



## Maternal serum beta-human chorionic gonadotropin levels as a predictor for pregnancy induced hypertension

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### Abstract

Pregnancy Induced Hypertension and its sequel are severe complications of pregnancy. The prognostic significance of high levels of serum free  $\beta$ -hCG in early pregnancy for subsequent obstetric and perinatal risks is still poorly documented. The primary aim of the present study was to investigate whether an isolated second trimester free  $\beta$ -hCG level in pregnancies could serve as a predictor of various pregnancy complications or adverse pregnancy outcome. The present results showed that the serum  $\beta$ -hCG levels were progressively increasing and were found to be significantly different between 3 groups of PIH in accordance with progressive increase of diastolic Blood Pressure. It is evident from the present study that the serum  $\beta$ -hCG levels were significantly higher and significantly correlated with increased risk of PIH in women with increased  $\beta$ -hCG levels in the hypertensive group as compared to those in the normotensive group; which indicates the strong correlation between higher serum  $\beta$ -hCG levels and development of PIH later on during pregnancy. Hence, the  $\beta$ -hCG levels can be considered as good predictor of PIH in early gestational age. It can be concluded that the maternal serum  $\beta$ -hCG levels can act as potential markers for early detection of PIH, thereby helping in initiating early treatment to minimize and/or avoid the complications of PIH.

**Keywords:** pregnancy Induced hypertension, free  $\beta$ -HCG, predictor, potential markers

### Introduction

Since years, there has been a search for an early predictor of Pregnancy Induced Hypertension (PIH), so that special care can be given to these patients [1]. Pregnancy Induced Hypertension (PIH) in particular, pre-eclampsia/eclampsia remain important causes of maternal mortality and morbidity worldwide [2]. A number of clinical studies have supported the possible association of unexplained elevated maternal serum (MS) human Chorionic Gonadotropin (hCG) in the second trimester with later pregnancy disorders. Pregnancy Induced Hypertension, Gestational Hypertension or Transient Hypertension of pregnancy are terms used to describe new hypertension which appears after mid-term (20 weeks) and resolves within 10 days postpartum without other symptoms of pre-eclampsia in a previously normotensive woman.

In pregnancy, the placenta forms especially large quantities of Human Chorionic Gonadotropin which is essential to a normal pregnancy and more so in Pregnancy Induced Hypertension. Elevated serum  $\beta$ -hCG in the second trimester has repeatedly been shown to be significantly associated with later PIH. The patients with abnormal  $\beta$ -hCG levels and in very few reports, the free  $\beta$ -subunit (free  $\beta$ -hCG) were reported as possible predictors of pre-eclampsia [3, 4, 5], pregnancy-induced hypertension [6, 7], spontaneous miscarriage, low birth weight,

preterm delivery [3, 6, 8] and intra uterine growth retardation (IUGR) [4, 8].

Pregnancy Induced Hypertension and its sequel are severe complications of pregnancy. The prognostic significance of abnormal free  $\beta$ -hCG serum levels in early pregnancy for subsequent obstetric and perinatal risks is still poorly documented. Therefore, the estimation of serum  $\beta$ -hCG may be helpful in the early detection of PIH later in the same pregnancy, in turn helps in early treatment by preventing complications of PIH. Hence, this will bring down the maternal and foetal morbidity and mortality.

Therefore, the present study was conducted to understand and investigate further the association of selected physical and biochemical parameters among pregnant women with PIH subjects (Experimental group) and without hypertension (Normotensive / Control group). To achieve this, biochemical parameters like maternal serum  $\beta$ -hCG, and the physical parameters like Gestational age, Systolic and Diastolic blood pressures of the subjects were estimated both in normotensive pregnant women and PIH women.

The study was aimed at estimation of the level of maternal serum  $\beta$ -hCG which included 18 normotensive women (control group) and 36 PIH women (Experimental group). Experimental group was further divided into group-1, group-2

and group-3 based on the degree of diastolic blood pressure of 90-95, 96-100 and >100 mmHg respectively.

**Materials and Methods**

The study was carried out in the Department of Biochemistry, Gandhi Medical College, Secunderabad, Telangana. The cases for the present study were selected from the antenatal outpatient Department of Gandhi Hospital, Secunderabad according to specific criteria like women with age group between 18-24 years, primigravida with known last menstrual period and gestational age between 20-30 weeks. If menstrual history and examination findings were not correlating, ultrasonography was done to find out the exact period of gestation. Those with known hypertension, diabetes mellitus, multiple pregnancy and ultrasound proven congenital malformations in the fetus were excluded. Ethical Committee approval was taken from the Institutional Ethical Committee Board.

All 54 women included in the present study were subjected to a detailed history taking, systematic examination, obstetric examination and routine antenatal investigations. Among 54 women, 36 were Pregnancy Induced Hypertensive (B.P. >140/90 mmHg) who were considered as experimental group and remaining 18 were normotensive (B.P. <140/90 mmHg) taken as controls. The experimental group was further categorized into three groups, having 12 women in each group, based on the degree of hypertension. The Group-1 was having diastolic blood pressure of 90 to 95 mmHg, the Group-2 with diastolic blood pressure of 96 to 100 mmHg and the

Group-3 having diastolic blood pressure more than 100 mmHg.

**Collection of samples**

Under strict aseptic conditions, 3 ml of venous whole blood sample was collected from each subject in a plain, dry and properly labelled bottle. Precautions were taken to prevent haemolysis. Samples were brought to Clinical Biochemistry Laboratory, Gandhi Hospital and centrifuged after clotting and retraction at room temperature. Clear serum was collected and subsequently analysed for the parameter serum β-human Chorionic Gonadotropin.

**Statistical analysis**

The data was subjected to descriptive statistical analysis to find out Means and Standard Deviation values and One Way Analysis of Variance (One Way ANOVA) to decipher the intra and inter group variations of the study subjects from both control and experimental groups. In addition, the correlation coefficients were also used for all the groups studied to understand the extent of relationships between the important variables pertaining to physical and biochemical parameters like gestational age, systole, diastole and serum β-hCG. P<0.05 and P<0.01 were considered statistically significant.

**Results**

The descriptive statistics (Mean and SD) for gestational age, systole, diastole, serum hCG of control (n=18) and experimental (n=36) group are presented in Table 1.

**Table 1:** Descriptive Statistics of Individual Clinical Data of Control Group (n=18) and Experimental group (n=36)

Parameter	Control Group Mean ± Std.	Experimental Group Mean ± Std.			
		GROUP-I (n=12)	GROUP-II (n=12)	GROUP-III (n=12)	TOTAL (n=36)
Gest. Age (Weeks)	26.89 ± 4.1	23.0 ± 1.60	27.3 ± 0.98	31.2 ± 1.03	27.17 ± 3.59
Diastole (mmHg)	76.67 ± 5.8	92.3 ± 1.67	96.7 ± 0.98	101.8 ± 1.80	96.9 ± 4.21
Systole (mmHg)	121.67 ± 7.5	142.0 ± 2.09	142.7 ± 2.15	147.2 ± 2.76	143.9 ± 3.26
hCG (mIU/ml)	440.94 ± 27.3	487.3 ± 12.34	516.4 ± 4.46	525.8 ± 5.26	509.8 ± 18.43

Gest. Age- Gestational age; hCG- serum β-hCG.

**Table 2:** Correlation coefficients of physical and biochemical parameters in control group (n=18) and experimental group (n=36)

Parameter	Control Group (n=18)				Experimental group (n=36)			
	G Age	Systole	Diastole	hCG	G Age	Systole	Diastole	hCG
G Age	1.000	.551**	.849**	.909**	1.000	.738**	.961**	.942**
Systole		1.000	.942**	.930**		1.000	.770**	.669**
Diastole			1.000	.965**			1.000	.910**
hCG				1.000				1.000

G Age- Gestational age; hCG- serum β-hCG. \*.Correlation is significant at (P < 0.05), \*\*.Correlation is significant at (P < 0.01), NS = Not significant.

Considering the blood pressure of control group, the mean systole and diastole was observed to be 121.67±7.46 and 76.7±5.86 respectively. Whereas, mean values of experimental PIH group were observed to be 143.9±3.26 and 96.9±4.21 respectively. Hence, the control group can be considered as normotensive. On the other hand, mean value of the biochemical parameter serum β-hCG was recorded to be 440.94±27.28 in the control group, while 509.83±18.43 in the experimental PIH group.

The correlation coefficient pertaining to physical and biochemical parameters of the control group and experimental group are presented in Table 2. Systole significantly correlated

with diastole and serum β-hCG (P<0.01) in the control group. Whereas, significantly correlated with gestational age, diastole and the biochemical parameter serum β-hCG (P < 0.01) in the PIH group. On the other hand, diastole was observed to be significantly correlated with systole and β-hCG (P<0.01) in the control group; whereas, significantly correlated with gestation age, systole and the biochemical parameter β-hCG (P<0.01) in the PIH group.

Further, it was observed that hCG was significantly correlated with systole and diastole (P < 0.01) in the control group. Whereas, significantly correlated with the biochemical parameter studied (P<0.01) in the experimental PIH group.

**Table 3:** One Way ANOVA of physical and biochemical parameters in Experimental group (n=36)

Parameter	Sum of squares	df	Mean square	F	Sig.
Gest. Age (Weeks)	400.667	2	200.333	131.344	.000
Diastole (mmHg)	542.889	2	271.444	116.333	.000
Systole (mmHg)	189.556	2	94.778	17.154	.000
hCG (mIU/ml)	9690.752	2	4845.376	72678	.000

**Table 4:** Multiple comparisons of different parameters studied in experimental group

Dependent variable	Groups	Mean difference	Std. Error	Sig.
Gestational Age (Weeks)	1 & 2	-4.33*	.504	.000
	1 & 3	-8.17*		.000
	2 & 3	-3.83*		.000
Diastole (mmHg)	1 & 2	-4.33*	.624	.000
	1 & 3	-9.50*		.000
	2 & 3	-5.17*		.000
Systole (mmHg)	1 & 2	NS	.960	NS
	1 & 3	-5.17*		.000
	2 & 3	-4.50*		.000
hCG (mIU/ml)	1 & 2	-29.092*	3.333	.000
	1 & 3	-38.558*		.000
	2 & 3	-9.467*		.008

**Table 5:** Comparison between controls Vs PIH subjects

Parameters	F	Sig.	T	df	Sig (2-tailed)
Diastole	4.195	.046	14.599	52	.000
Systole	19.749	.000	15.329	52	.000
hCG	5.963	.018	10.982	52	.000

**Table 6:** Comparison between Controls and Group I, Group II and Group III of PIH subjects

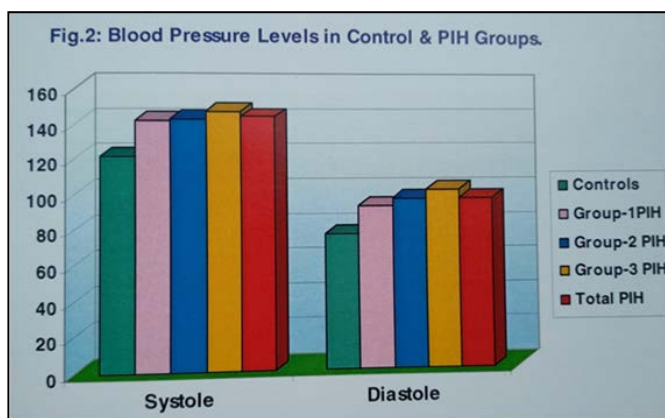
Parameters	Group I		Group II		Group III	
	F	Sig. (2-tailed)	F	Sig. (2-tailed)	F	Sig. (2-tailed)
Diastole	17.381	.000	23.593	.000	16.042	.000
Systole	14.446	.000	13.834	.000	11.618	.000
hCG	10.001	.000	24.275	.000	22.325	.000

The data presented in Table 3 shows One Way Analysis of Variance of physical and biochemical parameters in the experimental group was observed that all the parameters (systole, diastole, serum β-hCG) were found to be significantly different between the three groups of PIH (P<0.001).

Multiple comparisons of different parameters studied in the experimental group showed significant differences in the mean difference of the parameter like serum β-hCG (in group 1 & 2; group 1 & 3 (P<0.001) and group 2 & 3 (P<0.05), diastole (P<0.001), gestational age (P<0.001) in all the three groups. Considering the mean difference among the three groups of PIH with regard to systole, highly significant difference was observed between the groups 1 and 3 and 2 and 3 (P<0.001). However, no significant difference was observed in groups 1 and 2 (Table 4).

The data of comparisons between control and total experimental group of PIH women (Table 5) showed a significant increase in mean systole (P<0.01), diastole (P<0.05), serum β-hCG levels (P<0.05) in experimental group when compared with the control group. Statistical analysis on

comparison between controls and individual group of PIH women (groups 1 to 3 of experimental subjects) showed a significant increase in mean values of systole, diastole and serum β-hCG levels (P<0.001) in all the three groups of PIH (Figures 1 & 2) when compared to control group (Table 6).



**Fig 1:** Blood pressure levels in control and PIH Groups

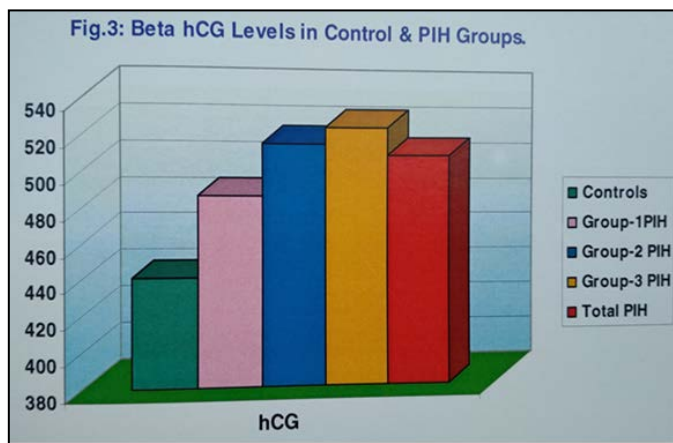


Fig 2:  $\beta$ -hCG levels in control and PIH groups

### Discussion

The primary aim of the present study was to investigate whether an isolated second trimester free  $\beta$ -hCG ( $\geq 2.0$  Multiple levels of Median MoM) serum levels in pregnancies could serve as a predictor of various pregnancy complications or adverse pregnancy outcome.

In the present study, it was observed that the biochemical parameter serum  $\beta$ -hCG significantly increased in experimental group compared to control group subjects [9]. Reported that the increased risk of development of PIH is associated with increased levels of serum  $\beta$ -hCG in second trimester.

The present results showed that the serum  $\beta$ -hCG levels were progressively increasing and were found to be significantly different between 3 groups of PIH in accordance with progressive increase of diastolic Blood Pressure.

Elevated serum  $\beta$ -hCG in second trimester has repeatedly been shown to be significantly associated with PIH [9]. It has been reported that women with markedly elevated maternal serum  $\beta$ -hCG levels has significantly increased risks of having spontaneous miscarriage, preterm delivery and IUGR [10, 11].

The estimation of serum  $\beta$ -hCG levels may be helpful in both the early detection of PIH and to initiate necessary treatment to avoid associated complications [12]. This will perhaps bring down the maternal and foetal morbidity and mortality [1, 11]. reported from their study that all those who developed PIH had higher levels of serum  $\beta$ -hCG confirmed 100% correlation between high serum  $\beta$ -hCG levels and development of PIH which in turn significantly increased risks of having poor/adverse pregnancy outcomes (Spontaneous miscarriage, Intra Uterine Growth Retardation (IUGR) and Preterm delivery), where the magnitude of risk correlates with the levels of  $\beta$ -hCG. The present study results indicate that  $\beta$ -hCG determination may have value in the prediction of Pre-eclampsia / PIH [13, 14].

reports provide some evidence that the  $\beta$ -hCG is elevated not only in established PIH but perhaps even before the clinical signs of the disease appears.

It is evident from the present study that the serum  $\beta$ -hCG levels were significantly higher (487 to 50 as IU/ml) and significantly correlated with increased risk of PIH in women with increased  $\beta$ -hCG levels in the hypertensive group as

compared to those in the normotensive group; which indicates the strong correlation between higher serum  $\beta$ -hCG levels and development of PIH later on during pregnancy. It is evident from the present study that by having significant positive correlation with gestational age, systolic and diastolic blood pressure. This observation was in tune with the studies reported by [1, 12] and hence, the serum  $\beta$ -hCG levels can be considered as good predictor of PIH in early gestational age.

On the other hand [11, 15], have also reported that there is a positive relationship between the PIH and increased  $\beta$ -hCG levels with increased risk of most pregnancy complications and outcome.

It seems reasonable to presume from the results of the present experimental study that the increased synthesis and secretion of free  $\beta$ -hCG is associated with immunosuppressive activity of hCG which helps to initiate early treatment so as to minimize and/or avoid adverse effects of PIH.

### Conclusion

It can be concluded that the maternal serum  $\beta$ -hCG levels can act as potential markers for early detection of PIH, thereby helping in initiating early treatment to minimize and or avoid the complications of PIH.

Thus, all the patients with high levels of serum free  $\beta$ -hCG in second trimester should be informed about the possible association between the biochemical findings and subsequent PIH (Pre-eclampsia). Furthermore, with more extensive investigations and better knowledge of the different risk factors, we can intervene on time with appropriate Obstetric management and possible therapeutic interventions for these pregnancies.

It is also opined further studies are needed on larger population to understand the detailed mechanisms/interactions between the biochemical molecule and development of PIH.

### References

1. Jaiswar SP, Nisha RM. Maternal Serum Human Chorionic Gonadotropin as a predictor for Pregnancy Induced Hypertension. J Obstet Gynecol Ind. 2003; 53:543-545.
2. Chamberlain G, Phillips E, Howlett B, Masters K. British births 1970, Obstetric care, 7. Heinemann, London. 1978; 2:80-100.
3. Wenstrom KD, Owen J, Boots LR, Du Bard MB. Elevated second-trimester human chorionic gonadotropin levels in association with poor pregnancy outcome. Am J Obstet Gynecol. 1994; 171:1038-1041.
4. Benn PA, Horne D, Briganti S, Rodis JF, Clive JM. Elevated second-trimester maternal serum hCG alone or in combination with elevated alpha-fetoprotein. Obstet Gynaecol. 1996; 87:217-222.
5. Fejgin MD, Kedar I, Amiel A, Ben-Tovim T, Chen R, Petel Y. Elevated hCG as an isolated finding during the second trimester biochemical screen: Genetic, ultrasonic, and perinatal significance. Prenat Diagn. 1997; 17:1027-1031.
6. Gonen R, Perez R, David M, Dar H, Merksamer R, Sharf M. The association between unexplained second-trimester maternal serum hCG elevation and pregnancy complications. Obstet Gynaecol. 1992; 80:83-85.

7. Palacio M, Jaumiaux E, Kingdom I, Sheldrake A, Rodeck CH. Perinatal outcome in pregnancies with a positive serum screening for Down's syndrome due to elevated levels of free beta subunit of hCG. *Ultrasound Obstet Gynaecol.* 1999; 13:58-62.
8. Lieppman RE, Williams MA, Cheng EY, Resta R, Zingheim R, Hickok DE, *et al.* An association between elevated levels of human chorionic gonadotropin in the midtrimester and adverse outcome. *Am J Obstet Gynaecol.* 1993; 168:1852-1856.
9. Sorensen TK, Williams MA, Zingheim RW, Clement SJ, Hickok DE. Elevated second-trimester human chorionic gonadotropin and subsequent pregnancy-induced hypertension. *Am J Obstet Gynaecol.* 1993; 169:834-8.
10. Walton DL, Norem, CT, Schen EJ, Ray CT, Colby CJ. Second Trimester Serum Chorionic Gonadotropin concentrations and complications and outcome of pregnancy. *N. Engl. J Med* 1999; 341:2033-2038.
11. Nathalie L, David C, John K, Tianhua. Association between second trimester isolated high maternal serum human chorionic gonadotropin levels and obstetric complications in singleton and twin pregnancies. *Am J Obstet Gynaecol.* 2003; 188:1354-1359.
12. Yaron Y, Maichele Cherry M, Krameer RL. Second trimester maternal serum marker screening: Maternal serum  $\alpha$ -fetoprotein,  $\beta$ -human chorionic gonadotropin, estriol and their various combinations as predictors of pregnancy outcome. 1999; 181:968-972.
13. Crosignani PG, Trojsi L, Attanasio AEM, Lombroso Finzi GC. Value of hCG and hCS measurement in clinical practice. *Obstet Gynaecol.* 1974; 44:673-681.
14. Said ME, Campbell DM, Azzam ME. Beta-human Chorionic Gonadotropin levels before and after the development of preeclampsia. *Br. J Obstet Gynaecol.* 1984; 9:772-775.
15. Sujata Chandra S, Heather Scott, Linda Dodds, Carolyn Watts, Claire Blight, Michiel Van Den Hof. Unexplained elevated maternal serum alpha-fetoprotein and/or human chorionic gonadotropin and the risk of adverse outcomes. *Amer J Obstet and Gynaecol.* 2003; 189:775-81.