Early Diagnosis of Pregnancy Induced Hypertension by Estimating Serum beta HCG and Lipid Profile

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Abstract:
Background:*Eclampsia is an important cause of maternalmortality in developing countries likeIndia. Eclampsia is also responsible for complications like heart failure, pre term labor, etc as well as adverse fetal outcomes. Hence this study is undertaken mainly to forecast the scenario of developing pregnancy induced hypertension at early trimester of 14 to 20 weeks of gestation by two main predictors – serum beta HCG and plasma lipid profile to prevent the development of eclampsia at near term.*
Methods:*A total of 150 pregnant women who had attended the department of obstetrics and gynaecology of the institute, from May 2016 to September 2017, were selected for the study. Pregnant women with known last menstrual period or first trimester sonography with gestational age between 14 to 20 weeks were included irrespective of parity and data analysed.*
Results:*This study has revealed a significant association between total cholesterol levels, HDL and LDL levels in lipid profile and higher beta HCG values and the incidence of PIH later on during pregnancy.*
Conclusion:*Thus, lipid control measures should start periconceptionally with frequent monitoring of lipid profile and beta HCG levels in early pregnancy period so that complications of PIH and eclampsia are avoided for the better healh care of mothers and fetaloucome.*
Keywords: *PIH, Eclampsia, Lipid profile, beta HCG*

I. Introducion

Hypertension complicates 5 to 10% of all pregnancies world wide.Pregnancy induced Hypertension accounts for 3.9% of all pregnancies[1].*Yagnik et al and Susane* proposed that Uncontrolled pregnancy induced hypertension can lead to maternal and fetal complications and increased risk of hypertension and diabetes in the fetus,in the later stages of life.

A systemic review by World Health Organisation reveals that "hypertensive disorders account for 16% of all deaths in the developed countries",with 9% maternal deaths in Africa and Asia,26% maternal deaths in Latin America and Carribean[2].

Severe morbidity associated with preeclampsia and eclampsia include renal failure, stroke,cardiac dysfunction or arrest,respiratory compromise,coagulopathy and liver failure.

The risk factors are multiparity, excess placental volume, higher maternal age maternal co morbidities like diabetes, hypertension[3].The most common mechanisms which lead to the causation of preeclampsia are vasospasm, endothelial cell injury, immunological factors and placental pathology like hyperplacentosis or abnormal placentation.

II. Materials & Methods

A total of 150 pregnant women who had attended the Department of obstetrics and gynaecology of the institute, from May 2016 to September 2017, were selected for the study. Pregnant women with known last menstrual period or first trimester sonography with gestational age between 14 to 20 weeks were included irrespective of parity. Women with hypertension diagnosed before 20 weeks of gestation, Diabetes Mellitus, multiple gestations, Ultrasound proved foetal congenital malformations or molar pregnancy were excluded. Detailed history regarding personal and obstetric details and family history of hypertension, physical activity during pregnancy was noted. Beta HCG was estimated by Enzyme Linked Immuno Sorbent Assay (ELISA test) and they were followed up till term. All the lipid parameters were estimated by enzymatic colour test. Mean and standard deviations (SD) for PIH and normotensive cases were calculated separately. Student unpaired t-test was employed for statistical analysis and p-value less than 0.05 was considered to be statistically significant.

III. Results

A total of 150 pregnant patients were included in our study. Out of these women, there were 83cases of PIH diagnosed in 2nd and third trimesters accounting for 55% of the sample while 67cases were normotensive throughout pregnancy, ie, 45% of the sample. Most of the women belonged to the age group of 21-30 years (81%), while 14% were less tahn 20 years and 5% were more than 30 years of age., the detailed age distribution of study population is as given below in Figure 1.

Figure 1: Age distribution of study population
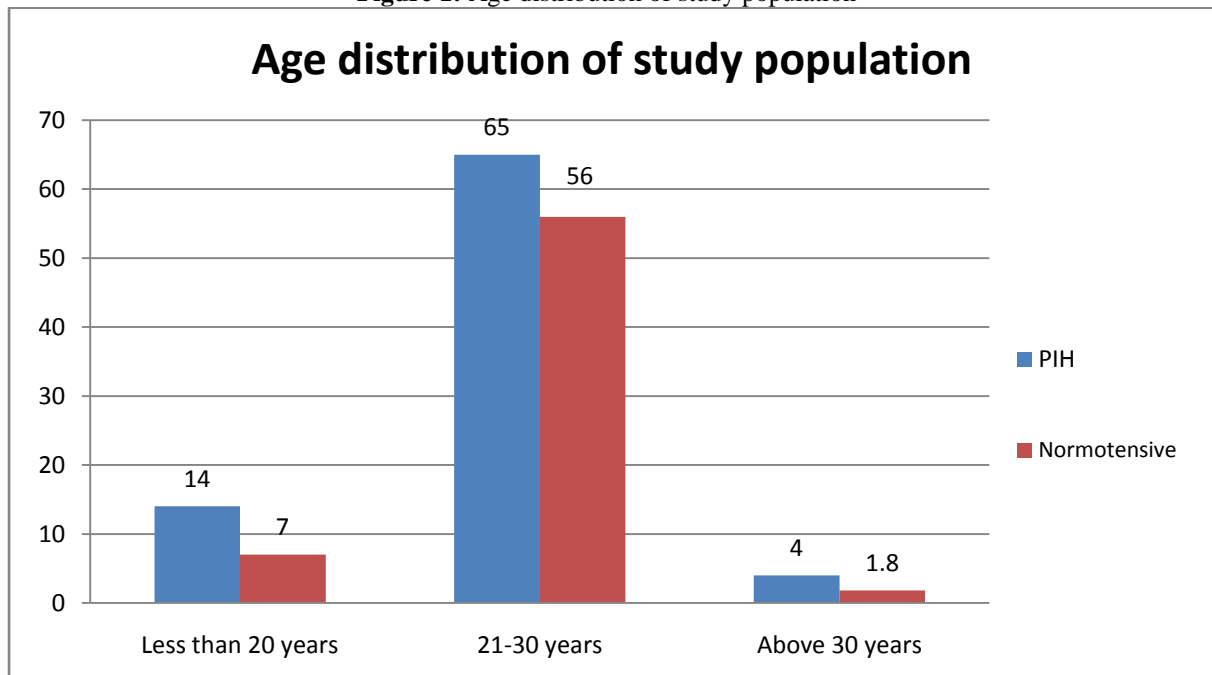
The mean age of PIH patients is 23.95 +/- SD of 3.7 years while that of normotensive women is 24.04 +/- SD of 3.9 years. There is no significant difference in the mean ages between both groups of women (Unpaired t test, p 0.83). Moreover, as per Kruskal Wallis test there is no significant difference in proportions of women across different age groups.

Pre-pregnancy weight and present weight:
The mean weight increases significantly from the pre-pregnancy range to the present weight with a P-value <0.0001 by paired t test.But there is no significant difference in the mean pre- pregnant weight (p 0.97) or present weight (p 0.99) among patients with preeclampsia and normotensive patients

Obstetric history:
Up to half of the women were primigravidae (44%), while 40% were second gravidae and 16% were having a parity of 3 or more, as depicted below in Figure 2. There was no significant association found between parity and incidence of PIH in these women on Chi-square test (p= 0.44).

Figure 2: Parity of the study population
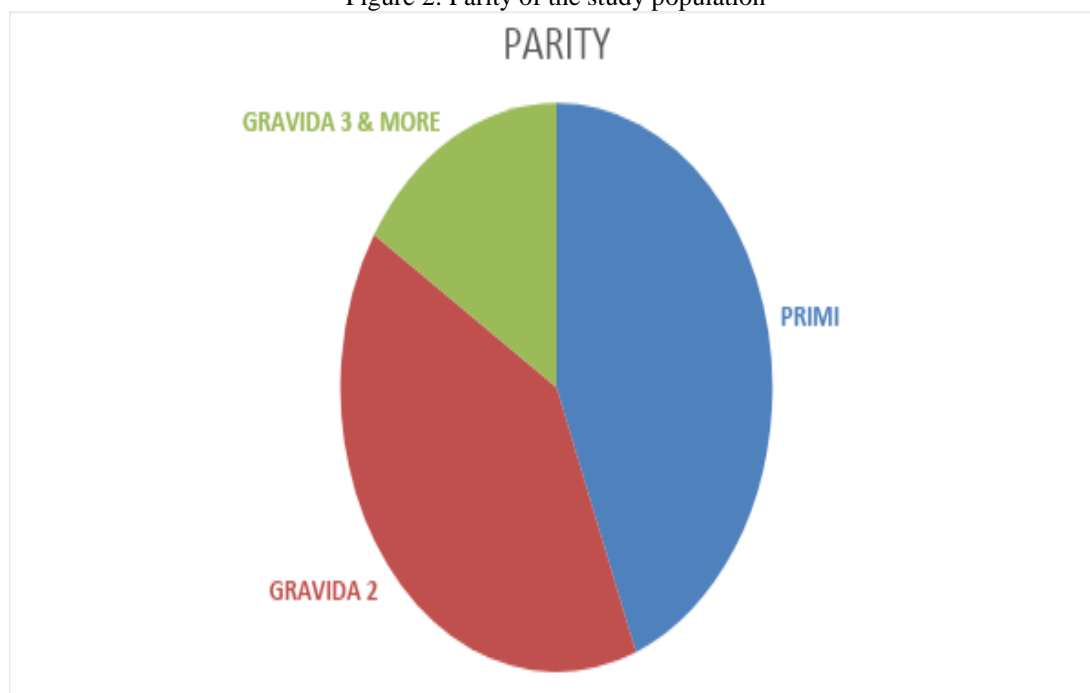
Family history of PIH was given by 52 women (35%) while majority (65%) had no family history of PIH. Out of women with PIH, a higher proportion of women gave positive family history than women without PIH. But this difference was not statistically significant as described below in Table 1.

Table 1: Association between parity and family history on PIH incidence:

PARITY	PIH	NORMOTENSIVE	P value
			0.441
Primi	34	32	
Gravida 2	37	23	
Gravida >/=3	12	12	
FAMILY H/O PIH			P value
	PIH	NORMOTENSIVE	
			0.145
Present	38	19	
Absent	50	48	

P value >0.05; Not significant

The gestational ages of the study population ranged from 14 to 20weeks. Majority of the women belonged to 16 weeks (22%) while the least common presentation was at 19 weeks (5.3%). The distribution of gestational ages of the women is as described below in Table 2.

Table 2: distribution of study population as per gestational age:

GESTATIONAL AGE	NO OF PATIENTS	PERCENTAGE
14 WEEKS	27	18%
15 WEEKS	25	16.70%
16 WEEKS	33	22%
17 WEEKS	22	14.70%
18 WEEKS	24	16%
19 WEEKS	8	5.30%
20 WEEKS	11	7.30%
TOTAL	150	100

BODY MASS INDEX (BMI) and its relation to PIH:

In this study, out of 150 patients, 110 (73%) had BMI within the normal range. The remaining 40 (27%) were overweight (BMI >30kg/m2). However, no significant relation between BMI and PIH was found on bivariate analysis (p=0.67; chi square test). The mean BMI was higher in the PIH group versus the normotensive group but this was not statistically significant as per unpaired t test (p=0.105).

Blood Pressure measurement& Pedal edema:

The Blood Pressure (BP) of the women was assessed during their second trimester and the distribution is as follows in Table 3. Out of 150 patients, only 57 had systolic blood pressure above 140 mm Hg (this includes PIH, mild and severe preeclampsia). The diastolic pressure was high in 67% patients of preeclampsia.

Table3: Distribution of Systolic BP& Diastolic BP

Variables	Elevated		Normal	
	Number	Percent	Number	Percent
Systolic BP	57	38%	93	62%
Diastolic BP	67	45%	83	55%

Out of 150 pregnant women, 66 had pedal edema while 84 did not have pedal edema. However,49/66 presented with PIH.Remaining 17 were normotensive.Hence, there was a higher incidence of PIH in patients with pedal edema (Figure 3). This difference was highly statistically significant as per Chi square test with p value of 0.002. The women who had PIH were 4.2 more likely to present with pedal oedema than those who were normotensive.

Figure 3: Presence of pedal edema in study population:
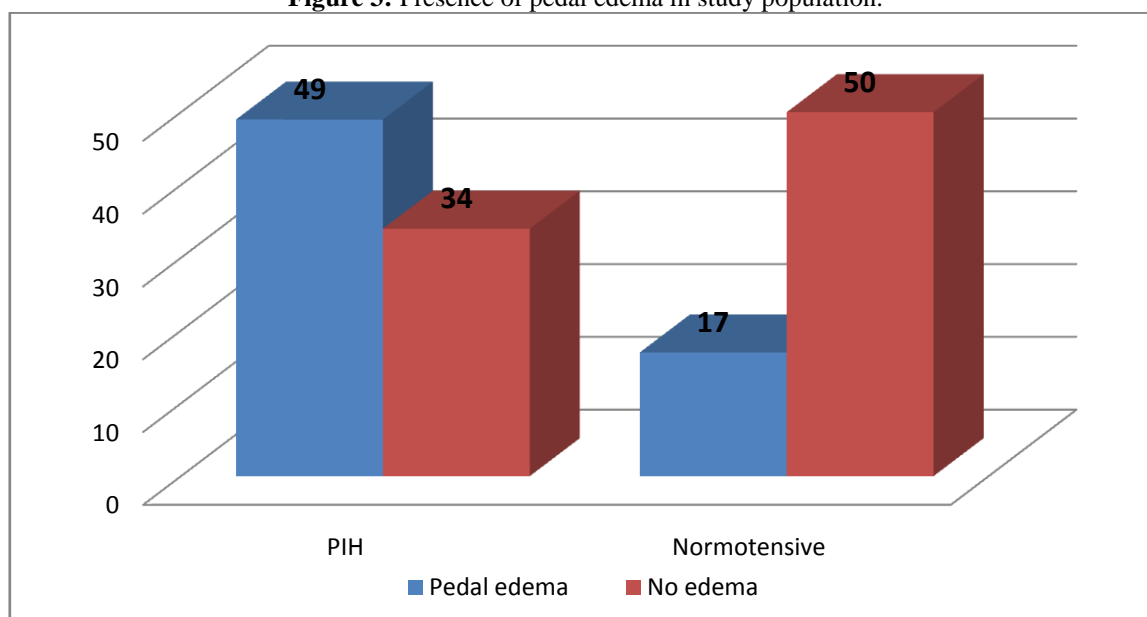
Lipid profile:

The detailed distribution of various parameters included in lipid profile is as given below in Table 4. The total cholesterol level (TC) is normal in 65% of study subjects. It is increased in 46 patients out of 83 PIH patients, whereas majority of the normotensives have normal cholesterol levels. The mean total cholesterol was elevated above normal levels and higher in PIH group than in normotensive group of women. This difference in means is significant at p value <0.013 as per unpaired t test. Also, 95% of patients in the study had normal triglyceride levels (TGL). There was no significant difference between mean TGL values of both groups.

Table 4: Lipid profile of study population:

Lipid Profile	Abnormal		Normal	
	Number	Percent	Number	Percent
TC	52	35%	98	65%
TGL	8	5%	142	95%
HDL	58	39%	92	61%
LDL	75	50%	75	50%
VLDL	90	60%	60	40%

Regarding High Density Lipoproteins (HDL) and their relation to PIH, HDL values were low in 39% of women while it was normal in 61% patients. The mean HDL level was lower in PIH group than in normotensive group of women and this was statistically significant at p value <0.012 as per unpaired t test. The level of LDL is equally high and of normal range in 50% of the patients in this study. The mean LDL level was higher in PIH group than in normotensive group of women, which was statistically significant as per unpaired t test. The levels of Very Low-Density Lipoproteins (VLDL) were also analysed. More than half of patients (60%) had elevated VLDL levels than normal. The mean VLDL level was higher in PIH group than in normotensive group but this difference was not significant (p value 0.734).

Association of lipid profile with PIH status of patients:

The proprtion of PIH patients with elevated total cholesterol levels were higher than those PIH patients with normal levels (44.6% versus 22.3%). This difference in proportions was statistically significant as per chi square test with a p value of 0.005. PIH patients were 2.78 times more likely to have elevated total cholesterol levels in the second trimester than normotensive patients. HDL levels were low in 53% of PIH patients and 44% of normotensive women. However, this difference was not significant as per bivariate analysis (p>0.05). LDL levels were high in 60.2% PIH patients when compared to 37.3% of normotensive women and this was highly statistically significant at p value of 0.005 in chi square analysis. PIH patients were 2.5 times more likely to have elevated LDL levels in second trimester than normotensive patients. A higher number of PIH patients (61.44%) had elevated VLDL levels than normotensive women (58.2%), but this was statistically not significant at p>0.05.

In effect, out of all parameters in the lipid profile done in second trimester, total cholesterol levels and LDL levels were found to be significantly associated with development of PIH status later on in the gestation.

Beta- HCG and its relation to PIH:

The mean betaHCG levels in PIH patients were higher than mean levels for normotensive patients at 14 to 16 weeks of gestation, with more predilections at 16 weeks - mean betaHCG in PIH being 72044.9 versus 58317.4 in normotensives. The mean+/- SD of the beta HCG values is significantly more than normal values in this study(14 to20 weeks) by Unpaired t test (p value is 0.0001).

IV. Discussion

Studies have shown that the circulating concentrations of triglycerides, low density lipoproteins, high density lipoproteins and total cholesterol increased during pregnancy. This is necessary because of the high energy required for the increased cellular proliferation of the maternal uterine enlargement, blood volume expansion and foetal implantation

In this study, there was significant association seen between elevated total cholesterol levels and LDL levels between 14 -20 weeks of gestationand PIH status later on in the gestation. However, though there was higher proportion of women with low HDL levels & high VLDL levels.

Lorentzen et al also concluded that patients in whom serum- free fatty acids and triglycerides were increased before 20 weeks of gestation ,later developed preeclampsia.

Cekemen et al showed that plasma triglycerides &LDL were higher in preeclampsia,whereas HDL levels were lower in preeclamptic patients.

De et al concluded that triglycerides and VLDL were raised and HDL levels decreased inpreeclamptic patients, indicating that an unfavourable lipid profile may forecast preeclampsia in pregnant women.

Vidyabati et al showed that total cholesterol,VLDL,LDL were significantly raised in preeclampsia patients[12].

Our study found a significant association between mean beta HCG above normal values and development of PIH during latter part of gestation. However, Mossink et al and Pouta et al concluded that rise in b-HCG was not observed in gestational hypertension cases but only in severe preeclampsia[13].

Weeks	Amount of HCG(mIU/l) Mean Level	Amount of HCG(mIU/l) Range of values
14weeks	56,600	13,300 – 254,000
15weeks	50,000	13,300 – 254,000
16 weeks	37,500	13,300 – 254.000
17 weeks	21,500	4,060 – 165,400
18 weeks	24,200	4,060 – 165,400
19 weeks	17,400	4,060 – 165,400
20 weeks	15,700	4,060 – 165,400

Parameters	Control	I trimester	II trimester	III trimester
TC	137.4+/- 11.4	176.4+/- 18.1	200+/- 13.4	209.3+/- 12.2
HDL-C	40.1+/- 4.4	43.7+/- 3.2	46.0+/- 3.3	54.0+/- 3.8
LDL-C	88.8+/- 13.5	87.3+/- 6.3	127.7+/- 9.9	161.5+/- 12.6
TG	43.7+/- 6.6	138.7+/- 11.1	168.5+/- 10.4	171.7+/- 10.8

Any elevation in the above lipid profile values in second trimester due to altered lipid metabolism is significantly related to preeclampsia in this study as follows.

V. Conclusion

This study has revealed a significant association between total cholesterol levels, HDL and LDL levels in lipid profile and higher beta HCG values and the incidence of PIH later on during pregnancy. However, studies with larger sample size are required to verify these factors as predictors of PIH among pregnant women.

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