A Study of Relationship Between Second Trimester Maternal Serum Beta Human Chorionic Gonadotropin and Hypertensive Disorder of Pregnancy

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Abstract

Objective: To test the hypothesis that women with high serum beta HCG levels in early second trimester (13-20 weeks) are at higher risk of developing hypertensive disorder of pregnancy and to compare beta HCG levels between normotensive and hypertensive pregnant women. *Method:* This prospective study was carried out in Department of Obstetrics & Gynaecology, GMCH, Udaipur from January 2017 to January 2018. Estimation of serum beta HCG level was done by enzyme linked fluorescence immunoassay. Followed up in antenatal clinic examined 4 weekly till delivery to note the development of hypertension and its complication. At every visit, blood pressure was recorded and urine was examined for albumin. PIH (pregnancy induced hypertension) included gestational hypertension and preeclampsia. *Results:* Incidence of PIH was 14% (28 out of 200 patients). Age, parity & socioeconomic status has no relation to development of PIH. There is significant difference in SBP & DBP between normotensive and PIH at the time of delivery (mean difference in SBP was 37.00 mmHg & DBP was 22.4 mmHg). Mean beta HCG in normotensive patients was 27500.10 mIU/ml and 45027.43 mIU/ml in PIH patients. 6.5% patients had beta HCG between 60,000 mIU/ml to 90,000 mIU/ml & among this 84.61% patients developed PIH. 92.50% patient had MOM of beta HCG <2. Among these 9.18% patients developed PIH. 7.50% patients had MOM of beta HCG >2, out of these 73.33% patients developed PIH. Sensitivity of beta HCG as predictor of PIH is 73.33% and specificity is 90.81%. *Conclusion:* Thus we can say that serum beta HCG level can be used as predictor of PIH as beta HCG is also already done as triple marker test in routine ANC. So it can be used without any extra burden on patient.

Keywords: Beta-HCG; Normotensive; PIH; MOM.

Introduction

Motherhood is nature's greatest gift to women. Having a baby is a joyous experience for all women. But sometimes this gift is wrapped with some complications which can endanger her life. Hypertensive disorders represent the most common medical complication of pregnancy affecting between 7-15% of all gestations and account for approximately a quarter of all antenatal admissions [1]. According to World Health Organization's (WHO) systemic review on

maternal mortality world-wide, hypertensive disease remains a leading cause of direct maternal mortality. Together they are one member of the deadly tried along with haemorrhage and infection that contributes greatly to maternal morbidity and mortality [2]. Of these disorders, the preeclampsia syndrome, either alone or superimposed on chronic hypertension, is the most dangerous.

The American College of Obstetricians and Gynaecologists (ACOG) has classified hypertensive disorder of pregnancy in four categories:

1.   Gestational hypertension.

2.   Preeclampsia-eclampsia.

3.   Chronic hypertension.

4.   Chronic hypertension with superimposed preeclampsia [3].

With increasing severity of the disease many complication occur in the mother like pre eclampsia, eclampsia, abruption, preterm labour, HELLP syndrome, DIC, PPH & renal failure [4]. The fetus of preeclamptic mothers have a significantly higher incidence of IUGR, IUD, birth asphyxia, neonatal death.

Although overt PIH rarely appears until third trimester, there are many studies which show that the disease begins early in pregnancy. The underlying patho-physiological mechanism responsible for the disease process seems to appear between 8 to 18 weeks of gestation which makes it logical to search for predictive indicators [5].

Numerous clinical, biochemical and biophysical tests in early or mid-pregnancy have been proposed for the prediction of preeclampsia. These predictive tests are related to placental perfusion and vascular response (mean arterial pressure, intravenous infusion of angiotensin-II, roll over test, 24-hour ambulatory BP monitoring), fetoplacental unit endocrinology (alpha-fetoprotein, inhibin A), renal function (serum uric acid, microalbuminuria), endothelial function and endothelial-platelet interaction (platelet count, antiphospholipid antibodies, homocysteine), and circulating anti-angiogenic factors [6].

At present, there is no single screening test that can be considered reliable and cost effective for predicting preeclampsia.

Now it is proved that gestational hypertension is mainly due to endothelial dysfunction and vasospasm. Endothelial dysfunction is due to oxidative stress and the inflammatory mediators. Vasospasm results from the imbalance of vasodilators (PGI_2, NO) and vasoconstrictors

(angiotensin-II, TXA_2 Endothelin-1). Hsu et al. hypothesized that during mid-trimester, immunological changes occurs in the trophoblasts, resulting in secretory response, which is seen as a rise in beta HCG levels [7].

The human chorionic gonadotropin (HCG) is produced by syncytiotrophoblast cells of placenta. It increases rapidly doubling every 2 days, with maximal level being attend at about 8-10 weeks of gestation. Peak level reach about 100,000 mIU/ml between 60th and 80th day and a nadir is reached by about 20th weeks [8]. Plasma level is maintains at this lower level for the remainder of pregnancy. It reflects proper placental function. Hence, if it remains high then it is a sign of placental dysfunction which may lead to gestational hypertension. Present study was aimed to find out the utility of beta HCG levels determined in early second trimester to predict the occurrence of gestational hypertension.

Aim and Objectives

•   To test the hypothesis that women with high serum beta HCG levels in early second trimester (13-20 weeks) are at higher risk of developing hypertensive disorder of pregnancy.

•   To compare beta HCG levels between normotensive and hypertensive pregnant women.

•   To know the incidence of PIH at GMCH.

Material And Methods

This prospective hospital based study was conducted on patients visiting during the period January 2017 to January 2018. Antenatal cases who visited GMCH antenatal OPD (at 13-20 weeks) in the Department of Obstetrics and Gynaecology, Geetanjali Hospital, Udaipur.

Inclusion Criteria

•   Non- hypertensive pregnant women with gestational age between 13-20 weeks according to last menstrual period or first trimester USG.

Exclusion Criteria

•   Chronic hypertension

•   Pre-existing renal, cardiac and vascular

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diseases

- Diabetes mellitus
- Molar pregnancy
- Twin pregnancy
- Systemic lupus erythematosus
- Patient with smoking habits

Methods

All the antenatal women who visited GMCH at 13–20 weeks of pregnancy were subjected to detailed history regarding age, parity, socioeconomic status, past obstetric history, medical history, and family history.

Detailed obstetric and systemic examination was done. Height, weight, blood pressure were measured. All patients were critically evaluated for gestational age depending upon their last menstrual period, regularity of menstrual cycle, clinical examination detail, or early ultrasound scan.

Routine antenatal investigation (Blood group, CBC, BT, CT, PT/INR, blood sugar, TSH, urea, creatinine, urine routine, and maternal infection like VDRL, HIV, & HbsAg) was done.

Estimation of serum beta HCG level was done by enzyme linked fluorescence immunoassay. The cases were followed up in antenatal clinic and were examined 4 weekly till 28 weeks, fortnightly upto 34 weeks and thereafter weekly till delivery to note the development of hypertension and its complication. At every visit, blood pressure was recorded and urine was examined for albumin. PIH (pregnancy induced hypertension) 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 patients who developed preeclampsia were followed till 6 weeks after delivery.

Assessment of serum beta HCG and its predictability for development of pregnancy induced hypertension was done.

Data analysis and interpretation

The data were analysed and interpreted according to the type of variables. The continuous variables were analysed in terms of mean and interpreted by student's t test. The discontinuous variables were described in terms of percentages and interpreted by $\chi 2$ (Chi-square) test. Correlation between serum ß-HCG and blood pressures were studied to see whether the two variables exhibit any linear correlation. The level of significance was fixed as 5% and the P-values less than or equal to 0.05 ($p \leq 0.05$) were considered as statistically significant.

Results

Equally distributed PIH and Normotensive mothers in respect to age were selected at the time of booking. The mean age of normal was 26.59 ± 3.47 years and that of PIH mothers was 26.07 ± 2.47 years. The difference was statistically not significant ($p > 0.05$) (Fig. 1).

The mean SBP of PIH mothers was 111.98 ± 9.02 mmHg and that of normotensive mothers was 107.86 ± 9.57 mmHg. The difference between them was statistically not significant ($p > 0.05$). The mean DBP of PIH mothers was 71.98 ± 7.31 mmHg and that of the normotensive mothers was 70.71 ± 6.04 mmHg. The difference between them was also statistically not significant ($p > 0.05$) (Table 1).
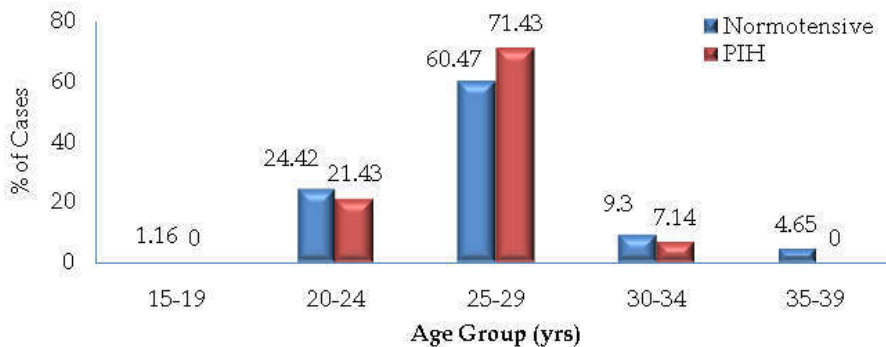
The increase in SBP and DBP were compared

Fig. 1: Comparison of PIH and Normotensive in respect of their age

within the PIH mothers from booking to delivery. The mean SBP of them at booking was 111.40 ± 9.19 mmHg and that at delivery was 149.29 ± 14.07 mmHg. The mean increase was 41.42 ± 17.76 mmHg which was statistically highly significant (p < 0.001). The mean DBP of them at booking was 71.80 ± 7.14 mmHg and that at delivery was 95.71 mmHg. The mean increase was 25.00 ± 12.30 mmHg which was also statistically highly significant (p < 0.001) (Table 2).

The mean increase of SBP in PIH mothers was 41.4 ± 15.1 mmHg. The mean increase of SBP in normotensive mothers was 4.4 ± 11.9 mmHg. The difference between them was statistically highly significant (p < 0.001). Similarly, the DBP mean increase in PIH mothers was 25.0 ± 8.5 mmHg. The mean increase of DBP of Normal mothers was 2.6 ± 9.7 mmHg. The difference between them was statistically highly significant (p < 0.001) (Table 3).

The mean serum beta HCG of PIH group mothers was 45027.43 ± 23020.54 mIU/ml and that of normotensive mothers was 27500.10 ± 12165.02 mIU/ml. The difference between the mean of PIH and normotensive mother was statistically highly significant (p < 0.001) (Table 4).

At the time of booking there was no significant correlation among serum beta HCG with SBP or DBP (p > 0.05), but at delivery the serum beta HCG had high correlation with both SBP and DBP (p < 0.001) (Table 5).

Out of 200 patients 185 (92.50%), had MOM <2 among these 17 (9.18%) patients developed PIH. 15 patients (7.50%) had MOM >2 among these 11 (73.33%) patients developed PIH (Table 6).

Above table shows sensitivity, specificity, positive predictive value and negative predictive value for beta HCG were 73.33%, 90.81%, 39.29% and 96.67% in our study respectively. Kaur G

Table 1: Comparison of systolic and diastolic blood pressure between PIH and Normotensive mothers at the time of booking

Blood Pressure	PIH		Normotensive		Differ b/w means	"t"	Significance
	Mean	SD	Mean	SD			
SBP	111.98	9.02	107.86	9.57	4.12	2.03	p>0.05
DBP	71.98	7.31	70.71	6.04	0.27	1.00	p>0.05

Table 2: Comparison of SBP and DBP in the PIH mothers at the time of booking & delivery

Blood Pressure	At Booking		At Delivery		Increase		Sig
	Mean	SD	Mean	SD	Mean	SD	
SBP	111.98	9.02	149.29	10.51	41.42	14.83	p<0.001
DBP	71.98	7.31	95.71	7.41	25.00	8.38	p<0.001

Table 3: Comparison of Increased SBP and DBP between PIH and Normotensive mothers

Blood Pressure	PIH		Normotensive		Difference of means	Significance
	Mean	SD	Mean	SD		
SBP	41.4	15.1	4.4	11.9	37.0	p<0.001
DBP	25.0	8.5	2.6	9.7	22.4	p<0.001

Table 4: Comparison of serum beta HCG between the PIH and normotensive mothers

Variable	PIH		Normotensive		Difference of means	Significance
	Mean	SD	Mean	SD		
β HCG (mIU/ml)	45027.43	23020.54	27500.10	12165.02	17527.32	p<0.001

Table 5: Correlation between serum beta HCG and SBP, DBP at the time of booking and delivery

Time	Variable-1	Variable-2	"r"	Sig	r^2
At booking	β HCG	SBP	-0.06	P>0.05	0.0036
	β HCG	DBP	-0.08	P>0.05	0.0064
At delivery	β HCG	SBP	+0.47	P<0.001	0.2209
	β HCG	DBP	+0.37	P<0.001	0.1369

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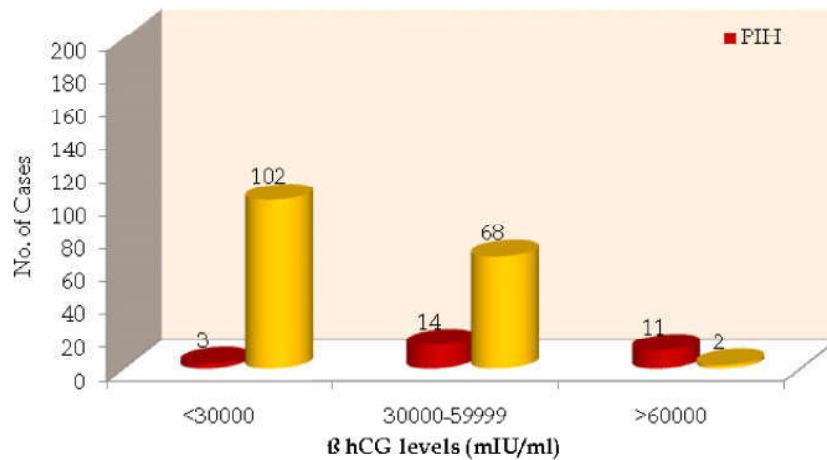Human Chorionic Gonadotropin and Hypertensive Disorder of Pregnancy

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Fig. 2: Relationship between serum beta HCG (absolute) levels and PIH

Table 6: Relationship between serum beta HCG in MOM (multiple of median) levels and PIH

	HCG >2 MOM	HCG < 2 MOM	Total
PIH	11	17	28
Normal	4	168	172
Total	15	185	200

Table 7: Comparison of predictive value of beta HCG with different studies

	Sensitivity	Specificity	PPV	NPV
Present study	70.33%	90.81%	39.29%	97.69%
Kaur G et al. [9]	90.91%	97.44%	83.33%	-
Chowdhary H et al. [10]	83.30%	96.90%	80.00%	97.50%

et al. [9] also reported that beta HCG levels obtained in early pregnancy have high sensitivity (90.91%), specificity (97.44%) and positive predictive value (83.33%) for prediction of gestational hypertension. Choudhary H et al. [10] have reported similar findings i.e. sensitivity, specificity, positive predictive value and negative predictive value for beta HCG were 83.30%, 96.90%, 80%, and 97.50% respectively (Table 7).

Discussion

The difference of age between them was not statistically significant which was in concordant with the results of study conducted by Aysel Kabuku et al. [11] and Sharma et al. [12] (Table 1).

The mean increase of SBP of PIH mothers was 41.4 ± 15.1 mmHg. The mean increase of SBP of normal mothers was 4.4 ± 11.9 mmHg. The difference of mean increase of SBP (37.00 mmHg) was statistically highly significant (p<0.001). Similarly, the DBP mean increase of PIH mothers was 25.0 ± 8.5 mmHg. The mean increase of DBP of

Normal mothers was 2.6 ± 9.7 mmHg. The difference between them was statistically highly significant (p < 0.001). Dayal M et al. [13] also reported similar mean Systolic BP levels and mean diastolic BP in hypertensive and normotensive. This difference was statistically significant (p < 0.05).

The mean beta HCG of PIH group mothers was 45027.43 ± 23020.54 and that of normotensive group was 27500.10 ± 12165.02. Thus difference between the mean of PIH & normotensive mothers was statistically significant (p < 0.001). Zhonghua et al. [14] also concluded that there was a positive correlation between the absolute beta-HCG levels and the severity of pregnancy induced hypertension (p<0.001). Basirat Z et al. [15] reported that the maternal serum Beta HCG levels in patients with preeclampsia (39840 ± 24630IU/L) was higher than in the control group (27460 ± 25862; p=0.031). Thus our findings are similar with the findings of Gubuz et al. [16] and Choudhury et al. [10]. There was no significant correlation between the β HCG with either SBP or DBP (p > 0.05). But at delivery the β HCG was highly correlated with both SBP and DBP (p < 0.001).

Out of 200 patients 105 (52.50%) had beta HCG below 30,000 mIU/ml, among this only 3 (2.85%) patients developed PIH. 82 (41%) had beta HCG between 30,000 mIU/ml to 60,000 mIU/ml & among this 14 (17.07%) patients developed PIH. 13 (6.5%) patients had beta HCG between 60,000 mIU/ml to 90,000 mIU/ml & among this 11 (84.61%) patients developed PIH. So, we can say that the higher absolute level of beta HCG strongly correlate with occurrence of PIH. Similar results have been shown by Zhonghua et al. [14], in which the author concluded that there was a positive correlation between the absolute Beta-HCG levels and the development of pregnancy induced hypertension. The serum level of Beta-HCG in the mild pregnancy induced hypertension group was 25,330 ± 17,800 and in severe pregnancy induced hypertension group it was 42,190 ± 17,720, that was significantly higher than the normotensive pregnant group, 12,330 ± 720, giving a highly significant p value < 0.001 [Zhonghua et al. [14]]. 185 (92.50%), had MOM < 2 among these 17 (9.18%) patients developed PIH. 15 patients (7.50%) had MOM >2 among these 11 (73.33%) patients developed PIH. Sharma V et al. [12] in their study observed that out of 387 cases with beta-HCG levels < 2MOM, only 6 cases (1.56%) developed pregnancy induced hypertension and out of 60 cases with beta-HCG values > 2MOM, 49 cases (81.67%) developed pregnancy induced hypertension (p<0.001). Present findings are also consistent with the findings of Kaur G et al. [9] who observed that 20 (83.33%) out of 24 cases with beta HCG levels > 2MOM developed PIH against 2 (1.2%) cases out of 154 having beta HCG levels ≤ 2MOM (p value <0.001). Soundararajan P et al. [17] reported similar findings.

Sensitivity, specificity, positive predictive value and negative predictive value for beta HCG were 73.33%, 90.81%, 39.29% and 96.67% respectively. Kaur G et al. [9] also reported that beta HCG levels obtained in early pregnancy have high sensitivity (90.91%), specificity (97.44%) and positive predictive value (83.33%) for prediction of gestational hypertension. Choudhary H et al. [10] have reported similar findings.

Conclusion

This study showed that measuring serum beta HCG in early second trimester (13-20 weeks) is a useful indicator to identify women who are likely to develop PIH in the same pregnancy. If beta HCG is < 30,000 mIU/ml there is less chance of development of PIH & if beta HCG is ≥ 60,000 mIU/ml there is very high chance of development of PIH. Thus we can say that serum *beta HCG* level can be used as predictor of PIH as *beta HCG* is also already done as triple marker test in routine ANC. So it can be used without any extra burden on patient.

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