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Original Research Article

Serum Beta HCG and Fasting Lipid Profile in Early Second Trimester as Predictors of Gestational Hypertension

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Abstract: Hypertensive disorders of pregnancy are one of the commonest medical problems encountered during pregnancy. It is the major cause of maternal and perinatal morbidity, complicating 5-10 % of pregnancies worldwide. A variety of biochemical and biophysical markers have been proposed for the purpose of predicting the development of gestational hypertension later in pregnancy. Early identification of at risk women may help in taking timely preventive and curative management to prevent or delay complications associated with gestational hypertension. The study aims at testing the hypothesis that women with high serum beta HCG and lipid profile in early second trimester have risk of developing gestational hypertension. 130 patients were included in the study using selection criteria. This prospective clinical study was being conducted in department of OBG, JMMC &RI in a time period of December 2013 to May 2015. The study group consisted of all pregnant women who were coming to the OBG department for antenatal visit except those who fall under exclusion criteria. Informed consent will be obtained as per proforma. Those with known last menstrual period or first trimester ultrasonography screening and gestational age between 14-20 weeks were selected irrespective of parity. Patients were screened for beta HCG and fasting lipid profile. The patients were followed up regularly in the antenatal OPD till delivery.All the detailed data were collected and data was analysed statistically. Total cholesterol, triglycerides, VLDL, and LDL values for those women who developed gestational hypertension were significantly higher than those who remain normotensive with p value of <0.05 which is statistically significant. HDL and beta HCG values for gestational hypertensive group were not higher than those in normotensive group with p value >0.05 which is statistically insignificant. Maternal lipid profile in second trimester is very good noninvasive test which can be used for prediction of gestational hypertension before its clinical onset. However, there is no correlation between maternal serum beta HCG and gestational hypertension.
Keywords: Gestational hypertension, beta HCG, total cholesterol, triglyceride, LDL, VLDL, HDL.

INTRODUCTION

Hypertensive disorders of pregnancy are one of the commonest medical problems encountered during pregnancy. It is the major cause of maternal and perinatal morbidity, complicating 5-10 % of pregnancies worldwide[1]. A variety of biological, biochemical, and biophysical markers are implicated in the pathophysiology of preeclampsia during the last two decades. Early identification of at-risk women may help in taking timely preventive and curative management to prevent or delay complications associated with hypertensive disorders of pregnancy, thus improving pregnancy outcome.

The onset of preeclampsia at or near to term is associated with low maternal and neonatal morbidity and mortality. In contrast, those patients who suffer early onset preeclampsia have significant maternal and perinatal morbidity and mortality[2]. Therefore, because of the lack of proven prophylaxis for preeclampsia, prediction of risk or identification of subclinical disease is desirable to identify patients for more intensive observation. Measurement of various biological, biochemical, and biophysical markers implicated in preeclampsia syndrome pathophysiology in early pregnancy or across pregnancy has been proposed to predict its development[3]. There is no cure for hypertensive disorders of pregnancy except delivery. The accurate identification of women at risk, early diagnosis, and prompt and appropriate management (eg, antenatal corticosteroids for fetal lung maturation, treatment of severe hypertension, early

delivery) may improve maternal outcome and possibly perinatal outcome as well.

Measurement during early pregnancy or across pregnancy of various biological, biochemical, and biophysical markers implicated in preeclampsia syndrome pathophysiology has been proposed to predict its development. Attempts have been made to identify early markers of faulty placentation, impaired placental perfusion, endothelial cell activation and dysfunction, and activation of coagulation. For the most, these have resulted in testing strategies with poor sensitivity and with poor positive-predictive value for preeclampsia. Currently, no screening tests are predictably reliable, valid, and economical. There are, however, combinations of tests, some yet to be adequately evaluated, that may be promising. Although most have been evaluated in the first half of pregnancy, some have been tested as predictors of severity in the third trimester. Others have been used to forecast recurrent preeclampsia

MATERIALS AND METHODS

Study setting

The study was conducted in the department of OBG, Jubilee Mission Medical College, and Thrissur

Study population

The study population includes 130 patients attending OBG department

Study design

Prospective study

Duration of study

One and half years

Inclusion criteria

Primi / Multi gravida with singleton pregnancy with gestational age 14-20 weeks as determined by last menstrual period or ultrasound scan

Exclusion criteria

The exclusion criteria were, a) multiple pregnancies; b) chronic hypertension; c) diabetes mellitus and d) liver and renal diseases.

Sample size

One hundred and thirty patients who fulfilled the selection criteria

METHODS

This was a prospective study, conducted on 130 patients. The study population included women with singleton pregnancy visiting antenatal outpatient department of the Obstetrics and Gynaecology of Jubilee Mission Medical College and Research Centre, Thrissur. All patients were screened for serum beta HCG and serum lipid profile in their early second trimester (14–20 weeks) by taking blood sample after 12 h of fasting. These values were recorded, and patients were followed up till their delivery. Serum beta HCG and serum lipid profile were compared between those who remain normotensive and those who developed gestational hypertension

Informed consents were taken from all the patients. Patients were called on a predetermined date after 12 h of fasting, and blood samples were collected for serum beta HCG and serum lipid profile in two different tubes. Serum beta HCG was determined by EIA (enzyme immune assay) using AIA 360 spectral equipment. Serum lipid profile was done using a fully automated machine-Beckmann coulter CX-5 Pro and Olympus AV-400 by means of enzyme calorimetric method. The cases were followed up regularly in the antenatal OPD till delivery. All the detailed data were collected and analysed statistically.

STATISTICAL ANALYSIS

The difference of means between the two groups was tested by t test. Chi square test was used to find out significant correlation

RESULTS AND DISCUSSION

This was a prospective study conducted in 130 patients. In this study 65 women(50%) were in the age group 19-24 years , 44 women (33.8%)were in the age group 25-29 years, and 15 women(11.5%) were in the age group 30-34 years. There were only 6 cases (4.6%) aged more than 35 years. The incidence of gestational hypertension in the present study is 17.7% which is higher than general population. Out of 130 cases studied, 23 developed gestational hypertension, the rest remained normotensive. (Table no: 1)

Table 1 Blood Pressure in 3rd Trimester

Blood Pressure in 3rd Trimester	No. of patients	%
>140/90	23	17.7
<140/90	107	82.3
Total	130	100.0

Out of the 130 cases in this study, 72 (55.4 %) cases were primigravida and 58 (44.6 %) were multigravida. 16 cases out of the 23 with gestational hypertension were primigravidawhich suggests that gestational hypertension is more common in primigravida cases, and this is similar to that reported by many studies.

Obese women are at a higher risk of pre-eclampsia, but the mechanisms involved are not known. Women with the lowest BMI are relatively protected against gestational hypertension. All the women in the

study were in the normal BMI group (18.5-24.9). As there were no women with elevated BMI, it is difficult to comment on the relation of gestational hypertension risk in patients with elevated BMI.

In this study, we did not find any correlation between serum beta HCG and gestational hypertension. (Table: 2) Morssink*et al.*[4]*;* and Pouta*et al*[5] did not find any correlation between serum beta HCG and gestational hypertension in their study. Also, Morssink*et al.*[4]*;* evaluated cases with pre-eclampsia and demonstrated that significantly rise of serum beta HCG was only associated with severe pre-eclampsia.

Table: 2 Beta HCG distribution of patients studied in relation to gestational hypertension

Beta HCG	Gestational hypertension		Total
	No	Yes	
<20000	29(27.1%)	7(30.4%)	36(27.7%)
20000-40000	52(48.6%)	8(34.8%)	60(46.2%)
>40000	26(24.3%)	8(34.8%)	34(26.2%)
Total	107(100%)	23(100%)	130(100%)

P=0.437, Not significant, Chi-Square test

In this study, we observed an association between maternal early pregnancy dyslipidemia and the subsequent risk of gestational hypertension. This finding is similar to many other studies. Lorentzen*et al.*[6] 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.*[7] concluded that hypertrigliseridemic dyslipidemia before 20 weeks of gestation is associated with the risk of developing early onset pre-eclampsia.

Cekmen*et al*[8].have shown that plasma triglyceride and LDL levels were significantly higher in pre-eclamptic subjects than in controls, whereas the plasma HDL levels were significantly lower in pre-eclamptic cases than in control group. De *et al.*[9]concluded that there is significant rise in triglyceride and VLDL levels and a fall in HDL levels in pre-eclamptic patients. Vidyabati*et al.*[10] concluded that total cholesterol; VLDL, and LDL in women who subsequently developed gestational hypertension were significantly higher than in normotensive patients.

Table 3: Lipid Distribution of patients studied in relation to gestational hypertension

Lipids	Gestational hypertension		Total (n=130)	P value
	No (n=107)	Yes (n=23)		
Total Cholesterol (mg/dl)				
<200	84(78.5%)	0(0%)	84(64.6%)	<0.001**
200-239	22(20.6%)	2(8.7%)	24(18.5%)	
>240	1(0.9%)	21(91.3%)	22(16.9%)	
TG (mg/dl)				
<150	100(93.5%)	1(4.3%)	101(77.7%)	<0.001**
150-199	3(2.8%)	14(60.9%)	17(13.1%)	
>200	4(3.7%)	8(34.8%)	12(9.2%)	
LDL (mg/dl)				
<100	71(66.4%)	0(0%)	71(54.6%)	0.001**
100-189	36(33.6%)	20(87%)	56(43.1%)	
>190	0(0%)	3(13%)	3(2.3%)	
VLDL (mg/dl)				
<30	100(93.5%)	1(4.3%)	101(77.7%)	<0.001**
30-59	7(6.5%)	22(95.7%)	29(22.3%)	
>60	0(0%)	0(0%)	0(0%)	
HDL (mg/dl)				
<40	5(4.7%)	0(0%)	5(3.8%)	0.138s
40-59	66(61.7%)	19(82.6%)	85(65.4%)	
>60	36(33.6%)	4(17.4%)	40(30.8%)	

Out of 23 patients who developed gestational hypertension, 2 patients had borderline high cholesterol values (200-239 mg/dL) and 21 had high values (>240mg/dL). In this study, 14 patients who developed gestational hypertension had borderline high values of triglycerides (200-239mg/dL) and 8 patients who

developed gestational hypertension had high values (≥240mg/ dL)

Out of 23 patients, 20 patients had borderline high values of LDL (100-189 mg/dL) and 3 patients had very high LDL values (>190mg/dL. 22 patients had high values of VLDL in gestational hypertensive group. Pregnant women who subsequently developed gestational hypertension had higher total cholesterol, TG, VLDL, and LDL cholesterol levels compared with pregnant women who remained normotensive. This finding is similar to that of many other studies.

In our study, we had 19 cases (82.6 %) out of the 23 with desirable values of HDL (40-59) and 4 cases (17.4 %) with protective values of HDL ≥60. None had HDL value < 40 (low value of HDL). The expected inverse relationship between pre-eclampsia risk and HDL concentration was not evident in this study. (Table no: 3)

So dyslipidemia particularly hypertriglyceridemia, high cholesterol and elevated lipoprotein precede the clinical manifestations of gestational hypertension and thus may be of etiologic and pathophysiologic importance in gestational hypertension. The association between dyslipidemia and the risk of pre-eclampsia is previously reported. In the literature, at least three hypotheses for association between dyslipidemia and pre-eclampsia have been postulated.

First, previous investigators have noted that increased plasma lipids and lipoproteins will induce endothelial dysfunction secondary to oxidative stress. Free radicals may be generated by different enzymatic processes. They are extremely reactive and interact with polyunsaturated fatty acids to produce lipid peroxides. Lipid peroxides are normally present in lipoproteins and may contribute to vascular tone regulation through stimulation of the arachidonic acid pathways. When oxidative stress reaches a certain level, cellular damage occurs, including structural damage in cellular membranes in mitochondrial and nuclear DNAs and impairment of enzymatic functions at multiple levels. Oxidative stress can have an affect mainly on vessel endothelium and on many tissues and organs both locally and systemically. During these processes, other molecules involved in vasodilatation such as nitric oxide (NO) are inhibited by high lipid peroxide concentration. All these circumstances might be the contributory factors for the etiopathogenesis of hypertension in pre-eclampsia. It is also noted that dyslipidemia may impair trophoblast invasion thus contributing to a cascade of pathophysiologic events that lead to the development of pre-eclampsia. In this disorder, there is under perfusion, ischemia, and hypoxia in the placenta, which is then thought to release a variety of mediators in the maternal circulation including hormones, cytokines, and reactive oxygen species such as NO, superoxide anion, and hydrogen peroxide, which cause endothelial dysfunction and permanent systemic vasoconstriction leading to pre-eclampsia.

The second mechanism is the pathologic process of preeclampsia via dysregulation of lipoprotein lipase resulting in dyslipidemic lipid profile. Serum from preeclamptic women had both, a higher ratio of free fatty acids to albumin and increased uptake of free fatty acids, which are further esterified to triglyceride.

A third possible mechanism may be via the metabolic syndrome. Metabolic characteristics of insulin-resistance syndrome namely, hyperinsulinemia and hyperuricemia, are also present in pre-eclampsia. Women with a history of pre-eclampsia, compared with their BMI matched counterparts without such a history, have higher circulating concentrations of fasting insulin, lipid, and inflammatory and coagulation factors, many years after delivery.

Therefore estimation of maternal lipid profile in the early second trimester will bring about early recognition and better management of patients at risk of gestational hypertension, before the clinical syndrome and complications of preeclampsia appear. Moreover early treatment of such cases is essential for a better feto-maternal outcome.

CONCLUSION

Hypertensive disorders of pregnancy are the second most common cause of maternal mortality and most common cause of morbidity. Despite a remarkable decline in morbidity and mortality from preeclampsia in the last half century, attributable to improvements in obstetric and perinatal care chiefly in the developed world, there have been no revolutionary advances in the treatment of preeclampsia. So prediction and prevention of the disease can solve the problem to some extent.Maternal lipid profile in the early second trimester is very good and effective non-invasive test, which is a reproducible, economical, and reliable technique which can be used for prediction of gestational hypertension, before its clinical onset. However, no correlation was found between maternal serum beta HCG and gestational hypertension.

Following conclusions were drawn from the present study

a. Elevated total cholesterol, triglycerides , LDL and VLDL in early second trimester can be taken as predictors of gestational hypertension
b. HDL had no correlation with gestational hypertension.

c. No correlation were found between maternal serum beta HCG and gestational hypertension
d. Gestational hypertension was found to be more common in primipara

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