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Original Research Article

Prediction of hypertensive disorders in pregnancy by estimation of maternal serum beta HCG levels in the mid-trimester (13-20 weeks) of pregnancy

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Abstract

Background: Hypertensive disorders of pregnancy (HDP) are one of the dreaded complications of pregnancy. Although improvements in obstetric and neonatal care have led to a reduction in morbidity and mortality from hypertensive disorders, our ability to predict the condition has not improved significantly.

Aims & Objectives: To study the correlation of the second trimester (13-20 weeks) maternal serum beta HCG levels and the development of hypertensive disorders during pregnancy.

Methods: This was a prospective study conducted in a Bihar medical college in the Department of Obstetrics and Gynaecology, over a period of 2 years. Total 100 pregnant patients, during the second trimester (13-20 weeks) were recruited from reproductive and child health OPD and serum beta HCG estimation were done in all the patients. Patients were followed till delivery and six weeks postpartum for the development of hypertensive disorders and pregnancy outcomes.

Results: Total 100 patients were recruited and only 90 patients completed the study. Results were analyzed statistically. Patients were divided into two groups, group 1 was normotensive patients 86.66% (78/90) and group 2 was patients who develop hypertensive disorders 13.33% (12/90), all were pre-eclampsia. Out of 40 cases with serum beta HCG levels >35,000 mIU/ml, 25% (10/40) cases developed hypertensive disorders and out of 50 cases with serum beta HCG levels < 35,000 mIU/ml, only 4.0% (2/50) cases developed hypertensive disorders. On comparison of the two groups, the p-value came out to be 0.003, which is statistically significant.

Conclusion: The present study concluded that the mid-trimester (13-20 weeks) maternal serum beta HCG estimation is a good predictor for the development of hypertensive disorders during pregnancy.

Keywords: Mid-trimester, Beta HCG, hypertensive disorders, pregnancy.

1. Introduction

Hypertensive Disorder is one of the most common medical complications affecting 5-10% of all pregnancies worldwide. [1] Hypertension during pregnancy is defined as a blood pressure of 140 / 90 mm Hg or more on two occasions at least 6 hours apart but within 7 days.

Proteinuria is defined as 24-hour urinary protein excretion ≥300 mg or persistent 30mg/dl (1+ dipstick) protein in a random urine sample or urine protein: creatinine ratio ≥0.3

Hypertensive disorder during pregnancy is classified according to report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy as. [2]

1) Gestational hypertension
2) Pre-eclampsia with and without severe features
3) Eclampsia
4) Chronic hypertension
5) Superimposed Preeclampsia on chronic hypertension

According to WHO systematic analysis published in 2014, worldwide Hypertensive Disorders during Pregnancy is the second leading cause of maternal mortality following hemorrhage. [3]

Pathogenesis of pre-eclampsia has not been exactly known but the placenta is clearly involved and endothelial cell dysfunction is believed to be the central theme. [4] Abnormal placentation has been considered as one of the initial events in the process of the disease. It has been hypothesized that during mid-trimester, immunological changes are occurring in the trophoblasts, which results in secretory response and subsequent rise in the beta HCG levels. [5]

Another hypothesis was given by some other researcher that placental vascular damage leading to decreased oxygen supply, which might result in increased HCG production by the hyperplastic cytotrophoblastic cells. [6] HCG, a pregnancy hormone is a glycoprotein and biologically similar to LH. It is almost entirely produced by placenta but some amount is also produced by fetal kidneys. [7] Levels peak at 8-10 weeks reaching 100000 mIU/ml. This is followed by a relatively sharp decrease beginning at 12 weeks and reaches a nadir by 20 weeks and maintained at these lower levels throughout the pregnancy. But it has been seen that patients with elevated second-trimester serum beta HCG levels develop hypertensive disorders later in the pregnancy.

Researchers work constantly to discover predictive factors which can identify risks during pregnancy and if prediction can be done, prevention will follow naturally. Many tests have been proposed for the prediction of hypertensive disorders during pregnancy but none achieved success or accepted widely because of the low predictive value.

The present prospective study was carried out to evaluate the clinical utility of second-trimester serum beta HCG levels as a predictive marker for the development of hypertensive disorders during Pregnancy.

1.1 Aims and objectives

To evaluate the correlation between maternal serum Beta HCG levels in the second trimester (13-20 weeks) of pregnancy and the development of hypertensive disorders during pregnancy.

2. Materials and methods

This prospective study was carried out in a medical college in the Department of Obstetrics & Gynaecology over a period of 2 years. Total 100 pregnant patients; normotensive, non-proteinuric between gestational ages of 13-20 weeks were recruited randomly from the RCH OPD (Reproductive and Child Health OPD, irrespective of the parity. Gestational age was calculated from the first-trimester ultrasonography (USG) and/ reliable menstrual dates if USG not available.

2.1 Inclusion criteria

- Gestational age between 13-20 weeks confirmed by first-trimester USG and/ reliable menstrual history
- Singleton pregnancy
- Normotensive
- Non- proteinuric
- No antenatal complications

2.2 Exclusion criteria

- Multiple pregnancies
- Congenital abnormalities
- Essential hypertension
- Diabetes Mellitus
- Molar Pregnancy

Selection of the patient was done on the basis of inclusion, exclusion criteria and consent to participate in the study. All the women were subjected to detailed history and examination along with the demographic details. Gestational age was calculated from the dates obtained from early first trimester USG (CRL) and/ reliable menstrual history. Serum beta HCG was done by chemiluminescent immunometric assay (CLIA) method.

The cases were followed up in antenatal OPD and were examined four weekly till 28 weeks, fortnightly till 34 weeks, weekly till delivery and thereafter till six weeks postpartum, for the development of hypertensive disorders during pregnancy. Hypertensive disorders during pregnancy are defined as the blood pressure ≥ 140/90 mmHg measured on two occasions 6 hours apart after 20 weeks of gestation with or without proteinuria in the previously normotensive non-proteinuric patient. In every visit, Blood pressure, urine for albumin, weight and antenatal examination was done.

2.3 Statistical analysis

The results so obtained were evaluated and analyzed statistically. Mean ± Standard Deviation (SD) of all the parameters of interest were calculated for hypertensive disorders in pregnancy group and for normotensive group 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 the diagnostic value of serum beta HCG for the development of hypertensive disorders in pregnancy. A p-value of < 0.05 or less was considered statistically significant.

3. Results

This study enrolled 100 pregnant women, who came to RCH out Patient department of Obstetrics & Gynaecology, Patna Medical College & Hospital over a period of two years. Only 90 (90%) patients were completely followed till six weeks postpartum and 10 patients (10%) were lost to follow up. Patients were divided into two groups, group 1 includes normotensive patients and group 2 includes patients who developed hypertension.

Out of 90 cases who completed the study, 12 (13.33%) cases developed hypertensive disorders in pregnancy (HDP) and 78 (86.66%) remained normotensive, making the prevalence of HDP 13.33%. (Table 1)

Table 1: **Distribution of patients according to hypertensive disorders in pregnancy (HDP)**

Groups	Number of cases	Percentage
Normotensive (Group 1)	78	86.66 %
HDP (Group 2)	12	13.33 %
Total	90	100 %

Maximum patients i.e. 64.44% (58/90) were in 20-24 year of age group. There were only 5.5 % cases (5/90) who were more than 35 years, and they remained normotensive till delivery. (Table 2)

Table 2: **Patient's distribution according to the age group**

Age in years	No. of Patients	Percentage
< 20	14	15.5%
20 – 24	58	64.4 %
25 – 29	13	14.4 %
30 – 36	5	5.5 %
Total	90	100%

All the cases who develop HDP (100%) had BMI between 20 – 25 kg/m^2 and only one case had BMI > 30, who remained normotensive. Due to a smaller number of patients with the BMI>30, it is very difficult to make an opinion on the relationship between HDP and obesity as a probable high-risk factor. (Table 3)

Table 3: **Patient's distribution according to BMI (kg/m^2)**

BMI (kg/m^2)	Total cases N=90	Group I (Normotensive) N=78	Group II (HDP) N=12
15-19.9	1	1	0
20-24.9	85	73	12
25-29.9	3	3	0
30-34.9	1	1	0
>35	0	0	0

91.66% cases (11/12) in group 2 (HDP) were primigravida. The chi-square statistic is 0.8449. The p-value is 0.357994. This result is not significant at $p < .05$ but the occurrence of HDP is more common among primigravida. (Table 4)

Table 4: **Patient's distribution according to parity**

Parity	Total no. of cases (N=90)	Group I (Normotensive) N=78	Group II (HDP) N=12
Primi	74 (82.22%)	63 (80.76%)	**11 (91.66%)**
Multi	16 (17.77%)	15 (19.23%)	1 (8.33%)

Comparison of blood pressure at the time of booking (13-20 weeks) between two groups did not vary significantly. Blood pressure for the pre-eclamptic (HDP) group at the time of delivery was significantly higher in comparison to the normotensive group. This was true for both systolic and diastolic blood pressure. (p value < 0.001) (Table 5)

Table 5: **Mean systolic and diastolic Blood Pressure (mm Hg) comparison between two groups at time of booking and delivery**

BP (mm Hg)	HDP (N=12)	Normotensive (N=78)	t Value	p- value
At 1st visit (13-20 weeks)				
Systolic	119.0 ± 6.4	114.9 ± 8.1	1.10	0.22 NS
Diastolic	75.0 ± 7.1	73.1 ±5.4	1.04	0.32 NS
At the time of delivery				
Systolic	154 .1± 8.5	119.4 ± 6.4	15.78	**< 0.001 HS**
Diastolic	100.1± 10.6	77.1 ± 5.7	11.44	**<0.001 HS**

[NS-not significant, HS-highly significant]

Out of 40 cases with serum beta HCG levels>35,000 mIU/ml, 25 % cases (10/40) developed hypertensive disorders and out of 50 cases with serum beta HCG levels<35,000 mIU/ml, only 4.0 % cases (2/50)) developed hypertensive disorders. The chi-square statistic is 8.4808. The p-value is 0.003589. This result is significant at $p < .05$. (Table 6)

Table 6: **Relation of Serum Beta HCG levels and Hypertensive disorders in pregnancy**

Beta HCG (mIU/ml)	Total No. of Cases (N=90)	Normotensive (N=78) No. (%)	HDP (N=12) No. (%)
< 25,000	18	18 (100%)	-
25,000 – 35,000	30	28 (93.3%)	2 (6.6%)
35,000 – 45,000	20	18 (90%)	2 (10%)
45,000 – 55,000	7	6 (85.71%)	1 (14.28%)
55,000 – 65,000	2	1 (50%)	1 (50%)
65,000 – 75,000	4	2 (50%)	2 (50%)
75,000 – 85,000	5	3 (60%)	2 (40%)
85,000 – 95,000	2	-	2 (100%)
>1,00,000	2	2 (100 %)	-
Total	**90**	**78**	**12**

This study establishes the validity of serum beta HCG level as a predictor of hypertensive disorders in pregnancy with a Sensitivity of 84%, Specificity of 60% and Accuracy of 61%. The PPV (Positive predictive value) is 20% and the NPV (Negative predictive value) is 97%.

However, there was no linear increase in the incidence of HDP with increasing absolute levels of serum beta HCG. Thus, genetic, immunological and environmental factors may contribute for the development of hypertensive disorders in pregnancy.

4. Discussion

Total 100 patients were enrolled in this study and 90 cases completed the study, 13.33% cases (12/90) subsequently developed Hypertensive Disorders in Pregnancy. Prevalence of HDP in this study is similar to the study conducted by Gurmandeep *et al* in 2012 on 178 women with the prevalence of 12.35%. [5] Vidyabati *et al* conducted a similar study on 164 women at 14-20 weeks of gestation and the prevalence was 17.7%. [8]

In our study, the mean age among group 1 and 2 was 22.2 years and 20.9 years respectively and there was no significant difference in the age group among both the groups. Results were similar to study conducted by Vidyabati *et al* with the mean age of 27.17 years and majority of patients in HDP group were elderly primigravida belonging to age group 31-35 years. [8] As the number of patients in present study was less in the age group>35 years, it is very difficult to make an opinion on the relationship between elderly patients and the risk of HDP. In another study by Satyanarayan *et al*, mean age among HDP group and the normotensive group was 24.14 years and 24.27 years respectively. [9]

In this study, 91.6% cases (11/12) of HDP were primigravida and the results were similar to the study conducted by Gurmandeep *et al*, where majority of patients, 72% cases who developed hypertensive disorders in pregnancy were primigravida. [5]

In the present study, the HDP group mean systolic and diastolic blood pressure was 119 mm Hg and 75 mm Hg respectively and in a normotensive group, it is 114 mm Hg & 73 mm Hg respectively.

Vidyabati *et al* [8] showed that the systolic BP among patients who later developed HDP was 120.7 mm Hg and diastolic BP was 78.96 mm Hg. In the normotensive group mean systolic and diastolic BP was 122.8 mmHg and 72.2 mm Hg respectively. Blood Pressure at the time of booking between the HDP and the normotensive group did not vary significantly.

Blood pressure for the HDP group at the time of delivery was significantly higher in comparison to the normotensive group. This was true for both systolic and diastolic blood pressure. (p-value < 0.001)

In the present study, the incidence of HDP in women with elevated beta HCG ≥ 35000 mlU/ml was higher compared to women with normal levels (25% versus 4%). However, there was no relationship between severity of HDP and beta HCG levels. Similar results were shown in a study by Sorensen *et al* [10] but in the study conducted by Jadab *et al* over 100 women in 2016 showed a positive correlation between serum β hCG concentration with the blood pressure levels both systolic and diastolic pressure. [11]

In the study done by Vidyabati *et al* [8] 17.68% cases (29/164) developed HDP. 72.4% (21/29) women had elevated beta HCG above 45000 mIU/ml similar to present study where 66.66% women (8/12) had beta HCG levels ≥45000 mIU/ml

In the present study, 25% cases (10/40) had HDP with beta HCG level > 35,000 mIU/ml as compared to only 4% cases (2/50) who had HDP with beta HCG level< 35,000 mIU/ml, which is statistically significant. (P value-0.003)

Gurmandeep *et al* [5] conducted a study which showed a sensitivity of 90.91%, specificity of 97.44% and PPV of 83.33% and in the present study, raised second trimester Serum beta HCG levels appears to be an efficient and promising predictor for hypertensive disorders in pregnancy with a Sensitivity of 84 %, specificity of 60 %, PPV of 20% and negative predictive value of 97%.

5. Conclusion

Serum beta HCG level measurement during mid-trimester (13-20 weeks) acts as an efficient non-invasive predictive marker for the development of hypertensive disorders in pregnancy. Predictive markers will help in preventing the dreadful complications like Pre-eclampsia and eclampsia and which will further reduce the maternal and fetal morbidity and mortality by improving the maternal and fetal outcome.

References

[1]. Cunningham FG, Leveno KJ, Bloom SL *et al*. Pregnancy Hypertension. Williams Obstetrics, 23rd edition: p.706 – 709.

[2]. Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. *Am J Obstet Gynecol*. 2000; 183(1): S1-S22.

[3]. Global causes of maternal deaths: A WHO systematic analysis. *The Lancet Global Health*, June 2014; 2 (6).

[4]. Majumdar S, Dasgupta H, *et al*. A study of Placenta in Normal and Hypertensive Pregnancies. *J Ant Soc India*. 2005; 54(2): 1-9.

[5]. Kaur G, Jain V, Mehta S *et al*. Prediction of PIH by Maternal Serum Beta HCG Levels in the Second Trimester (13–20 Weeks) of Pregnancy. *J Obstet Gynaecol India*. 2012 Feb; 62(1): 32–34.

[6]. Gratacos E. Lipid mediated endothelial dysfunction: a common factor to pre-eclampsia and chronic vascular disease. *Eur J Obstet Gynaecol Reprod Biol*. 2000; 92: 63-6.

[7]. Sharma P, Maheshwari S, Barala S. Correlation between second trimester beta human chorionic gonadotropin levels and pregnancy outcome in high risk group. *Int J Reprod Contracept Obstet Gynecol* 2016; 5: 2358-61.

[8]. Vidyabati R K, Davina H, Singh NK, *et al*. Serum βhCG level and lipid profile in early second trimester as predictors of pregnancy induced hypertension. *J Obstet Gynaecol India*. 2010; 60(1): 44-50.

[9]. K Satyanarayan, Harjeet Sawhney, Kala Vasishta. Association between second trimester maternal serum hCG levels and PIH. *Journal of Obs & Gyn of India*. 2001; 51: 85-88.

[10]. Sorensen TK, Michelle A, Williams SD. Elevated second trimester hCG and subsequent PIH. AJOG 1993; 170:834.

[11]. Phulkan KJ, Paul T. A comparative study of serum β hCG concentration and lipid profile in pregnancy induced hypertensive and normotensive women in third trimester of pregnancy. *International Journal of Advanced Research* 2016; 4 (7): 680-686.