



## A comparative Study of Serum $\beta$ HCG Concentration in Pregnancy Induced Hypertensive and Normotensive Women in 3rd Trimester of Pregnancy

## KEYWORDS

Human chorionic gonadotropin, pregnancy induced hypertension, pre-eclampsia, eclampsia.

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**ABSTRACT** *Background: Hypertensive disorders are among the commonest and unpredictable medical disorders during pregnancy contributing significantly high to maternal and perinatal morbidity and mortality. Human chorionic gonadotropin (hCG) is a glycoprotein that is produced during pregnancy by the developing embryo and later by the syncytio trophoblast of the placenta mainly. hCG is found to be abnormally raised in the urine and serum of pregnant women with pregnancy induced hypertension.*

*Aims: To evaluate the level of serum human chorionic gonadotropin and its correlation with pregnancy induced hypertension and to compare the serum  $\beta$  hCG level between study and control group.*

*Materials and Methods: The study was carried out in the department of Biochemistry, Assam Medical College and Hospital, Dibrugarh. The study includes two group cases and controls. The cases included in the study were taken from Obstetrics and Gynaecology Department, Assam Medical College & Hospital during the period of study. The cases comprised of 50 clinically established cases of Pregnancy Induced Hypertension (PIH) in their third trimester and the control group comprised of 50 cases of normotensive pregnant patients in the third trimester.*

*Results: The differences of mean serum  $\beta$  hCG concentration in cases and in controls were statistically very highly significant ( $p < 0.001$ ). It is also found that there is positive correlation between serum  $\beta$  hCG concentration with Blood pressure levels both systolic and diastolic pressure.*

*Conclusion: Pregnant women with pregnancy induced hypertension have higher level of serum  $\beta$  hCG in comparison to normotensive women.*

## INTRODUCTION

Pregnancy is a physiological stress in which many changes occur in the milieu interior of the body, with more and more stress being laid on the biochemical changes, which occur in the haematopoietic system, during the normal pregnancy and becomes exaggerated in complications of pregnancy like in PIH. Hypertensive disorders are among the commonest and unpredictable medical disorders during pregnancy contributing significantly high to maternal and perinatal morbidity and mortality. It is one of the deadly triad along with hemorrhage and infections. Preeclampsia is the 3rd leading etiology of maternal mortality and can complicate 3-14% of all pregnancies<sup>1</sup>.

In studies carried out in Asian countries of China, Myanmar, Thailand and Vietnam, preeclampsia was seen in 15% in Vietnam to 8.3% in China. Women over the age of 35 years and below the age of 20 years who are pregnant for the first time are potentially at high risk of eclampsia. Socioeconomic status and nutritional standard of a nation and the quality of antenatal care have a remarkable bearing on the incidence of this disease and maternal and perinatal loss<sup>2</sup>.

A number of biochemical and biophysical markers have been proposed as predictors for development of PIH in later pregnancy and the role of Placental hormones being one of them. Human chorionic gonadotropin (hCG) is a glycoprotein that is produced during pregnancy by the developing embryo and later by the syncytio trophoblast of the placenta mainly. Estimation of blood hCG titres

are especially helpful in the diagnosis and management of trophoblastic disease and ectopic pregnancies. Other clinical conditions associated with increased secretion of  $\beta$  hCG are Down's syndrome, neural tube defects, fetal aneuploidy and twin or higher pregnancies. Decreased levels are found in women at risk of carrying fetus with trisomy 18, ectopic pregnancy and blighted ovum. Besides the above diseases and chromosomal anomalies, hCG was also found to be abnormally raised in the urine and serum of pregnant women with pregnancy induced hypertension<sup>3</sup>.

Soheila Akbari *et al* (2009) studied to assess association between preeclampsia and serum level of  $\beta$  human chorionic gonadotropin ( $\beta$ hCG) on 75 pregnant women. Subjects divided into 3 groups: Normotensive pregnancies, mild preeclampsia and severe preeclampsia. Then level of  $\beta$  hCG was measured using Enzyme linked Immunosorbent Assay (ELISA) method. The mean level of  $\beta$  hCG was significantly higher ( $p < 0.001$ ) in severe preeclampsia than normotensive and mild preeclamptic groups. However, there was no significant difference between normotensive and mild preeclamptic groups regarding mean level of  $\beta$  hCG. They concluded that  $\beta$  hCG may be a good indicator for severe preeclampsia but it is not suitable for early diagnosis of the disease<sup>4</sup>.

Dayal Meena *et al* (2011) did a retrospective clinical study of serum markers ( $\beta$  hCG,  $\alpha$  -fetoprotein and inhibin A) as predictors of preeclampsia in 50 antenatal women by ELISA technique and found that 10 women developed preeclampsia (20%). A significant rise of mean serum  $\beta$  hCG was

found in those who developed preeclampsia<sup>5</sup>.

So, keeping the above facts in mind and preeclampsia being much prevalent in our part of the country, this study was done with to evaluate the concentration of serum Beta human Chorionic Gonadotropin ( $\beta$  hCG) and its correlation with pregnancy induced hypertension and to compare the serum  $\beta$  hCG concentration between study and control group.

## MATERIALS AND METHODS

The study was carried out in the department of Biochemistry, Assam Medical College and Hospital, Dibrugarh. The study includes two group cases and controls. The cases included in the study were taken from Obstetrics and Gynaecology Department, AMCH during the period of study. The cases comprised of 50 clinically established cases of Pregnancy Induced Hypertension (PIH) in their third trimester and the control group comprised of 50 cases of normotensive pregnant patients in the third trimester.

## AIMS

- 1) To evaluate the level of serum human chorionic gonadotropin and its correlation with pregnancy induced hypertension.
- 2) To compare the serum  $\beta$  hCG level between study and control group.

**Inclusion criteria:** Pregnant woman with systolic blood pressure of at least 140mmHg with a >30 mmHg rise and /or diastolic blood pressure at least 90mmHg with rise of >15 mmHg occurring on two or more occasions after 24weeks of gestation was included in the study.

## Exclusion criteria:

- 1) Woman with hypertension diagnosed before 24weeks of gestation.
- 2) Woman with diabetes mellitus.
- 3) Multiple pregnancies
- 4) Ultrasound proved congenital malformation.

All the patients in the study was subjected to detail history regarding age, parity, height, pre pregnancy weight and weight at the time of blood collection. Maternal family history of preeclampsia, past obstetric history, past medical history, smoking habit, medical histories of first degree family members and physical activity during pregnancy was noted. Systemic examination with special reference to oedema, blood pressure and gestational week was carried out and routine antenatal investigation was done.

## Blood sampling and preparation of serum Beta hCG

The venepuncture was done in the cubital fossa. About 2 ml of blood was drawn using perfectly dry and sterile syringe. The sample is allowed to clot for thirty minutes at room temperature. Samples were centrifuged at 5000 rpm for 10 minutes as soon as after formation of the clot. The supernatant clear serum was then pipetted out using dry piston pipettes with disposable tips. The samples were analysed on the same day.

**Principle of the test:** The BRIA MAGII is a sandwich immune-radiometric assay for hCG. In this method, two antibodies generated against different epitopes of the hCG antigen are used. One antibody is coupled to magnetisable cellulose and the other antibody is radiolabelled with <sup>125</sup>I. hCG antigen from sample or standard binds simultaneously to the anti hCG antibody coupled magnetisable cellulose as well as radio labelled anti-hCG antibody. The

'bound complex' is separated from the 'free' radiolabelled antibody using antibody coupled magnetisable cellulose particles using a magnetic rack. The radioactivity in the bound fraction is directly related to the concentration of the antigen and quantitated using gamma counter calibrated for <sup>125</sup>I.<sup>6</sup>

**Statistical analysis:** The present study is a randomised case control study and results were expressed as Arithmetic Mean  $\pm$  Standard Deviations (SD) and analysed by unpaired Student's t-test on continuous measurements and results on categorical measurements were presented in Number (%). Pearson coefficient of correlation ( $r$ ) was used to find out the correlation between Blood pressure and the serum  $\beta$  hCG concentration.

**P-Value:**  $p < 0.05$  is considered significant,  $p < 0.01$  is considered highly significant,  $p < 0.001$  is considered very highly significant,  $p > 0.05$  is considered not significant.

**Coefficient of Correlation:** To see the correlation between two variables coefficient of correlation ( $r$ ) was applied. The correlation coefficient ' $r$ ' tends to lie between  $-1.0$  and  $+1.0$ . If  $r$  is near  $+1$ , it indicates a strong positive correlation i.e. when one variable increases, the other also increases. A value in minus side indicates inverse correlation, i.e. when one variable increases, the other decreases. If  $r = 0$ , it indicates no correlation.

The Mean  $\pm$  S.D, Median and Range of the  $\beta$  hCG values obtained for normotensive group of patients was calculated. The serum  $\beta$  hCG values obtained for the hypertensive group of patients were compared with the median level of serum  $\beta$  hCG in the normotensive group the outcome of pregnancy noted. The results were expressed as Multiple of Median (MoM) for normal pregnancy.

## RESULTS

In the present study it is found that the mean serum  $\beta$  hCG concentration in cases was  $42.94 \pm 18.91$  ranging from 15-78 IU/mL and in controls was  $24.18 \pm 11.34$  ranging from 10-49 IU/mL and it was statistically very highly significant ( $p < 0.001$ ). Thus, the serum  $\beta$  hCG concentration increases in PIH patients.

**TABLE 1: AGE WISE DISTRIBUTION OF MEAN  $\beta$  hCG CONCENTRATIONS OF PIH PATIENTS AND NORMAL PREGNANT WOMEN**

Age Group (years)	$\beta$ -hCG (IU/mL)			
	PIH patients		Normal pregnant women	
	Range	Mean $\pm$ SD	Range	Mean $\pm$ SD
16-20	18-78	<b>45.2 <math>\pm</math> 21.82</b>	11-46	<b>22.44 <math>\pm</math> 13.49</b>
21-25	21-76	<b>42.21 <math>\pm</math> 18.73</b>	10-42	<b>21.65 <math>\pm</math> 9.45</b>
26-30	15-65	<b>36.07 <math>\pm</math> 16.00</b>	10-49	<b>28.21 <math>\pm</math> 12.82</b>
31-35	16-76	<b>49.92 <math>\pm</math> 19.18</b>	10-43	<b>24.4 <math>\pm</math> 10.08</b>
Total	15-78	<b>42.94 <math>\pm</math> 18.91</b>	10-49	<b>24.18 <math>\pm</math> 11.34</b>

It is also found that there is positive correlation between serum  $\beta$  hCG concentration with Blood pressure levels both systolic and diastolic pressure with Pearson Correlation co-efficient " $r$ " values 0.64 for systolic pressure and 0.62 for diastolic pressure.

**TABLE-2: PEARSON COEFFICIENT OF CORRELATION AND P-VALUE OF BLOOD PRESSURE WITH SERUM  $\beta$ -hCG CONCENTRATION OF PIH PATIENTS AND NORMAL PREGNANT WOMEN**

BLOOD PRESSURE	$\beta$ -hCG			
	PIH patients		Normal pregnant women	
	r value	p value	r value	p value
SYSTOLIC	0.64	<0.0001	0.06	0.68
DIASTOLIC	0.62	<0.0001	0.17	0.24

## DISCUSSION

In the 50 hypertensive cases which were studied, the maximum number of 16 cases (32%) belonged to the 16-20 years age group and 8 (16%) were from the age group of 20-25 years. After combining both the groups, we get the highest number of 26 cases (48%) were found 16-25 years age group. Similar findings were also found by Farnoosh et al (2012)<sup>7</sup> who recorded maximum incidence in age group 15-25 age group. In the age group of  $\leq 20$  years there were 16 hypertensive cases which constitute 32% of total number of participants. In 31-35 years age group 32% were hypertensive. This can be attributed to the fact that increased episodes of preeclampsia occurs in extremes of maternal age.

In the present study there were 32 (64%) who were primigravidas and 18(32%) were multigravidas in the hypertensive study group. Surraya H et al (2010)<sup>8</sup>, D.S. Seidman et al (1990)<sup>9</sup> also found in their study that hypertensive disorders of pregnancy affects mainly the first pregnancy.

Analysis of serum  $\beta$  hCG in the study participants the mean serum  $\beta$  hCG values for the patients in PIH (42.94 IU/mL) was significantly higher ( $P < 0.0001$ ) than found in the normotensive group (24.18 IU/mL). Pearson's coefficient between blood pressure and serum  $\beta$  hCG of hypertensive group shows positive correlation and are statistically very highly significant. Similar results were observed by, Basirat Z et al (2006)<sup>10</sup>, Yousefnejad et al (2008)<sup>11</sup> and Vidyabati RK et al (2010)<sup>12</sup> Gurmandeep K et al (2012)<sup>13</sup>

## CONCLUSION

From the present study it can be concluded that pregnant women with pregnancy induced hypertension have higher level of serum  $\beta$  hCG in comparison to normotensive women. Serial estimation of serum  $\beta$  hCG can very well be used as biochemical markers of the disease and also can be used in better management of established cases of eclampsia or preeclampsia.

The metabolic disorder that occurs in pregnancies with pregnancy induced hypertension may be important and may be a predictor of future systemic diseases in these women. Therefore more studies are warranted into the implications of these predictors of hypertension during pregnancy.

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