International Journal of Advanced Research in Medicine

Madhuri S
Assistant Professor,
Cardiology, Katuri Medical
College, Guntur, Andhra
Pradesh, India

Shyamala Devi S
Professor, Obstetrics and
Gynecology, Guntur Medical
College, Guntur, Andhra
Pradesh, India

Babulal S
Principal, Guntur Medical
College, Guntur, Andhra
Pradesh, India

Gayatri S
Assistant Professor,
Endocrinology, Narayana
Medical College, Nellore
Andhra Pradesh, India

Prediction of pregnancy induced hypertension by maternal serum βhCG levels in second trimester

Madhuri S, Shyamala Devi S, Babulal S and Gayatri S

Abstract
Background: There is no single test that is reliable and cost-effective for predicting pregnancy induced hypertension (PIH). It is hypothesized that during mid-trimester, immunological changes occur in the trophoblast resulting in secretory response which is seen as a rise in βhCG levels. An initial screening test like serum βhCG might help in categorizing patients who require special attention throughout pregnancy.
Methods: This is a prospective observational study conducted at Government General Hospital (GGH), Guntur, in the department of Obstetrics and Gynecology on 100 pregnant women in their second trimester (13-20 weeks) attending the outpatient department (OPD) from December 2020 to December 2021, who were followed up till term. Maternal serum βhCG levels were estimated.
Results: Twenty three women developed PIH and 77 remained normotensive. Out of the 23 cases, 20 cases showed elevated βhCG values in 13-20 weeks.
Conclusion: Elevation in maternal serum βhCG levels in early second trimester is a good non-invasive, reliable and economical test which can be used as a predictor of PIH before the clinical onset of the disease.

Keywords: Beta human chorionic gonadotropin, pregnancy induced Hypertension

Introduction

In pre-eclampsia, TGFβ levels remain high and the trophoblast is arrested at an immature state while its invasiveness is decreased. These hormones are elevated in maternal serum long before preeclampsia is detected and has been proposed as early predictor of preeclampsia. HCG secretion may be raised as a consequence of abnormal placental invasion or placental immaturity. It may also be linked to the trophoblast response to hypoxia with the development of a hypersecretory state [1-5]. In this study, we therefore intend to find out the correlation between raised βhCG levels and hypertensive disorders of pregnancy, to know the association of βhCG levels with the severity of the disease, and the association between systolic and diastolic blood pressure and βhCG values with maternofetal outcomes.

Methods

This prospective observational study was conducted on 100 normotensive non-proteinuric patients, between 18 to 35 years of age, with singleton pregnancy, who were selected randomly between the gestational age 13-20 weeks attending the outpatient department of OBG in Government General Hospital, Guntur from December 1st 2020-December 1st 2021 over a period of 12 months, irrespective of parity. Women with multiple pregnancies, chronic hypertension, diabetes mellitus, molar pregnancy or anomalies in fetus or any other condition that could interfere with the study and those who did not consent were excluded. Blood pressure was recorded using a sphygmomanometer with auscultatory method and the average of three readings was taken. Maternal serum sample of 2ml was taken and sent for βHCG level estimation, using enzyme linked immune-fluorescence assay. The data was entered in an excel sheet and analyzes statistically using IBM SPSS Version 28 for windows.

Results

Out of 100 women enrolled in the study, 23 cases developed PIH and 77 remained normotensive.

Corresponding Author:
Gayatri S
Assistant Professor,
Endocrinology, Narayana
Medical College, Nellore
Andhra Pradesh, India

Table 1: Age distribution of normotensive and women with PIH

Age in yrs	PIH Group	Normal Group
19-23	9	26
24-28	5	39
29-33	8	11
>33	1	1
Total	23	77
Chi Square test $p<0.04$, Sig		

Table 1 shows the age distribution of cases. Mean age among PIH is 25.96 years with standard deviation being 4.78 and mean age among normotensive group is 24.87 and standard deviation being 3.57. This association was found to be statistically not significant (p value<0.241).

Table 2: Distribution of normotensive and women with PIH with respect to BMI

BMI	PIH Group	Normal Group
Normal Weight	20	76
Over Weight	3	1
Total	23	77
Chi Square test $p<0.04$, Sig		

BMI in the two categories is shown in table 2. Mean BMI among the PIH cases is 23.04 with standard deviation being 1.57 and the mean BMI in normotensive group is 22.16 and standard deviation was 1.31. This association was found to be statistically significant (p value<0.008).

The association of parity with PIH was not found to be statistically significant.

Table 3: Comparison of normotensive and PIH group with mean serum βhCG scores by independent t test

Variables	Groups	N	Mean	Sd	SE	T Value	P-Value
Serum Beta hCG	PIH Group	23	84841.70	30826.53	6427.78	13.152	0.001
	Normal Group	77	26280.04	13328.66	1518.94		

The mean βhCG value of PIH group mothers was 84841.70 IU/l with standard deviation being 308265.53 IU/l and that of normotensive group was 26280.04 IU/l with standard deviation being 13328.66 IU/l. The difference between the means was statistically significant, as seen in table 3.

Table 4: Comparison of mode of delivery between PIH and normotensive groups

Mode of delivery	No. of cases	Women with PIH	Women without PIH
Vaginal	51	6	45
Caesarean section	44	16	28
Vacuum	3	1	2
Forceps	2	0	2
Total	100	23	77
Chi Square test $p<0.03$, Sig			

The difference in the mode of delivery in the two groups was statistically significant, as shown in table 4.

Table 5: Comparison between PIH and normotensive groups with respect to the period of gestation at the time of delivery

Age	No of cases	Women with PIH	Women Without PIH
Term	83	13	70
Preterm	17	10	7
Total	100	23	77
Chi Square test $p<0.001$, Highly Sig			

The term and preterm deliveries among the total study group was 83% and 17% respectively. The difference in the two groups is shown in table 5.

The difference in perinatal outcomes between the PIH and normotensive group was highly significant statistically with p value<0.001. Among the three severe PIH cases, all their babies had preterm deliveries with abnormal perinatal outcomes and thus the comparison of the perinatal outcome with the severity of the disease was also very significant statistically with p value <0.001.

Discussion
The prevalence of PIH in our study was 23%. Yadav Kiran et al. [6] during a prospective study on 120 pregnant women observed that 21 women developed PIH which constitutes about 17.5%. At SSG Hospital, Baroda, Dipti A Modi et al. [7] found that 26 women out of 100 developed hypertension which accounted to 26% of cases.

In our study, majority of the women were in the age group of 24-28 years. Mean age among hypertensive group was 25.96 years and mean age among normotensive group was 24.87 years. In a study conducted by Josephine Latha et al. [8] on 100 women with PIH and 100 normotensive pregnant women, the mean age of women with PIH was 24.57±3.27 years and that of normotensive pregnant women was 23.9±3.50 years. In a study conducted by Pradeepa Soudaranjan [9], maximum cases of preeclampsia were in the age group of 24.48±2.08 years and in normotensive group, it was 23.65±2.47 years.

In our study, mean BMI among PIH was 23.04 and mean BMI among normotensive group was 22.16. This association was found to be statistically significant. In a study conducted by Anuradha et al. [10] during the year 2015 at Government Medical College, Ananthapuram on 80 cases, it was found that the mean BMI of normotensive pregnant women was 24.32±8.03 kg/m^2 and that of preeclamptic women was 28.13±5.62 kg/m^2 with a p value of 0.0162. There was a high statistical significance in the maternal pre-pregnancy BMI which was more in the pre-eclamptic women.

In our study, the mean systolic blood pressure of PIH women was 151.13 and that of normotensive pregnant women was 117.25 mm of Hg. The mean diastolic blood pressure of PIH women was 101.30 and that of normotensive women was 77.22, which was found to be statistically very significant. In a study conducted by Aparna Rajesh et al. [11] in K.S. Hedge Medical Academy, Mangalore during November 2015 to January 2017, the mean systolic blood pressure of PIH women was 139.1±20.6 mm Hg and that of normotensive pregnant women was 118.4±8.3 mm Hg and the mean diastolic blood pressure of PIH women was 90±7.3 mm Hg and that of normotensive pregnant women was 77.8±4.8 mm Hg with a p value of <0.001.

In our study, elevated βhCG levels were associated with preeclampsia. The mean βhCG value of PIH group mothers

was 84841.70 IU/l and that of normotensive group was 26280.04 IU/l. The difference between the means was statistically significant. The cut-off point of βhCG for predicting PIH was 25590 IU/l with a sensitivity of 95.6% and specificity of 44.2%. In a study conducted by Kaur G *et al*. [12], estimation of beta HCG at midtrimester was a good predictor of PIH and higher levels were associated with increased severity. The sensitivity of the test was 90.91%, specificity was 97.44% and positive predictive value (PPV) was 83.33%. Similar findings were echoed in the study by Hui-Qiang Liu *et al*. [13]. Ayse Gurbuz *et al*. [14] study states that high serum HCG values can be a helpful marker in diagnosis and clinical management by preventing possible complications resulting from severe and superimposed preeclampsia. In a study conducted by Megha Panwar *et al*. [15], 440 primigravida between 16-18 weeks of gestation were included in the study and the mean values of neutrophilic lymphocytic ratio and serum betah CG were significantly raised in patients developing pre-eclampsia and suggested that these can be used as excellent biomarkers in predicting both pre-eclampsia and its severity. In a study conducted by Vidyabathi [16], 29 cases developed preeclampsia out of 164 women. Out of 29 cases, 21 women had elevated βhCG above 45,000IU/ml. In the study conducted by Pradeepa Soudaranjan, out of 100 women, 32 women who had high βhCG value of more than 25,000 IU/ml developed preeclampsia with a significant p value of less than 0.01. Specificity was 80% and PPV was 86%. Yousefnejad Y *et al*. [17] stated that the mean of serum βHCG levels in patients with pre-eclampsia was significantly higher.

Conclusion
Serum βhCG in the early second trimester is an effective non-invasive test, economical and reliable technique which can be used in the prediction of preeclampsia before the clinical onset of the disease. However, larger studies would help in implementation of such practices. If prediction is possible, prevention will follow naturally.

References
1. Nirupama R, Divyashree S, Janhavi P, Muthukumar SP, Ravindra PV. Preeclampsia: Pathophysiology and management. J Gynecol Obstet Hum Reprod. 2021 Feb; 50(2):101975.
2. Allerkamp HH, Clark AR, Lee TC, Morgan TK, Burton GJ, James JL. Something old, something new: digital quantification of uterine vascular remodelling and trophoblast plugging in historical collections provides new insight into adaptation of the utero-placental circulation. Hum Reprod. 2021 Feb 18; 36(3):571-586.
3. Wang Y, Zhao S. Vascular Biology of the Placenta. San Rafael (CA): Morgan & Claypool Life Sciences; c2010.
4. Lokki AI, Heikkinen-Eloranta JK, Laivuori H. The Immunogenetic Conundrum of Preeclampsia. Front Immunol. 2018 Nov 13;9:2630.
5. Hitzerd E, Broekhuizen M, Neuman RI, Colafella KMM, Merkus D, Schoenmakers S, Simons SHP, Reiss IKM, Danser AHJ. Human Placental Vascular Reactivity in Health and Disease: Implications for the Treatment of Pre-eclampsia. Curr Pharm Des. 2019;25:505-27.
6. Yadav K, Aggarwal S, Verma K. Serum βhCG and Lipid Profile in Early Second Trimester as Predictors of Pregnancy-Induced Hypertension. J Obstet Gynaecol India. 2014 Jun; 64(3):169-74.
7. Dipti A Modi, Bijal D Rami, Gurleen K Wander. Role of Serum Bhcg and Lipid Profile in Early Second Trimester as Predictors of Hypertensive Disorders of Pregnancy. Int J Res Med. 2015;4(4):34-37e.
8. Latha PJ, Ganesan S. Evaluation of serum uric acid and lipid profile in gestational hypertension. Int J Pharm Bio Sci. 2013;4(2):496-502.
9. Soundararajan P, Muthuramu P, Veerapandi M, Mariyappan R. Serum beta human chorionic gonadotropin and lipid profile in early second trimester (14-20 weeks) is a predictor of pregnancy-induced hypertension. Int J Reprod Contracept Obstet Gynecol. 2016;5(9):3011-6.
10. Anuradha R, Durga T. Estimation of lipid profile among preeclampsia woman by comparing with normal pregnancy. Int J Contemp Med Res. 2016;3(7):1958-1961.
11. Rajesh A, Muralidharan V. Serum beta hCG in early second trimester as a predictor of gestational hypertension. Int J Reprod Contracept Obstet Gynecol 2018 Jun 1;7(6):2355-60.
12. Kaur G, Jain V, Mehta S, Himani S. 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):32-4.
13. Liu HQ, Wang YH, Wang LL, Hao M. Predictive Value of Free β-Hcg Multiple of the Median for Women with Preeclampsia. Gynecol. Obstet. Investig. 2015;81:137-147.
14. Gurbuz A, Karateke A, Mengulluoglu M, Gedikbasi A, Ozturkmen M, Kabaca C, Sahinoglu Z. Can serum HCG values be used in the differential diagnosis of pregnancy complicated by hypertension? Hypertens Pregnancy. 2004 Jan; 23(1):1-2.
15. Panwar M, Kumari A, Arora R, Singh V, Bansiwal R. Raised neutrophil lymphocyte ratio and serum beta hCG level in early second trimester of pregnancy as predictors for development and severity of preeclampsia. Drug Discov Ther 2019 Feb; 13(1):34-7.
16. Vidyabati RK, Hijam D, Singh NK, Singh WG. Serum β-hCG and lipid profile in second trimester as predictors of pregnancy induced hypertension. J Obstet Gynecol India. 2010;60(1):44-50.
17. Moslemizadeh N, Moslemizadeh KY. Serum β-hCG levels in diagnosis and management of preeclampsia. J Med Sci. 2008;8(8):722-7.