WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 7, Issue 2, 722-727. Research Article ISSN 2277– 7105

SECOND TRIMESTER MATERNAL SERUM BETA HCG LEVEL AS A PREDICTOR OF PREGNANCY INDUCED HYPERTENSION

Dr. Asha Sadanand Joshi,* Dr. Kanchan Kunal Joshi, Dr. Sadanand Balkrushna Joshi, Dr. Kunal Sadanand Joshi

Consultant Anand Hospital, Islampur.

Article Received on
18 November 2017,

Revised on 09 Dec. 2017,
Accepted on 31 Dec. 2017

DOI: 10.20959/wjpr20182-10651

***Corresponding Author**
Dr. Asha Sadanand Joshi
Consultant Anand Hospital, Islampur.

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 400 women between 13 and 20 weeks of gestation, from Jan 2015 to March 2017. 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. **Results:** Out of 400 cases, 356 (89%) were finally evaluated. Of whom 44(12.36%) cases developed PIH. Beta HCG levels were considered raised if the levels were >2MOM. 40 (83.33%) out of 48 cases with beta HCG levels >2MOM developed PIH against 4 (1.2%) cases out of 308 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.

KEYWORDS: Beta HCG, Pregnancy Induced Hypertension (PIH).

INTRODUCTION

Pregnancy-induced hypertension (PIH) includes both gestational hypertension and preeclampsia. It is considered as common pregnancy complication for which the pathogenesis remains unclear. Pregnancy induced hypertension is considered one of the main public health issues worldwide and major cause of mortality both in mother and foetus.[1],[2],[3] 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 American College of Obstetricians and Gynaecologists (ACOG) has classified pregnancy induced hypertension (PIH) into four groups of disorders: gestational hypertension, where resting BP is 140/90 mmHg or higher after the 20th week of gestation; Chronic hypertension, that exists before pregnancy or begins in the first 20 weeks of gestation; preeclampsia (raised BP and edema or proteinuria)/Eclampsia (preeclampsia and seizures); and preeclampsia superimposed on chronic hypertension.[4],[5] PIH may be followed by acute renal failure, maternal death, premature delivery, intra-uterine growth restriction etc. It is seen only in pregnancy, affecting 12–15 % of all pregnant women.

The abnormal placentation has been considered as one of the initial event in the disease process. Hsu et al[6] 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 METHODS

This study was conducted in Anand Hospital, Islampur, Maharashtra from Jan 2015 to March 2017 on 400 pregnant, normotensive, nonproteinuric women 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 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 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

Four hundred women were enrolled but only 356 (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 356 cases finally evaluated, 308 cases (86.51 %), had beta HCG levels ≤2MOM, whereas 48 cases (13.48 %), had values ≥2 MOM. Out of 308 cases with beta HCG levels ≤2 MOM, only 4 cases (1.2 %) developed PIH. And out of 48 cases with beta HCG values ≥2MOM, 40 cases (83.33 %) developed PIH, and only 8 cases (16.66 %) were normotensive. The P value for this parameter was\0.001, which was highly significant.

Table 1: Outcome of pregnancy after recruitment.

Total No cases	Missed Abortions	Spontaneous abortions	Lost to follow up	Congenital malformations	No. Of cases followed
400	6 (1.5%)	20 (5%)	8 (2%)	10 (2.5%)	356 (89%)

Table No 2: Distribution of cases according to parity and occurrence of PIH.

Parity	No. Of cases	Women with PIH	Women without PIH
Primi para	188 (52.80%)	32 (17.02%)	156 (82.98%)
Multi para	168 (47.20%)	12(7.14%)	156 (92.86%)
Total	356 (100%)	44 (13%)	312 (87%)

Chi square= 3.136, degree of freedom 1, p value= 0.07

Table No 3: Distribution of cases according to hypertensive status and HCG levels.

HCG levels (MOM)	No. Of cases	Normotensive	PIH patients	
			Mild PIH	Severe PIH
≤2	308 (86.51%)	304 (98.70%)	4(1.30%)	0
≥2	48 (13.49%)	8 (16.66%)	14(29.16%)	26(54.16%)
Total	356	308	18	26

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

Table No 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	18	18 (100%)	-	-
30,000-40,000	156	142 (98.61%)	2(1.38%)	-
41,000-50,000	130	128 (98.46%)	2(1.53%)	-
51,000-60,000	20	20 (100%)	-	-
61,000-70,000	10	2 (20%)	4 (80%)	-
71,000-80,000	4	-	2 (50%)	2 (50%)

81,000-90,000	8	2 (25%)	-	3 (75%)
91,000-1,00,000	10	-	2 (20%)	8 (80%)
>1,01,000	12	-	2(16.66%)	10(83.33%)
Total	356	312 (87%)	18 (5%)	26 (7%)

Table No 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	14 (77.78%)	2 (7.69%)	16 (36.36%)
≥80,000	4 (22.72%)	24 (92.31%)	28 (63.64%)
Total	18 (100%)	26 (59.09%)	44 (100%)

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

As is seen from Tables 4 and 5 the increasing beta HCG levels have a direct association with the severity of PIH. Two cass (7.69 %) out of 16 in<80,000 mIU/ml group had severe PIH, while for >80,000 mIU/ml group24 cases (85 %) out of 28, had severe PIH, giving a P value of <0.01, which is statistically significant. 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[7], 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,[8] 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.[9] 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 gonadotropins 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. [10] 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 concluded that measuring second trimester serum Beta- HCG levels is a good predictor of pregnancy induced hypertension and helps in risk stratification of women destined to develop pregnancy induced hypertension 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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