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Serum Beta HCG and Lipid Profile in Second Trimester as Predictors of Pregnancy Induced Hypertension

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Abstract

Objective: To study whether serum βhCG and lipid levels during second trimester of pregnancy are associated with the development of pregnancy induced hypertension (PIH). Methods: 100 pregnant women between 14-20 weeks gestation with singleton pregnancy irrespective of parity were selected randomly and serum βhCG and lipid profile were estimated by chemiluminescent immunometric assay (CLIA) and enzymatic colorimetric test respectively. Regular follow up of the cases was done till delivery. Results were analyzed statistically. Results: Out of 93 cases followed up till delivery, 10 cases developed PIH. Serum βhCG (median ≥ 35000 mIU/dl) has sensitivity of 80%, specificity of 59% and accuracy of 61%. Dyslipidemia especially LDL > 117 mg/dl had higher sensitivity (80%) but specificity and accuracy was similar to total cholesterol (≥200mg/dl) and triglycerides (156mg/dl). Serum βhCG seems to be a more efficient marker in predicting PIH at second trimester. Conclusion: The present study indicates an increased risk of PIH in patients with elevated βhCG and dyslipidemia, especially elevated cholesterol and LDL in second trimester. As yet there is no practical, acceptable and reliable screening test for PIH, Serum βhCG seems to be a very good noninvasive early predictor for the development of PIH.

Keywords: *Serum beta Hcg; Pregnancy; Preeclampsia; Serum lipid profile.*

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Introduction

Hypertensive disorder is one of the most common medical complications affecting 5-10 % of all pregnancies. Understanding the disease process and the impact of hypertensive disorders on pregnancy is of utmost importance, as these disorders remain the leading cause of maternal and perinatal morbidity and mortality.

Preeclampsia is a multisystem disorder of unknown etiology unique to pregnancy with the onset after 20 weeks of gestation. It is characterized by the hypertension and proteinuria. Various clinical and laboratory parameters have been used to predict Pregnancy Induced Hypertension (PIH) with varying degree of success. The maternal plasma lipid levels are elevated prior to the clinical onset of preeclampsia. Altered lipid metabolism can cause endothelial dysfunction, one of the hypothesized factors in the pathogenesis of PIH.

Women with PIH have hyperplacentosis or an abnormal placentation. Serum βhCG (â human Chorionic Gonadotrophin) level in mid trimester is elevated in the patients who later develop preeclampsia.

The present study was carried out to evaluate the clinical utility of second trimester serum âhCG levels and serum lipid profile as a predictive tests for PIH. In this study PIH refers to gestational hypertension and preeclampsia.

Objectives

- To study whether serum βhCG and lipid levels during second trimester of pregnancy are associated with the development of pregnancy induced hypertension (PIH).

Methodology

This prospective study was conducted in Women and Children Hospital, Bapuji Hospital and Chigateri General Hospital, Davangere from November 2010 to October 2012 over a period of 2 years on 100 pregnant normotensive, non proteinuric women selected randomly between the gestational periods of 14-20 weeks attending the ANC clinics, irrespective of parity. Women with multiple pregnancy, chronic hypertension, diabetes mellitus and congenital mal- formation were excluded from the study. Gestational age was calculated from the reliable menstrual history dates and/or early ultrasonography.

All the women were subjected to detailed history regarding age, parity, past obstetric history, medical history, and family history. Height, weight, blood pressure were measured. Routine antenatal investigation was done. 5 ml of venous blood sample was collected and tests were carried out. Estimation of serum βhCG level was done by Chemiluminescent immunometric assay (CLIA) method. Serum lipid profile (Total cholesterol, triglycerides and HDL) estimation was done by enzymatic colorimetric test. LDL cholesterol and VLDL cholesterol values were indirectly calculated.

The cases were followed up in antenatal clinic and were examined 4 weekly till 28 weeks, fortnightly up to 34 weeks and thereafter weekly till delivery. At every visit, blood pressure was recorded. Urine was examined for albumin, if blood pressure was found to be raised. PIH included gestational hypertension and preeclampsia. Gestational hypertension was defined as blood pressure ≥ 140/90 mmHg on two occasions at least 6 hours apart after 20 weeks of gestation. Preeclampsia was defined as gestational hypertension and proteinuria of at least 1 + on dipstick. The patient who developed PIH was followed till 6 weeks after delivery.

Statistical analysis

Results so obtained were evaluated and analyzed statistically. Mean ± standard deviation (SD) of all the parameters of interest were calculated for PIH and for normotensive separately and difference of means between the two groups was tested by unpaired 't' test. Chi-square test was applied for categorical data. Diagnostic validity tests were performed to assess diagnostic value of βhCG and lipid profile in the prediction of PIH.

A p-value of 0.05 or less was considered for statistical significance.

SPSS version16 software was used for all the analysis.

The following diagnostic validity tests[58] were used.

Results

One hundred women were enrolled, but only 93 (93%) women were completely followed till term. 7 were lost to follow up. Out of 93 cases that completed the study, 10 (10.7%) cases developed PIH (all were preeclampsia) and 83 remained normotensive.

Graph 1: Shows the distribution of the age of the cases. Majority of them were aged between 20-24 years

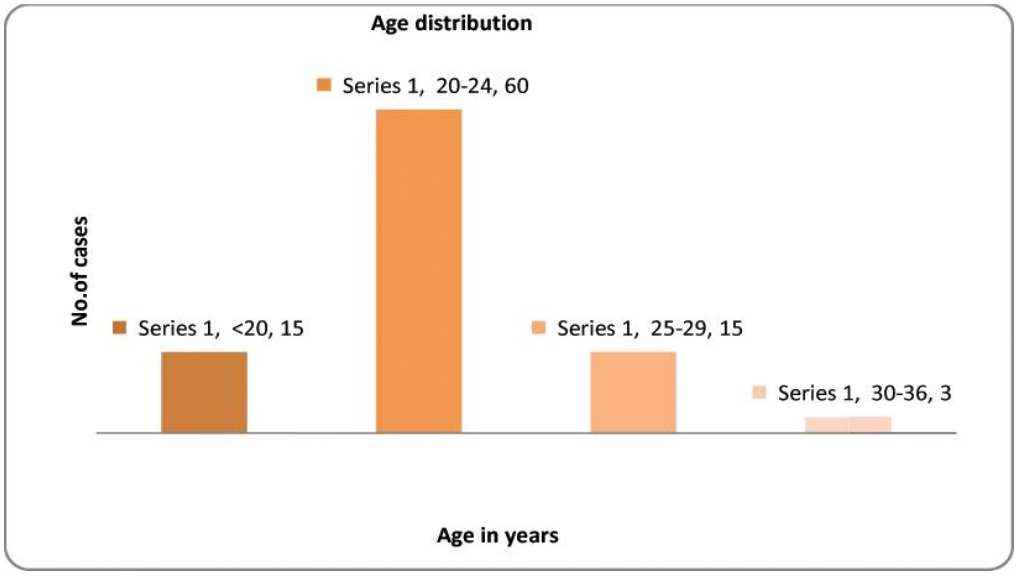


Table 1: Characteristics of subjects

		PIH (10)	Normal (83)	p-value
Age (years)	Mean ± SD	20.8 ± 1.5	22.1 ± 3.2	0.20 NS
	Range	18-23	18-32	
BMI (kg/m^2)	Mean ± SD	22.76 ± 1.08	22.72 ± 2.20	0.96 NS
	Range	21.7 – 24.6	17.54 – 31.2	

NS: Not significant

Mean age among PIH group is 20.8 years and mean BMI in this group is 22.76 kg / m^2. Normotensive group has mean age of 22.1 years and BMI of 22.72 kg / m^2. Comparison of the age and BMI for both PIH and normotensive groups are almost alike.

Table 2: Comparison of mean ± SD of systolic and diastolic blood pressure (mm Hg) between PIH and normal group

BP	PIH (n=10)	Normal (n=83)	t value	p-value
At 1st visit (14-20 weeks)				
Systolic	118.0± 6.3	114.8 ±8.0	1.20	0.23 NS
Diastolic	75.0 ± 7.1	73.1 ± 5.4	1.03	0.31 NS
At delivery				
Systolic	154.0±8.4	118.4±6.5	15.77	<0.001 HS
Diastolic	100.0±10.5	76.1±5.6	11.43	<0.001 HS

NS: Not significant HS: Highly significant

Comparison of blood pressure at the time of booking (14-20 weeks) between the PIH and the normotensive group did not vary significantly. Blood pressure for PIH cases at the time of delivery was significantly higher in comparison to the BP of the normotensive group. This is true for both diastolic and systolic blood pressure.

Table 3: Comparison of mean ± SD of serum b hCG and serum lipid profile between PIH and normotensive group

Variable	PIH (n=10) Mean ± SD	Normal (n=83) Mean ± SD	t value	p-value
Serum βhCG (mIU/ml)	55115.7 ± 18183.3	37759.3 ± 21270.5	2.47	0.02 Significant
Total cholesterol (mg/dl)	238.5±79.5	204.6±40.2	2.22	0.03 Significant
Triglycerides (mg/dl)	153.8 ± 33.8	164.0 ± 59.9	0.53	0.60 NS
HDL (mg/dl)	51.1 ± 13.7	50.7 ± 14.4	0.08	0.94 NS
LDL (mg/dl)	156.8 ± 47.1	123.5 ± 42.4	2.32	0.02 Significant
VLDL (mg/dl)	20.8 ± 4.3	25.6 ± 9.3	1.62	0.11 NS

NS: Not significant

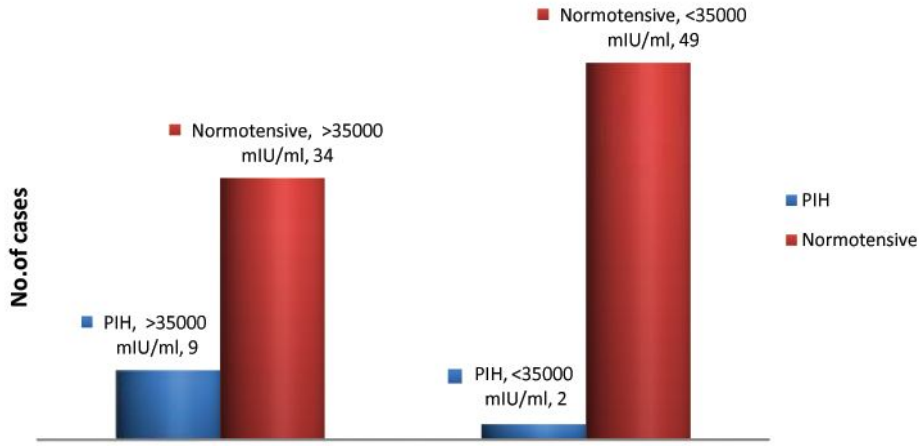
Mean ± SD concentration of serum βhCG is increased significantly in those women who developed PIH. Total cholesterol and LDL (low density lipoprotein) values for those women who developed PIH were found significantly higher than the corresponding values for normotensive women. The mean value of triglyceride and VLDL was slightly higher in normal than PIH but statistically not significant. The mean value of HDL for both the groups was almost alike.

Table 4: Relation of serum bhCG levels and hypertensive status

βhCG (mIU/ml)	PIH (n=10) No (%)	Normotensive No (%)	No. of cases
<20000	-	12 (100%)	12
20000 – 30000	-	24 (100%)	24
30000 – 40000	3 (10.3%)	26 (89.7%)	29
40000 – 50000	2 (16.7)	10 (83.3%)	12
50000 – 60000	-	2 (100%)	2
60000 – 70000	3 (75%)	1 (25%)	4
70000 – 80000	1 (16.6%)	5 (83.3%)	6
80000 – 90000	1 (50%)	1 (50%)	2
>1,00,000	-	2 (100%)	2
Total	10	83	93

Those pregnant women having serum βhCG level above the median value i.e. 35000 mIU / ml at the second trimester of pregnancy are at the risk of developing PIH. The absolute βhCG levels did not correlate with the severity of PIH.

Graph 2: Distribution of cases according to hypertensive status & βhCG levels



Out of 42 cases with βhCG> 35000 mIU / mL, 8 (19%) cases developed PIH and out of 51 cases with β hCG<35000 mIU / mL only 2 cases developed PIH. The p-value is 0.02, which is significant.

Table 5: Distribution of cases according to lipid profile and hypertensive status

Variable (mg/dl) median	PIH (n=10)	Normal (n=83)	Total
Total cholesterol			
≥ 200	6 (60%)	41 (49.4%)	47
<200	4 (40%)	42 (50.6%)	46
	$X^2 = 0.40$, P=0.53 (NS)		
Triglyceride			
≥156	7 (70%)	40 (48.2%)	47
<156	3 (30%)	43 (51.8%)	46
	$X^2 = 1.70$, P=0.19 (NS)		
LDL – Cholesterol			
≥117	8 (80%)	40 (48.2%)	48
<117	2 (20%)	43 (51.8%)	45
	$X^2 = 3.62$, P=0.05 significant		

NS: Not significant

Out of 47 cases with total cholesterol more than the median (≥200mg / dl), 6 (12.76%) developed PIH. 4 cases (40%) in spite of cholesterol levels < 200mg / dl developed PIH later.

Seven out of 10 cases with PIH had triglycerides ≥156mg / dl (median), but 40 cases in spite having high triglycerides levels did not developed PIH.

8 cases (80%) had LDL values above median. p – value is significant. With LDL values more than the median i.e., 117 mg / dl, 8 out of 48 cases (16.67%) had PIH.

Table 6: Diagnostic value of bhCG and lipid profile in the prediction of PIH

Variable	βhCG	Total cholesterol	Triglyceride	LDL
Sensitivity	80%	60%	70%	80%
Specificity	59%	51%	52%	52%
PPV	19%	13%	15%	16%
NPV	96%	91%	93%	96%
Overall accuracy	61%	52%	54%	55%

Serum βhCG(e" 35000 mIU / dl) has sensitivity of 80%, specificity of 59% and accuracy of 61%. Dyslipidemia especially LDL > 117 mg / dl had higher sensitivity (80%) but specificity and accuracy was similar to total cholesterol (≥200mg / dl) and triglycerides (156mg / dl).

Serum âhCG seems to be a more efficient marker in predicting PIH at second trimester.

Discussion

Among the 93 cases that completed the study, 10 (10.75%) cases subsequently developed PIH and 83 remained normotensive. In the study conducted by Vidyabati [1] et al, 164 women at 14-20 weeks gestation completed the study out of 180 selected.

29 (17.7%) developed PIH. In our study, majority (64.5%) belonged to age group between 20 -24 years. Mean age among PIH group is 20.8 years and 22.1 years among normotensive group. In Vidyabathi [1] study, mean age was 27.17 years. Maximum PIH was observed in elderly primi belonging to age group of 31-35 years.

In our study, mean systolic blood pressure in PIH group is 118mmHg and diastolic blood pressure is 75 mmHg. In normotensive group it is 114mmHg and 73 mmHg respectively. In Vidyabathi [1] study, systolic BP among group who later developed PIH was 120.7mmHg and diastolic BP in normotensive group was 78.9mmHg.In Satyanarayan [2] et.al, study, mean systolic BP was 105 mmHg and mean diastolic BP was 71.64mmHg. Mean arterial BP on recruitment in PIH group is 83.92 mmHg and 82. 45mmHg in normotensive group.

Blood pressure at the time of booking between the PIH and the normotensive group did not vary significantly.

In the study done by Vidyabathi, WG Singh [1] et al, 29 cases developed PIH out of 164 women. Out of 29 cases, 21(72.4%) women had elevated βhCG above 45000mIU/ml. For every 1000 mIU/ml increase in serum βhCG a pregnant women has 10.7% increasing chance of having PIH.

In study conducted at Jaipur [3], 20 cases had PIH out of 24 women with βhCG> 2 MOM (multiple of median) as compared to 2 cases had PIH out of 154 women with βhCG ≤ 2 MOM which is statistically significant. Increasing âhCG had direct association with the severity of PIH. One case out of 8 in <80000 mIU/ml group had severe PIH, while for >80000mIU/ml group 12 out of 14 had severe PIH (P value <0.01significant).

In study conducted by Pankaj Desai [4], 62 cases had PIH out of 90 women with βhCG> 2 MOM as compared to 21 cases had PIH out of 130 women with âhCG ≤ 2 MOM (p value <0.01, significant). It was also significant that 59 out of 62 women who developed PIH had βhCG levels > 2MOM before 32 weeks. On the other hand 18 out of 21 women with βhCG ≤ 2 MOM did it after 32 weeks (p<0.001).

In Satyanarayan et al, [2] study, there was no correlation between elevated hCG levels and PIH. Mean hCG levels at mid-trimester were non-significantly higher in normotensive women (17112mIU/ml) compared to those with PIH (15666mIU/ml). Twenty four women (12.3%) had elevated hCG levels on recruitment, of which 21(87.5%) remained normotensive and 3 (12.5%) developed PIH. Elevated hCG levels were found 3 of 21 women (14.2%) with PIH and 21 (12%) normotensive women [2].

In the present study, incidence of PIH in women with elevated hCG ≥35000 mIU/dl was higher compared to women with normal levels (19% versus 4%). However, there was no relation between severity of PIH and hCG levels. Similar results were shown in study by Sorensen et al [5].

The present study shows that maternal âhCG has a significant influence in predicting preeclampsia with sensitivity 80%, specificity 59%.

Vidyabathi [1] et al., showed an association between maternal early pregnancy dyslipidemia, particularly hypertriglyceridemia, and the subsequent risk of preeclampsia.

In present study, dyslipidemia especially, raised LDL and hyper- cholesterolemia was associated with development of PIH. Serum β hCG seems to be a more efficient marker than dyslipidemia, in predicting PIH.

Conclusion

The present study indicates an increased risk of PIH in patients with elevated βhCG and dyslipidemia, especially elevated cholesterol and LDL in second trimester. As yet there is no practical, acceptable and reliable screening test for PIH, Serum âhCG seems to be a very good noninvasive early predictor for the development of PIH.

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