ORIGINAL RESEARCH PAPER

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EARLY SECOND TRIMESTER MATERNAL SERUM β-HCG LEVEL AS PREDICTOR MARKER OF HYPERTENSIVE DISEASE OF PREGNANCY

KEY WORDS:

Dr. Chhitar Mal Yadav Resident Doctor Dept. of Obs & Gynae, JLN Medical College Ajmer.

Dr. Purnima Pachori Senior Professor Dept. of Obs & Gynae, JLN Medical College Ajmer.

Dr. Dharmendra Singh Fatehpuriya* Associate Professor Dept. of Obs & Gynae, JLN Medical College Ajmer. *Corresponding Author

ABSTRACT

INTRODUCTION - Hypertensive disorders of pregnancy (HDP) are one of the dreaded complications of pregnancy contributing significantly to maternal and fetal morbidity and mortality. It affects about 12-15% of the pregnancies. They have been found to be linked with complications like intra uterine growth retardation (IUGR), premature delivery, and increased perinatal morbidity and mortality. Although improvements in obstetric and neonatal care have led to reduction in morbidity and mortality from hypertensive disorders, our ability to predict the condition has not improved significantly. 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. **MATERIAL & METHOD-**The study was carried out on 200 pregnant women attending the ANC OPD at antenatal visit in the Department of Obstetrics and Gynaecology, JLN Medical College, Ajmer. **RESULT-** There was a statistically notable association between absolute values of Beta HCG and the severity of P.I.H (p value<.01.). So higher the maternal serum levels of beta HCG, more are the likelihood of developing severe P.I.H. **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.

INTRODUCTION

Hypertensive Disorder is one of the most common medical complications affecting 12-15% of all pregnancies. [1] It is among the leading causes of maternal mortality, along with thromboembolism, haemorrhage. 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 occurring after 20 weeks gestation and resolves within 12 weeks postpartum.

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.

The pathogenesis of PIH appears to be reduction of uteroplacental perfusion as a result of abnormal cytotrophoblast invasion of spiral arterioles. Placental ischaemia is thought to cause widespread activation or dysfunction of the maternal vascular endothelium which results in enhanced formation of endothelin and thromboxane, increased vascular sensitivity to angiotensin II, and decreased formation of vasodilators such as nitric oxide and prostacyclin (Granger et al. 2001). Human chorionic gonadotrophin (hCG) hormone is a sialylated glycoprotein with a mass of 37 kDa, which is secreted by syncytiotrophoblastic cells of the normal placenta. The hCG molecule is made up of 237 amino acids and consists of two dissimilar□ and □ subunits. The □-subunit is unique to hCG. During pregnancy, serum hCG concentration increases gradually and reaching a peak at 8 to 10 weeks of gestation and progressively declines from 12 weeks of pregnancy to a plateau at 18 to 20 weeks of gestation (Yaron et al. 1999) & and maintained at these lower levels throughout the pregnancy. Early recognition of PIH is essential to prevent adverse fetomaternal outcome. 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.

AIMS AND OBJECTIVES

To find out the sensitivity of early 2nd Trimester (13 to 20 weeks) serum beta HCG in prediction of hypertensive disease of pregnancy and its severity, thereby to follow up the at risk patients and to prevent the development of hypertensive disease of pregnancy by prophylactic measures and to prevent its complications.

MATERIAL AND METHODS

The study was carried out on 200 pregnant women attending the ANC OPD in the Department of Obstetrics and Gynecology, JLN Medical College, Ajmer. This study will be conducted from Jan 2019 to Dec 2019, after obtaining informed consent.

INCLUSION CRITERA

Pregnant women with Non protein uric, Normotensive, Primi/Multi gravida, Singleton, Gestational age 14-20 weeks as determined by last menstrual period or ultrasound scan.

EXCLUSION CRITERIA

Chronic hypertension, Molar Pregnancy, Diabetes mellitus, Anomalous foetus, Multiple pregnancies.

METHODOLOGY:

All 200 women included in this study were subjected to a detailed examination history regarding age, parity, past obstetric history, systemic examination, routine antenatal investigations, medical history, and family history. Height, weight, blood pressure was measured.

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. At every visit, blood pressure was recorded and urine was examined for albumin. HDP included gestational hypertension, preeclampsia and eclampsia. 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 protenuria of atleast 1 + on dipstick. Eclampsia is development of convulsion in a woman with preeclampsia.

COLLECTION OF SAMPLES

Under strict aseptic conditions, 3 ml of venous whole blood sample was collected from each subject in a plain, dry and properly labeled bottle. Precaution was taken to prevent haemolysis. (Samples were brought to Biochemistry Laboratory, JLN Medical College, Ajmer) Samples were centrifuged after clotting and retraction at room temperature, Clear serum was collected and subsequently analyzed for the parameter serum -human Chorionic Gonadotrophin. Estimation of serum hCG level was done by enzyme linked fluorescence immunoassay.

STATISTICAL ANALYSIS :

The data was subjected to descriptive statistical analysis to find out Means and Standard Deviation values and One Way Analysis of Variance (One Way ANOVA) to decipher the intra and inter group variations of the study subjects from both control and experimental groups. In addition, the correlation coefficients was also used for all the groups studied to understand the extent of relationships between the important variables pertaining to physical and biochemical parameters like gestational age, systole, diastole and serum □-hCG. P<0.05 and P<0.01 will be considered statistically significant.

RESULTS

The present study was carried out to find out the sensitivity of serum beta HCG in prediction of hypertensive disease of pregnancy and its severity on 200 pregnant women attending the ANC OPD in the Department of Obstetrics and Gynecology, JLN Medical College, Ajmer. In our study, out of the 200 total cases selected for this study, ultimately 178 could be evaluated for the final results. The 22 cases that were left out were due to, missed abortion (3), Spontaneous abortion (10), Congenital malformations (5) and 4 cases were lost to follow up. In all, 178 cases i.e. 89% of the initially selected cases were followed till the final outcome.

Table 1: Distribution of cases according to hypertensive status and HCG

HCG levels (MOM)	Number of cases	NORMOTENSIVE	PIH	
			MILD PIH	SEVERE PIH
≤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

The above table shows the distribution of number of cases according to levels of beta HCG in multiples of median (MOM) and occurrence of PIH for the present study. Out of a total 178 cases final evaluated, 154 cases (86.51%), had beta HCG levels, ≤MOM, whereas 24 cases (13.48%), had values >2 MOM. Out of 154 cases with Beta HCG levels ≤2 MOM, only 2 cases (1.2%) developed PIH.

The remaining cases, 152 (98.70%), were normotensive. 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 when calculated for the development of PIH, came out to be <0.001, which is highly significant.

Table 2: Distribution according to gestational age, beta HCG levels and PIH occurrence

Gestational age gp. (in wks.)	No. of cases	Beta HCG levels (MOM=Multiples of Median)		Women with PIH	Women without PIH
13-14	62	<2MOM	54(87%)	1(1%)	53(98.14%)
		>2MOM	8(12%)	7(87%)	1(13%)
15-16	54	<2MOM	47(88%)	1(2%)	46(97.87%)
		>2MOM	7(11%)	6(85.71%)	1(14.28%)
17-18	53	<2MOM	44(86%)	-------	44(100%)
		>2MOM	9(13%)	7(77.77%)	2(22.22%)
19-20	9	<2MOM	9(100%)	------	9(100%)
		>2MOM	------	------	-----
Total	178			22(13%)	156(87%)

The above table shows the relationship between the gestational age, the beta HCG levels, and the subsequent PIH development in the 178 cases taken up for final evaluation. As is evident from the table, majority of the cases belonged to the 13-14 wk. gestational age group and had a 12% incidence of the cases where beta HCG levels were >2MOM, and out of these, 87% cases had subsequent PIH development, which is significant. When similar figures are seen for the 15-16 wks and 17-18 wks, 85.71% and 77.77% cases respectively, having beta HCG levels >2 MOM developed PIH.

Table 3: Relation of beta HCG level with severity of P.I.H

Beta HCG levels(Miu/ml)	No of cases	Normotensive	PIH patients	
			Mild PIH	Severe PIH
<30,000	9	9	------	-------
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%)	------	-------
61000,70,000	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%)**

The above table defines the association between the individual beta HCG levels (in mlU/ml), and the severity of PIH. As is seen above, the maximum PIH cases, 14 out of 22, are seen to be developing in the group with beta HCG levels in the higher ranges, i.e. > 80,000 mlU/ml. Also, it can be seen that the severe PIH cases are proportionately on the increase, as the beta HCG levels rise.

Table 4: Distribution of cases showing validity of HCG as Predictor of PIH

	Test Normal (HCG≤2)	Test Abnormal (HCG>2)	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value
With PIH	2	20	90.91	97.44	83.33	98.70
Without PIH	152	4				

DISCUSSION

In the present study, the increasing Beta HCG levels (in mlU/ml) showed a direct association with the severity of PIH. While 1 case out of 8, i.e. 12% with a Beta HCG value<80,000 mlU/ml, group had PIH, the similar figure for >80,000 mlU//ml group was 12 out of 17 i.e. 70.50%. Giving a p value of <.01, which is statistically significant. So, it was concluded that as the Beta HCG levels rise, the probability of developing severe PIH also increases with a positive association between these parameters.

Similar results have been shown by Zhonghua et al, 2000[51], in which the author concluded that there was a positive correlation between the absolute Beta HCG levels and the severity of PIH, (p value <.05). The serum level of Beta HCG in the mild PIH gp was 25,330±17,800 and in severe PIH gp, 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.

In my study, it was seen that as the severity of PIH increases, so do the chances of having caesarean section, rather than the vaginal delivery. While only 32 cases out of 156 normotensive mothers (20.51%), had LSCS (lower segment Caesarean Section), 13 out of 22 mothers with PIH had LSCS (59.09%). Among these cases also, most belonged to the severe PIH group (84.6%). P value for this association was highly significant (<0.001), indicating that the patient is at more risk of operative delivery with the increasing severity of PIH.

In our study out of 156 normotensive pregnant women 125 (80.12%) delivered vaginally and 31 (19.18%) delivered by LSCS and out of 9 mild PIH pregnant women 7(77.8%) were delivered vaginally and 2(22.2%) delivered by LSCS and out of 13 severe PIH pregnant women 3(23.07%) were delivered vaginally and 10(76.93%) delivered by LSCS. This implies that LSCS rate was more in PIH patients. Similar result found by Sanyukta S Dawle et al, 28.75% women delivered vaginally at term in women with pregnancy-induced hypertension as compared with 54.375% normotensive women; 71.25% women had cesarean sections in women with pregnancy-induced hypertension as compared with 45.625% normotensive women. There were no instrumental deliveries. The difference in mode of delivery in both the groups was statistically significant (p = 0.0001). The most common indication for cesarean section in women with pregnancy-induced hypertension was abnormal Doppler and fetal distress.

As regards to the fetal outcome and pregnancy related fetal complications, as the severity of PIH increases, there is an increase in fetal complications, namely in terms of IUGR (38.46% in severe PIH vs. 3.85% in normotensive) and IUD (15.38% in severe PIH vs. 1.92% in normotensive). This has been shown in a study by Song KC et al, 2001[41], women with unexplained elevation of Beta HCG level showed increased risks of PIH (p<.001) and preterm delivery (p<.003). This further necessitates the need for continuous fetal health monitoring and timely active management in PIH cases. In another study of 6011 women by R.Gonen et al, 1992[15], 284(4.7%) had unexplained levels of Beta HCG, and had a significant higher risk for Fetal growth restriction (odds ratio 2.8; 95% CI 1-7) Women with HCG levels >4 MOM also had an increased risk of preterm delivery (odds ratio 3.3; 95% CI 1.3-8.2).

CONCLUSIONS

Serum beta HCG level measurement during midtrimester (13-20 weeks) acts as an efficient non-invasive predictive marker for the development of hypertensive disorders in pregnancy. There was statistically significant association among absolute values of Beta HCG and the severity of P.I.H (p value<.01.). The legitimacy of Beta HCG as a predictor of PIH was established with a sensitivity of 90.91%, specificity of 97.44%, and a positive predictive value of 83.33%. 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.

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