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ORIGINAL ARTICLE

Prediction of PIH by Maternal Serum Beta HCG Levels in the Second Trimester (13–20 Weeks) of Pregnancy

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Abstract

Objective To test the hypothesis that women with high serum beta-HCG levels in early pregnancy are at higher risk of developing PIH.

Methods Serum beta-HCG estimation was done by CLIA method in 200 women between 13 and 20 weeks of gestation, selected randomly for this study from July 2008 to Aug 2009. Multiple of median (MOM) was calculated from charts of norms available for that week of pregnancy. They were followed till delivery for development of PIH and pregnancy outcome and results analysed statistically with Chi-square test and *Z* test.

Results Out of 200 cases, 178 (89 %) were finally evaluated. Of whom 22 (12.36 %) cases developed PIH. Beta HCG levels were considered raised if the levels were >2MOM.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 ≤2 MOM (*P* value <0.001). Also, higher levels of beta HCG are associated with increased severity of PIH (*P* value <0.01). The sensitivity was 90.91 %, specificity was 97.44 % and positive predictive value was 83.33 %.

Conclusion The study concluded that the serum beta HCG estimation at mid trimester (13–20 weeks) is a good predictor of PIH and higher levels of beta HCG are associated with increased severity of PIH.

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Introduction

Pregnancy induced hypertension (PIH) is a unique disease seen only in pregnancy affecting 12–15 % of all pregnant women. In spite of improvement in maternal and neonatal care, PIH and its sequelae are a dreaded complication of pregnancy. It is indeed a constant endeavour of obstetricians to identify the risk involved in pregnancy and if possible its prediction. If prediction become possible, prevention will follow naturally. Several test have been proposed but none has been accepted widely due to their low predictive value.

The abnormal placentation has been considered as one of the initial event in the disease process. Hsu et al. [1] hypothesized that during mid trimester, immunological changes occur in the trophoblasts, resulting in secretory response, which is seen as a rise in the beta HCG levels. In this study we have tried to find out whether beta HCG can predict the development of PIH.

Materials and Method

This study was conducted in Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur from July 2008 to August 2009 on 200 pregnant, normotensive, nonproteinuric women selected randomly between the gestational age of 13–20 weeks attending the ANC clinics, irrespective of parity. Women with multiple pregnancy, congenital malformation, essential hypertension, diabetes mellitus, molar pregnancy and history of down syndrome were excluded from the study. Gestational age was calculated from the reliable menstrual history dates and early ultrasonographical measurement of fetal crown-rump length. The serum beta-HCG estimation was done by chemiluminescent immunometric assay (CLIA) method. The multiple of median (MOM) was calculated from the median of the diagnostic test employed for the current study (Diagnostic Products Corporation, U.S, Immulite 2000-HCG) for the HCG was considered raised if levels were more than 2MOM.

The cases were followed till delivery and observed for development of PIH. PIH is defined as hypertension $\geq$140/90 mmHg after 20 weeks of gestation with or without proteinurea in previously normotensive and normoproteinuric women measured on two occasions at least 6 h apart.

Result so obtained were evaluated and analyzed statistically. Chi-square test was applied.

Results

Two hundred women were enrolled but only 178 (89 %) women were completely followed till term. Table 1 shows the recruitment of the cases.

There was no statistically significant association found between maternal age, parity and religion but occurrence of PIH was more among primiparas (Table 2).

As shown in Table 3 out of a total 178 cases finally evaluated, 154 cases (86.51 %), had beta HCG levels $\leq$2MOM, whereas 24 cases (13.48 %), had values >2 MOM. Out of 154 cases with beta HCG levels $\leq$2 MOM, only 2 cases (1.2 %) developed PIH. And out of 24 cases with beta HCG values >2MOM, 20 cases (83.33 %) developed PIH, and only 4 cases (16.66 %) were normotensive. The P value for this parameter was <0.001, which was highly significant.

Table 2 Distribution of cases according to parity and occurrence of PIH

Parity	No. of cases (%)	Women with PIH (%)	Women without PIH (%)
Primi para	94 (52.80)	16 (17.02)	78 (82.98)
Multi para	84 (47.20)	6 (7.14)	78 (92.86)
Total	178 (100)	22 (13)	156 (87)

Chi-square = 3.136, degree of freedom 1, P value = 0.07

Table 3 Distribution of cases according to hypertensive status and HCG levels

HCG levels (MOM)	No. of cases	Normotensive	PIH	
			Mild PIH	Severe PIH
$\leq$2	154 (86.51 %)	152 (98.70 %)	2 (1.30 %)	0
>2	24 (13.49 %)	4 (16.66 %)	7 (29.16 %)	13 (54.16 %)
Total	178	156	9	13

Chi-square = 126.514 with 1 degree of freedom, $P < 0.001$

Table 4 Relation of beta HCG level with severity of PIH

Beta HCG levels (miu/ml)	No. of cases	Normotensive (%)	PIH patients	
			Mild PIH (%)	Severe PIH (%)
<30,000	9	9 (100)	–	–
30,000–40,000	72	71 (98.61)	1 (1.38)	–
41,000–50,000	65	64 (98.46)	1 (1.53)	–
51,000–60,000	10	10 (100)	–	–
61,000–70,000	5	1 (20)	4 (80)	–
71,000–80,000	2	–	1 (50)	1 (50)
81,000–90,000	4	1 (25)	–	3 (75)
91,000–1,00,000	5	–	1 (20)	4 (80)
>1,01,000	6	–	1 (16.66)	5 (83.33)
Total	178	156 (87)	9 (5)	13 (7)

As is seen from Tables 4 and 5 the increasing beta HCG levels have a direct association with the severity of PIH. One case (7.69 %) out of 8 in <80,000 mIU/ml group had severe PIH, while for >80,000 mIU/ml group 12 cases (85 %) out of 14, had severe PIH, giving a P value of <0.01, which is statistically significant.

Table 1 Outcome of pregnancy after recruitment

Total no. of cases	Missed abortion (%)	Spontaneous abortion (%)	Lost to follow up (%)	Congenital malformations (%)	No. of cases followed till delivery (%)
200	3 (1.5)	10 (5)	4 (2)	5 (2.5)	178 (89)

Table 5 Distribution of cases according to beta HCG level and severity of PIH

Beta HCG level (miu/ml)	PIH severity		Total (%)
	Mild (%)	Severe (%)	
≤80,000	7 (77.78)	1 (7.69)	8 (36.36)
>80,000	2 (22.72)	12 (92.31)	14 (63.64)
Total	9 (100.00)	13 (59.09)	22 (100.00)

Chi-square = 7.167, degree of freedom = 1, $P < 0.01$

The study establishes the validity of beta HCG as a predictor of PIH with the sensitivity of 90.91 %, specificity of 97.44 %, and a positive predictive value of 83.33 %.

Discussion

Since the year 1950 HCG is reported to be elevated in toxemic pregnancy. In our study women with higher levels of beta HCG (>2 MOM) during the second trimester of pregnancy, developed PIH later in their pregnancy, with *P* value <0.001 which was statistically significant. 83.33 % of women with elevated levels of beta HCG developed PIH with sensitivity 90.91 %, specificity 97.44 % and the positive predictive value 83.33 %.

In a study by Desai and Rao [2], 62 cases out of 90 (68.9 %) with values of beta HCG > 2MOM developed PIH against 21 cases out of 130 (16.15 %), having a beta HCG value < 2 MOM. The difference was statistically significant (*P* value <0.001).

Roiz-Hernandez et al. [3], showed that with a cut off value of 2 MOM for beta HCG in multipara and primigravida during second trimester, area below the curve was 0.96 and 0.95, respectively, sensitivity was 88.5 and 100 %, respectively, the positive predictive value was 0.46 and 0.25, respectively, and the negative predictive values were 0.99 and 1.0.

Kabukcu et al. [4] studied 610 pregnant women in second trimester, grouping them according to the multiple of median (MOM) of beta HCG and found that women with elevated second trimester human chorionic gonadotropin levels (>2 MOM) are at increased risk for preeclampsia (Odds ratio 5.93, 95 % confidence interval 1.97 to 15.88).

In the present study, the increasing beta HCG levels (in mIU/ml) showed a direct association with the severity of PIH. Similar results were shown in study by Jaiswar et al. [5] in which the author concluded that there was a positive correlation between the absolute beta HCG levels and the severity of PIH.

Conclusion

The study showed that measuring second trimester beta HCG levels is useful in clinical practice to identify women who will develop PIH in the same pregnancy. Also, higher levels of beta HCG are associated with increase severity of PIH. The sample size for this study being small, necessitate the need of further large scale studies considering the importance of BETA-HCG in PIH prediction.

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