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Maternal Serum Beta Human Chorionic Gonadotropins as a Predictor for Pregnancy Induced Hypertension

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Abstract

Context: If it is possible to predict PIH, then its prevention can be undertaken. In this direction many attempts have been made to find out a suitable test which can predict the occurrence of PIH in pregnancy, but till date such type of test was not found. *Aims:* To study the role of maternal serum beta human chorionic gonadotropins as a predictor for pregnancy induced hypertension. *Settings and Design:* Hospital based follow up study carried out at Chalmeda Anand Rao Institute of Medical Sciences, Karimanagar. *Methods and Material:* Present study was carried out among women of 13-20 weeks gestation. They were divided into two groups. Group I consisted of 90 normotensive women and group II consisted of 10 women with Pregnancy induced hypertension. Maternal serum beta hCG was measured and mean values were compared in both the groups. *Statistical Analysis:* Chi square test was applied to study significance of difference between proportions and t test was used to study significance of difference between mean values. *Results:* It is found that severity of PIH correlated with serum beta hCG levels in hypertensive patients. The mean serum beta hCG levels were significantly higher in PIH group compared to normotensive group. The sensitivity of beta hCG in predicting occurrence of PIH was 100%, specificity was 97.7%, positive predictive value was 83.3% and negative predictive value was 100%. Women with > 2 MOM of beta hCG had 6 times more risk of having PIH compared to women with beta hCG < 2 MOM. The mean Serum beta hCG for low birth weight, IUGR and pre-term delivery was significantly higher in PIH group compared to normotensive group. *Conclusion:* Early detection by screening tests and appropriate treatment may prolong pregnancy long enough to ensure a satisfactory outcome for both mother and fetus. Serum beta hCG levels were found to be effective in early prediction of PIH.

Keywords: IUGR; Beta hCG Levels; Normotensive.

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Introduction

The incidence of Pregnancy induced hypertension (PIH) is 12-15%. It leads to many complications of pregnancy which are grave in nature. If it is possible to predict Pregnancy induced hypertension, then its prevention can be undertaken. In this direction many attempts have been made to find out a suitable test which can predict the occurrence of Pregnancy induced hypertension in pregnancy, but till date such type of test was not found [1].

Pregnancy induced hypertension is harmful for mother as well as baby. It is difficult to predict. It is not easy to understand the progression of Pregnancy induced hypertension [2]. Exact causes could not be found. Various hypotheses have been suggested as cause of Pregnancy induced hypertension. It has been related with few biochemical markers. Some studies have highlighted that serum β-hCG levels are increased in mother during second trimester

and such women subsequently developed Pregnancy induced hypertension [3]. hCG is secreted by placenta. Various studies correlated increased levels of serum β-hCG and occurrence of Pregnancy induced hypertension [4].

Pregnancy induced hypertension can cause various complications like intra uterine growth retardation, pre term labor, low birth weight etc. it can be harmful to the baby also. Various screening tests were tried; for example diastolic blood pressure more than 80 mmHg before 20 weeks of gestation. But this was found to be only 32-46% sensitive and specificity ranged between 84-91%. Second trimester mean arterial blood pressure more than 90 mmHg was tried; but it shows a huge variability in sensitivity ranging from 8-73% with a specificity ranging from 48-90%. Certain biochemical tests like increased uric acid was tried which has shown a reasonable sensitivity of 88% and a high specificity of 97%. Increased fibronectin test showed a very low sensitivity of 38% with high specificity of 97%. But these also were not relied upon by the practitioners.

Hence based on previous studies we attempted to study efficacy of maternal serum β-hCG in predicting the occurrence of pregnancy induced hypertension in our settings.

Materials and Methods

A hospital based follow up study was carried out at Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar for a period of two years from September 2014 to August 2016. A total of 100 women were randomly selected for the present study.

Women in the gestational age of 13-20 weeks willing to participate in the present study were included. Women with known case of diabetes, known case of hypertension, women with Rh negative blood group, women having multiple pregnancy and any women who had fetus with congenital anomalies as seen from ultra sonography and finally women not willing to participate in the present study were excluded from the present study. The reason for excluding these women from the present study was that the conditions mentioned above will be associated with hyper placentosis and therefore exhibit increased levels of maternal serum β-hCG levels. This would have confounded the findings of the present study. Hence they were excluded from the present study.

After obtaining detailed history, and carrying out thorough clinical examination, 2 ml of blood was drawn; serum was separated and stored at 2-8^{0}C. maternal serum β- hCG was estimated by ELISA method.

The women were followed till they developed pregnancy induced hypertension. all women were followed till delivery to note any evidence of pregnancy induced hypertension and fetal outcome like low birth weight, intra uterine growth retardation, pre term delivery etc. in comparison to their maternal serum β-hCG levels. In the present study we found that out of 100 women who finally were counted till the end of the present study, after considering lost to follow up or lost to development of complications, 10 women developed pregnancy induced hypertension. 90 women did not develop pregnancy induced hypertension. Hence these 90 normotensive women were placed in group I. 10 women developing complications were placed in pregnancy induced hypertension group or group II. All the data was properly recorded. Mean values of maternal serum β-hCG levels in different groups like normotensive women, women with pregnancy induced hypertension, women with low birth weight babies, women with intra uterine growth retardation, women with pre term deliveries were tabulated and compared. Student's t test was used to find significance of difference between the mean values. Chi square test with Yate's correction was used to find significance of difference between the proportion values. P value of less than 0.05 was taken as statistically significant.

Results

Table 1 shows serum β-hCG levels in both the groups. It is found that severity of PIH correlated with serum β-hCG levels in hypertensive patients. A rise is seen in serum β-hCG levels with rise in severity of pregnancy induced hypertension. The mean serum β-hCG levels were significantly higher in PIH group compared to normotensive group.

Table 2 shows efficacy of serum β-hCG levels in predicting PIH. The cut off value for sensitivity and specificity was taken as 2 multiple of median (MOM). Total 12 patients had β-hCG > 2 MOM and 88 had < 2 MOM. Out of 12 who had > 2 MOM (true positives), 10 developed PIH compared to only 2 who had > 2 MOM out of 88 normotensive (false positives). There were no false negatives. 88 out of 90 normotensive were true negatives. Thus the sensitivity of β-hCG in predicting occurrence of PIH was 100%, specificity was 97.7%, positive predictive value was 83.3% and negative predictive value was 100%. All this was statistically significant. ($p < 0.001$).

Odds ratio was 6 (95% CI = 1.69-21.26), which meant that women with > 2 MOM of β-hCG had 6 times more risk of having PIH compared to women with β-hCG < 2 MOM.

Table 3 shows effect of serum β-hCG levels on pregnancy outcome. The mean Serum β-hCG for low birth weight was significantly higher in PIH group compared to normotensive group. The mean Serum β-hCG for intra-uterine growth retardation (IUGR) was significantly higher in PIH group compared to normotensive group. The mean Serum β-hCG for pre term delivery was significantly higher in PIH group compared to normotensive group.

Table 1: Serum β-hCG levels in both the groups

Serum beta hCG (mIU/ml)	Group I (normotensive)	Group II (PIH)	P value
1000-2000	1	0	
2000-3000	7	0	
3000-5000	71	0	
5000-10,000	10	0	
10,000-15,000	1	0	
15,000-20,000	0	1	
> 20,000	0	9	
Total	90	10	< 0.0001
Mean levels	4313.4±1564	32793.6±7888	< 0.0001
Median levels	4044	32842	

Table 2: Efficacy of serum β-hCG levels in predicting PIH

Serum beta hCG (mIU/ml)	PIH	Normotensive
> 2 MOM (multiple of median) (> 8340)	10 (a)	2 (b)
< 2 MOM (multiple of median) (< 8340)	0 (c)	88 (d)

Table 3: Effect of serum β-hCG levels on pregnancy outcome

Pregnancy outcome	Mean Serum beta hCG (mIU/ml)		P value
	Group I (normotensive)	Group II (PIH)	
Low birth weight	6744.5	36620	< 0.001
IUGR	6652.6	37889.2	< 0.001
Pre term delivery	6081.9	34417.6	< 0.001

Discussion

It is found that severity of PIH correlated with serum β-hCG levels in hypertensive patients. A rise is seen in serum β-hCG levels with rise in severity of pregnancy induced hypertension. The mean serum β-hCG levels were significantly higher in PIH group compared to normotensive group. The cut off value for sensitivity and specificity was taken as 2 multiple of median (MOM). Total 12 patients had β-hCG > 2 MOM and 88 had < 2 MOM. Out of 12 who had > 2 MOM (true positives), 10 developed PIH compared to only 2 who had > 2 MOM out of 88 normotensive (false positives). There were no false negatives. 88 out of 90 normotensive were true negatives. Thus the sensitivity of β-hCG in predicting occurrence of PIH was 100%, specificity was 97.7%, positive predictive value was 83.3% and negative predictive value was 100%. All this was statistically significant. ($p < 0.001$). Odds ratio was 6 (95% CI = 1.69-21.26), which meant that women with > 2 MOM of β-hCG had 6 times more risk of having PIH compared to women with β-hCG < 2 MOM. The mean Serum β-hCG for low birth weight was significantly higher in PIH group compared to normotensive group. The mean Serum β-hCG for intra-uterine growth retardation (IUGR) was significantly higher in PIH group compared to normotensive group. The mean Serum β-hCG for pre term delivery was significantly higher in PIH group compared to normotensive group.

Jaiswar et al [5] estimated Serum β-hCG by ELISA in 150 pregnant women of 13-20 weeks of gestation age and followed them till delivery to assess the occurrence of pregnancy induced hypertension and fetal outcome. They found that incidence of pregnancy induced hypertension was 12%. The maternal serum β-hCG correlated with development of pregnancy induced hypertension and this finding was statistically significant. We also observed similar findings.

Ramsey P et al [6] studied 515 pregnant women and carried out estimation of serum hCG, progesterone and estriol levels between 11-20 weeks of gestation. They followed up the mothers till delivery

and found that in high risk women, it is the hCG, and not the estriol or progesterone was associated with pregnancy induced hypertension. Women with elevated hCG were 2.6 times more at risk of developing mild pregnancy induced hypertension as compared to their counterparts who demonstrated normal hCG levels. Women with elevated hCG were 3 times more at risk of developing severe pregnancy induced hypertension as compared to their counterparts who demonstrated normal hCG levels.

Vyas N et al [7] studied 48,028 women of which 166 had hCG levels greater than 4 MOM (multiple of median) for gestational age. These patients had markedly higher rate of still birth i.e. 3%, pregnancy induced hypertension i.e. 19%, abruption in 6%, and second trimester fetal loss in 7%. Intra uterine growth retardation was seen in 4% of the cases while pre term delivery was seen in 7% of the cases. The women who were screened too early, who had an indeterminate screening result or who had multiple gestations were excluded. These findings support the findings of the present study.

Sujatha Chandra et al [8] carried out a study among 14,374 women. They found that among these 5,789 was high risk. Women with elevated hCG were 1.45 times more at risk of developing pregnancy induced hypertension as compared to their counterparts who demonstrated normal hCG levels. Women with elevated hCG were 4.09 times more at risk of having fetal death as pregnancy outcome as compared to their counterparts who demonstrated normal hCG levels.

Endres LK et al [9] studied women at 15-20 weeks of gestation. They divided them into two groups. 146 were in experimental group and 292 were in control group. They observed that women with low hCG levels had better pregnancy outcome as compared to their counterparts with higher hCG levels. We also observed similar findings.

Satyanarayana K et al [10] studied women at 16-20 weeks of gestation in their follow up study. The incidence of pregnancy induced hypertension was 10.8%. We also observed an incidence of 10% for pregnancy induced hypertension. They also noted that the incidence of elevated hCG levels was more in women with pregnancy induced hypertension than women without pregnancy induced hypertension. We also noted similar observation in the present study.

Conclusion

We conclude that maternal serum hCG levels can be used to predict occurrence of pregnancy induced hypertension in pregnant women from second trimester as this test has given 100% sensitivity and a very high degree of specificity of 97.7%. Positive predictive and negative predictive value was also very high being 83.3% and 100% respectively. Other studies also support this concept. Hence maternal serum hCG levels can be used to predict occurrence of pregnancy induced hypertension in pregnant women.

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