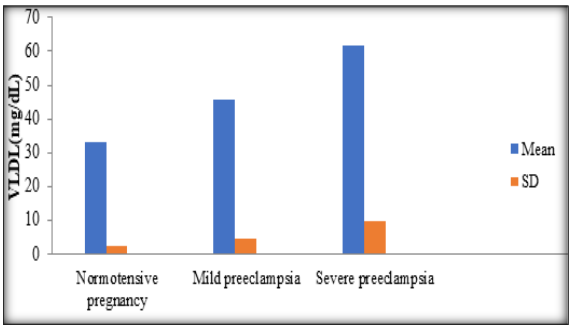

Figure 7: Comparison of serum VLDL levels in severe and mild preeclampsia with normotensive pregnancy

The mean serum VLDL levels were higher in groups with mild and severe preeclampsia when compared with that in normotensive pregnancy. The differences were statistically significant in between the study groups.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

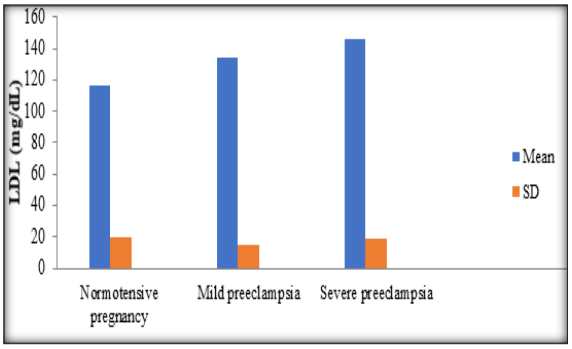

Figure 8: Comparison of serum LDL levels in severe and mild preeclampsia with normotensive pregnancy

The mean serum LDL levels were higher in groups with mild and severe preeclampsia when compared with that in normotensive pregnancy. The differences were statistically significant in between the study groups.

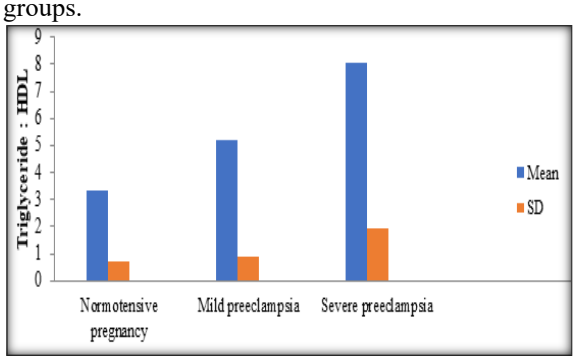

Figure 9: Comparison of serum triglyceride: HDL in severe and mild preeclampsia with normotensive pregnancy

The mean serum Triglyceride / HDL ratio were higher in groups with mild and severe preeclampsia when compared with that in normotensive pregnancy. The differences were statistically significant in between the study groups.

DISCUSSION

The serum concentrations of β-hCG, total cholesterol, LDL, HDL, VLDL, triglycerides and triglyceride:HDL ratio were determined among 3 groups – normotensive pregnant women, mild preeclamptic women and severe preeclamptic women.

The mean serum β-hCG level in mild preeclampsia was 27304.3 ± 9991.93 mIU/mL compared to 8751.45 ± 3124.62 mIU/mL in normal pregnancy (Figure 1). This difference was found to be statistically significant and is comparable to the value reported by Soheila Akbari et al[21] in mild preeclampsia. The mean serum β-hCG level in severe preeclampsia was also significantly higher compared to the levels in mild preeclampsia. This finding is supported by the findings reported by Zahra Basirat et al.[22] There was a significant positive correlation between serum β-hCG and the mean systolic (r=0.665) and diastolic (r=0.685) blood pressures in preeclampsia cases (Figure 2, 3). This is consistent with the studies of Muhd El Hadi Farag, [23] and Gurbuz et al[24] in which β-hCG concentration was positively correlated with disease severity. This increase in β-hCG secretion may be a consequence of abnormal placental invasion or placental immaturity.[10] It may also be linked to reactive hyperplasia of syncytiotrophoblast cells in response to placental hypoxia secondary to hypertensive disorder. Thus there is increased secretion of β-hCG into the maternal circulation.[2]

The mean total cholesterol in severe preeclampsia, mild preeclampsia and normal pregnancy was 247.68 ± 15.93 mg/dL, 224.53 ± 13.34 mg/dL and 200.75 ± 15.02 mg/dL respectively (Figure 4). The mean total cholesterol level in severe preeclampsia was significantly higher when compared to mild preeclampsia and normal pregnancy. There was also significant difference in total cholesterol levels between mild preeclampsia and normal pregnancy. This finding is in accordance with Usha Adiga et al[25] which states that lipid peroxidation occurring in preeclampsia can be attributed to hypercholesterolemia.

The mean serum triglyceride (TG) level in severe preeclampsia (308.8 ± 48.8 mg/dL - Figure 5) was significantly higher compared to the levels in mild preeclampsia (227.68 ± 22.94 mg/dL) and normal pregnancy (165.38 ± 13.42 mg/dL). There was also significant difference in triglyceride levels between mild preeclampsia and normal pregnancy. The studies of Jayanta De et al,[20] and Rubina Aziz et al[26] also obtained similar results. This significant hypertriglyceridemia in preeclampsia could be attributed to the markedly high gestational insulin resistance seen during the third trimester which in turn cause increased activity of hormone sensitive lipase and decreases adipose tissue lipoprotein lipase activity than seen during third trimester of normal pregnancy.

There was significant reduction in serum HDL levels in severe preeclampsia (39.48 ± 5.75 mg/dL (Figure 6) compared to mild preeclampsia (44.45 ± 6.16 mg/dL) and normotensive pregnancy (51.23 ± 8.8 mg/dL). The serum HDL level was significantly lower in mild preeclampsia compared to normotensive pregnancy. Similar results were obtained by Rubina Aziz et al.[26] Estrogen is responsible for induction of TG and HDL, but in toxaemia of pregnancy there is a fall in estrogen levels as compared to normal pregnancy. Hence the low HDL in preeclampsia is due to hypoestrogenemia and increased triglycerides. Oestrogen levels decrease because of the impairment in the formation of Dehydroepiandrosterone sulphate (DHEA) due to decreased utero-placental blood flow which is the main pathophysiological event in preeclampsia. Moreover, decrease in utero-placental blood flow leads to relative stasis of maternal blood in the intervillous space resulting in redistribution of steroids formed in syncytium back to the fetus instead

ISSN (O): 2687-5365; ISSN (P): 2753-6556

of entering into maternal circulation which also results in a state of hypoestrogenemia.[27] Decreased HDL could also result from hypertriglyceridemia since the two are metabolically linked. Increased triglycerides leading to low HDL cholesterol is due to actions of Cholesteryl Ester Transfer Protein (CETP) which mediates the exchange for cholesteryl esters from HDL with triglycerides from chylomicrons or VLDL.[26,28]

The serum VLDL level in severe preeclampsia, mild preeclampsia and normal pregnancy was 61.76 ± 9.76 mg/dL, 45.54 ± 4.59 mg/dL and 33.08 ± 2.68 mg/dL respectively (Figure 7). There was significant difference in VLDL levels between the three groups. Studies by Jayanta De et al[20] observed that serum VLDL rose significantly in the third trimester of pregnancy in comparison to non-pregnant women perhaps due to hypertriglyceridemia leading to enhanced entry of VLDL that carries endogenous triglycerides into circulation. These findings are in accordance with Barkhai et al[17] and Sattar et al[18] which suggests increased VLDL lipoproteins accumulation over the maternal vascular endothelium, particularly those of uterine and renal vessels.

There was significant increase in mean serum LDL levels in severe preeclampsia (146.44 ± 19.19 mg/dL) (Figure 8) compared to mild preeclampsia (134.29 ± 14.48 mg/dL) and normal pregnancy (116.44 ± 19.49 mg/dL). This observation is in accordance with Sahu et al.[29] Increase in LDL level can be due to decreased level of oestrogen in preeclampsia.[30]

The mean serum triglyceride:HDL ratio was significantly higher in severe preeclampsia (8.03 ± 1.92 -Figure 9) compared to mild preeclampsia (5.22 ± 0.89) and normal pregnancy (3.34 ± 0.71). The ratio was also significantly higher in mild preeclampsia compared to normal pregnancy. Gaziano et al,[31] reported that this ratio of triglycerides to HDL indicate presence of dyslipidemia is a strong predictor of myocardial infarction. Increased triglyceride levels results in endothelial cell dysfunction in preeclampsia.[20] Thus the assessment of blood lipids may be helpful in the prevention of complications of preeclampsia.

Heikkila et al[32] showed that an elevated maternal serum β-hCG concentration is a marker of early onset and severe disease with significant maternal and perinatal morbidity. This finding reinforces the association between elevated hCG concentrations and placental damage in early pregnancy. Elevated maternal serum hCG levels identify a subgroup of preeclamptic patients who needs intensive observation.

CONCLUSION

According to the results of this study β-hCG may be a good indicator for mild and severe preeclampsia. Therefore, measuring β-hCG may be an early sign for the early diagnosis of the disease. Frequent antenatal visits may assist in early recognition of hypertensive complications of pregnancy and this may help to achieve a favourable outcome.

Limitations of the Study

In this study correlation was obtained between serum β-hCG and systolic and diastolic blood pressures when the preeclamptic cases were taken as a whole without grouping. Groupwise correlation between serum β-hCG and systolic and diastolic blood pressure would have been possible if a larger number of preeclamptic cases were available for the study

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ISSN (O): 2687-5365; ISSN (P): 2753-6556