Original Research Article

Early predictors of PIH: Serum β-HCG and lipid profile

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Abstract

Background: Preeclampsia is a disease that continues to be a leading cause of morbidity and mortality to both mothers and fetuses in 5-8% of pregnancies, of which up to 11% end in preterm deliveries.
Aim: The objective of the study was to evaluate β-HCG and lipid profile in early second trimester and monitored as predictors of PIH.
Materials and methods: 100 antenatal women in second trimester (14-20 weeks) attending antenatal clinic were taken into study. Serum triglycerides, total cholesterol, LDL, VLDL, HDL, β-hCG was measured. All patients were followed till delivery and observed for development of PIH.
Results: Serum β HCG, Total cholesterol and triglycerides are significant on comparison with normotensive groups of subjects. 23 out of 28 (82%) had serum βhCG level more than or equal to 40,000 mIU/ml (P<0.000, statistical significant), Number of patients with increased with Serum βHCG levels indicating its association.
Conclusion: β-HCG and lipid profile in early second trimester can help in predicting PIH. So early detection and better management of PIH and its complications is possible which would improve the maternal and fetal outcome.

Key words

Lipids, Preeclampsia, Human Chorionic Gonadotropin.

Introduction

Incidence of preeclampsia is between 3% and 10% of pregnancies and there is no evidence that this has changed appreciably. Preeclampsia is characterized by vasospasm, increased peripheral vascular resistance and reduced organ perfusion. It has been proposed that blood pressure

decreases from the first trimester to the second trimester and rises again in third trimester for healthy pregnant women. For women who developed gestational hypertension or preeclampsia, blood pressure is stable during first half of pregnancy and then continuously increased until delivery. During pregnancy placenta is the site of production of hCG, due to hypoxia there is abnormal placental trophoblastic cell invasion, increased lipid peroxidation and oxidative stress leads to dyslipidemia and increased placental βhCG production which menifests as preeclampsia later on [1].

Lipid peroxidation is a process normally occurring at low levels in all cells and tissues. It involves oxidative conversion of unsaturated fatty acids to primary products known as lipid hydroperoxides and a variety of secondary metabolites. An important mechanism for lipid peroxidation detectable in all cells is commonly referred to as the free radical process of lipid peroxidation. Any imbalance between prooxidant and antioxidant forces in which former dominates may be broadly defined as oxidative stress of which lipid peroxidation is one important manifestation. Although lipid peroxidation affects many cellular components, the primary reaction sites involve membrane associated polyunsaturated fatty acids and protein thiols [2]. Oxidative stress is a key factor in disease process. In the placenta the synthesis of reactive oxygen species is increased and activities of antioxidant enzymes are reduced. There is also evidence of lipid peroxidation in the maternal blood and placenta [3]. The endothelium seems to be the target organ for preeclampsia process. Altered endothelial cell function in preeclampsia includes activation of coagulation cascade, increased membrane permeability, enhanced response to pressor agents and increased vasoconstriction, which all contribute to reduced perfusion of affected organs.

Early pregnancy dyslipidemia is associated with an increased risk of preeclampsia. Women with a history of preeclampsia have significant differences in lipid parameters and an increased susceptibility to lipoprotein oxidation when compared with women who had normal pregnancy. Therefore simple measurements of serum lipid profile may be of good predictive value in preeclampsia. Women with PIH have hyperplacentosis or an abnormal placentation. Beta subunit of human chorionic gonadotropin (β hCG) is secreted in abundance from placenta.β hCG level in mid trimester is elevated in patients with chromosomally normal fetus who later on develop preeclampsia.

Materials and methods

A prospective study was carried out in the department of Obstetrics and Gynecology, for a period of one year. The study was conducted on 100 antenatal women with gestational age between 14 and 20 weeks.

Inclusion criteria: Primi/multigravida, singleton pregnancy, between 14 - 20 weeks of gestation as determined by last menstrual period or ultrasound scan.
Exclusion criteria: Twin gestation, chronic hypertension, diabetes mellitus, fetus with congenital anomaly, pre-existing heart disease, pre-existing renal disease.

All the patients in the study were subjected to detailed history regarding age, parity, height, maternal education, religion, socio economic status, family history of preeclampsia, past history, medical history were noted. Systemic examination and routine antenatal investigation were done. Informed consent was taken from the patient, and a fixed protocol was followed as per the proforma. Apart from routine hematological investigation, estimation of maternal serum βhCG and lipid profile was done Patients were called on a predetermined date after 12 hours of fasting, and blood sample was collected for serum βhCG and serum lipid profile in two different tubes.

Estimation of serum βhCG level was done by ELISA (Enzyme Linked Immune Absorbant

Assay). The quantitative determination of human chorionic gonadotropin in human serum was carried out. For Lipid profile Estimation after collection of blood sample, the blood was allowed to clot for 10 minutes and serum was separated by centrifugation at 2500 rpm for 20 minutes. Estimation of total cholesterol was done using enzymatic kit. Normal value of total cholesterol is <250 mg/dl. Estimation of triglyceride was done by GPO – PAP method. Normal value of triglyceride is <150 mg/dl. The HDL, VLDL, LDL cholesterol were calculated only if the total cholesterol was more than 200 mg/dl. Estimation of HDL cholesterol was done by direct enzymatic method using enzymatic method. Normal value of HDL is >40 mg/dl. Estimation of LDL cholesterol was done by enzymatic method. Normal value is <130 mg/dl. The VLDL cholesterol was calculated by the formula VLDL = TC – (HDL + LDL). Normal value is <35 mg/dl.

Means ± SD of all parameters of interest were calculated for both groups, and the difference of means between the two groups was tested by *t* test. Chi square test was used to find out significant correlation.

Results

In present study, a total of 100 subjects were recruited. Out of 100 subjects, 28 cases developed hypertensive disorders of pregnancy, 20 developed mild or severe preeclampsia, 7 developed gestational hypertension and 1 patients developed eclampsia.

Out of 28 who developed hypertension, 12 (42.8%) were of age group between 18 to 21 years and 16 (57%) were illiterate, 20 (71%) delivered vaginally and 8 (28.5%) delivered by cesarean section, 21 (75%). 4 (17.8%) developed complications like eclampsia, abruptio and acute renal failure. 20 out of 28 (71%) were primigravida out of which 1 developed eclampsia, showing hypertensive disorders more common in primigravida.
Serum β HCG, Total cholesterol and triglycerides were significant on comparison with normotensive groups of subjects.

30 who had total cholesterol level more than or equal to 250 mg/dl out of 100 cases, 15 had HDL level less than 40 mg/dl, 17 had LDL level more than 130 mg/dl and 14 had VLDL level more than 35 mg/dl. 17 out of 20(85%) had mild preeclampsia and 3(15%) had severe preeclampsia (**Table – 1**).

23 out of 28 (82%) had serum βhCG level more than or equal to 40,000 mIU/ml (P<0.000, statistical significant) as per **Table – 2**.

Number of patients with increased with Serum βHCG levels indicating its association as per **Figure - 1**.

Table - 1: Measurement values of serum βhCG and serum lipid profile between Hypertensive and Normotensive group.

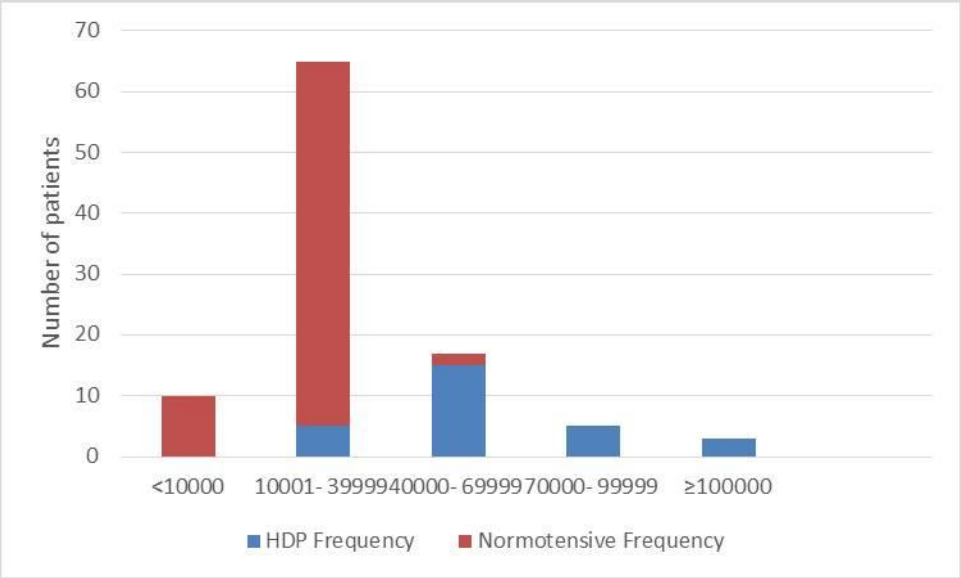
Variable	**HDP (n=28) Mean ± SD**	**Normotensive (n=72) Mean ± SD**	**p-value**
Serum β HCG	61254±39004	22134.04±9567	0.000
TC	234.45±42.3	189.2±34.5	0.000
TG	129±43.09	103±30.1	0.005
LDL	154±28.4	148±26.1	>0.05
HDL	48.3±10.45	50.2±9.81	>0.05
VLDL	46.99±25.4	46.4±30.2	>0.05

P- Value<0.05 was significant

Table - 2: Serum βHCG and development of hypertensive disorders of pregnancy.

Beta HCG (mIU/ml)	HDP Frequency (%)	Normotensive Frequency (%)	Total
<10000	0 (0.0)	10(13.8)	10
10000- 39999	5(17.8)	60(83)	65
40000- 69999	15(53.5)	2(2.7)	17
70000- 99999	5(17.8)	0(0.0)	5
≥100000	3(10.7)	0(0.0)	3
Total	28	72	100

Figure - 1: Serum βHCG with development of hypertensive disorders.



Discussion

Recent evidence suggests that there may be several underlying causes or predisposing factors in PIH leading to endothelial dysfunction and causing signs of hypertension, proteinuria and edema. Despite active research for many decades, the etiology of these disorders is Unknown. Many hypotheses have been offered for the pathogenesis of disease and include prostacyclin – thromboxane imbalance, endothelial dysfunction, immunogenetic and absolute or relative placental ischemia [12].

In our study women with elevated levels of β-HCG in early 2nd trimester had more chance of developing PIH which is comparable to the study done by Chandra, et al. and Vidyabati, et al. [4, 5]. In our study Beta HCG is significant on comparison with normotensive groups of subjects. Women developed PIH if TC >200mg/dl which in comparable with the study done by Vidyabati, et al. [4]; Morssink, et al. [6] and Pouta, et al. [7] did not find any correlation between serum βhCG and pregnancy-induced hypertension in their study. Also, Morssink, et al. [8] evaluated cases with pre-eclampsia and demonstrated that significantly rise of serum βhCG was only associated with severe pre-eclampsia. In our study also, we did not find any correlation between serum βhCG and pregnancy-induced hypertension. The divergent points of maternal serum βhCG with wide range of cut-off values may be responsible for this result. Also, the small-sized sample could be a contributing factor.

Women with preeclampsia display additional alteration in blood lipids, reflecting a disordered lipid and lipoprotein metabolism. In present study, Total cholesterol is significant on comparison with normotensive groups of subjects which is comparable with the

metaanalysis study published in BJOG by Gallos, et al. and Amarlal, et al. [5, 9]. Abnormal levels of TG are associated with pregnancy complication [10].

In this study significant difference in triglyceride levels in preeclamptic groups as compare to control group were found. PIH which is comparable with the metaanalysis study published in BJOG by Gallos, et al. and Amarlal, et al. [5, 9]. Abnormal levels of TG are associated with pregnancy complication [7]. Lorentzen, et al. [11] concluded that serum-free fatty acids and triglyceride are increased before 20 weeks of gestation in women who later develop pre-eclampsia. Clausen, et al. [12] concluded that hypertriglyceridemic dyslipidemia before 20 weeks of gestation is associated with the risk of developing early onset pre-eclampsia.

De, et al. [13] concluded that there is significant rise in triglyceride and VLDL levels and a fall in HDL levels in pre-eclamptic patients. Vidyabati, et al. [4] concluded that total cholesterol; VLDL, and LDL in women who subsequently developed PIH were significantly higher than in normotensive patients.

We have observed that lipid profile levels are strongly associated with preeclampsia. This suggests that elevated lipids may be involved in pathogenesis with preeclampsia and risk marker of this in women. Our results, when taken together with those of earlier studies, indicate that dyslipidemia particularly hypertriglyceridemia and elevated lipoprotein precede the clinical manifestations of pre-eclampsia and thus may be of etiologic and pathophysiologic importance in pregnancy-induced hypertension. The association between dyslipidemia and the risk of pre-eclampsia is biologically plausible and is compatible with what is known about the pathophysiology of pre-eclampsia. So from this study we add evidence supporting that altered lipid profile (mainly hyper triglyceridaemia) and increased β-HCG as early predictors of PIH.

Conclusion

The present study showed that maternal dyslipidemia as well as abnormally elevated maternal serum βhCG level at second trimester are very good non-invasive predictors of hypertensive disorders of pregnancy. However, considering the percentage of detection, maternal serum βhCG seems to be more efficient marker in predicting hypertensive disorders of pregnancy at second trimester. It may be concluded that the estimation of maternal lipid profile in early second trimester will bring about early recognition of patients at risk of hypertensive disorders of pregnancy before the clinical syndrome and complications of hypertensive disorders of pregnancy appears for a better fetomaternal outcome.

Ethical approval: The study was approved by the Institutional Ethics Committee.

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