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Original Research Article

Serum beta hCG in early second trimester as a predictor of gestational hypertension

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ABSTRACT

Background: Hypertensive disorders of pregnancy complicate upto 10% of pregnancies worldwide, and constitute one of the greatest causes of maternal and perinatal morbidity and mortality. The goal of this study is to evaluate the serum beta hCG levels in pregnant women as a predictor of gestational hypertension.

Methods: This is a prospective study done at K. S. Hegde Medical Academy during the month of November 2015 to January 2017. Serum beta hCG was estimated between 14-20 weeks of gestation in 90 women with singleton pregnancy irrespective of parity. Regular follow up of the cases were done till delivery. Results were analysed statistically.

Results: Out of 90 women, 81 women were followed till term and 12 (14.8%) cases developed gestational hypertension. β HCG levels (Mean \pm SD) were higher (69808.66 \pm 54764.7 vs. 38126.49 \pm 97419.2; $p < 0.28$) in subjects who developed gestational hypertension. Serum beta hCG (median > 32726 mIU/ml) has a sensitivity of 75%, specificity of 72.5% and accuracy of 72.8%.

Conclusions: Our study indicate an increased risk of gestational hypertension in women with elevated levels of serum beta hCG. As yet there are no practically acceptable and reliable screening tests for gestational hypertension, serum beta hCG seems to be good noninvasive early predictor for the development of gestational hypertension.

Keywords: Gestational hypertension (GH), hCG

INTRODUCTION

Hypertensive disorders of pregnancy complicate up to 10% of pregnancies worldwide, and constitute one of the greatest causes of maternal morbidity and mortality and perinatal morbidity and mortality. Preeclampsia either alone or superimposed on preexisting chronic hypertension presents the major risk.¹ The incidence of pre-eclampsia in India is about 8-10% and maternal mortality due to preeclampsia reported to be 8%. Preeclampsia complicates about 2-8% of all pregnancies.²

According to the National High Blood Pressure Education Program Working Group Report (2000), hypertensive disorders of pregnancy is classified as;

gestational hypertension, preeclampsia and eclampsia syndrome, superimposed preeclampsia on chronic hypertension and chronic hypertension.³

Numerous clinical, biophysical and biochemical tests have been proposed during the past two decades for the early detection of preeclampsia. Few of these tests are simple whereas others are non-invasive. Some studies have been studied extensively while others are still under clinical investigations. A review of literature indicates considerable disagreement regarding the sensitivity and predictive values of the various tests studied. The reported differences in the predictive values of these tests are attributed to one or more of the following; definition and prevalence of the disorder, population studied,

methodology and techniques in performing these tests, etc. Hence, there is a disagreement regarding the ideal screening test to be used for identifying women for clinical trials dealing with prevention of disorder.⁴

Most current hypothesis regarding the pathophysiologic mechanisms point to early placental abnormalities. Women with gestational hypertension have an abnormal placentation or hyperplacentosis. As placenta remains the primary source for hCG production, plasma hCG measurement has been proven to be effective screening tool for pregnancies with altered placental function or mass.

There is low oxygen tension in first trimester in a normal pregnancy which prevents the trophoblasts from differentiating towards an invasive phenotype. This mechanism is mediated by TGF β . This physiological increase in oxygen tension between 10-12 weeks of gestation determines a decrease in TGF β and allows trophoblasts to differentiate into a more invasive type. The levels of TGF β remains high in a preeclamptic women and hence the trophoblasts are arrested at an immature state, and their invasiveness is reduced. Because trophoblasts play a vital role in the development of preeclampsia, it is not surprising that few placental hormones change in maternal circulation, indicating a derangement of placental function. These hormones are increased in the maternal serum long before the onset of preeclampsia and have been proposed as early predictors of preeclampsia.

Women with overt preeclampsia in the third trimester have an elevated maternal serum beta hCG levels. Some advocate that the hCG secretion may be increased as a consequence of abnormal placental maturity or invasion. It may also be linked to the trophoblast response to the hypoxia as a result of a hypersecretory state.⁵

The goal of this study is to evaluate the serum beta hCG levels in pregnant women as a predictor of gestational hypertension.

METHODS

This prospective study was conducted in the Department Obstetrics and Gynecology, K. S. Hegde Medical Academy, Deralakatte, which is a tertiary care teaching institute in the state of Karnataka, India. This study was conducted between November 2015 and January 2017 including complete follow-up of the last case registered for the study. Patients were enrolled in the study after taken approval from hospital ethical committee and written informed consent from the patients.

Inclusion criteria

Primi/multi gravida with singleton pregnancy with gestational age 14-20 weeks as determined by last menstrual period or ultrasound scan.

Exclusion criteria

Patients having multiple pregnancy, chronic hypertension, diabetes mellitus, congenital anomalies were excluded from the study.

All the subjects were informed about the study and informed consent was taken before they were enrolled in the study. Women were subjected to detailed history including age, parity, height, pre-pregnancy weight, and weight at the time of blood collection. Family history, past obstetric history, past medical history, smoking habits, medical histories of first degree family members was taken. Systemic examination with special reference to edema, blood pressure and gestational week was carried out and routine antenatal investigations were done. Gestational age was calculated from reliable last menstrual history and early ultrasonographic measurement of fetal crown rump length. Venous blood (3 ml) was collected. Estimation of serum beta hCG was done by enzyme linked immune absorbent assay. All patients were followed up in antenatal clinic and examined 4 weekly till 28 weeks, fortnightly up to 34 weeks and thereafter weekly till delivery. At every visit, blood pressure was recorded.

Statistical analysis

The collected information was summarized using frequency, percentage, mean and standard deviation. The $p < 0.05$ was considered statistically significant.

The following diagnostic validity tests were used.⁶

- Sensitivity = true positive /true positive & false negative $\times 100$
- Specificity = true negative /false positive & true negative $\times 100$
- Positive predictive value (PPV) = true positive /true & false positive $\times 100$
- Negative predictive value (NPV) = true negative /true & falsenegative $\times 100$.
- Overall accuracy = true positive + true negative / total $\times 100$.

RESULTS

90 women were enrolled in this study, but only 81 (90%) women were followed completely till term. 9 women were lost to follow up. Out of the 81 women who completed the study, 12 (14.8%) cases developed GH and 69 women remained normotensive.

Table 1 depicts the comparison between the subjects. Mean age among GH group is 27.08 years and BMI in this group was 24.5kg/m². Normotensive group had a mean age of 26.8 years and BMI of 23.9kg/m². Comparison of age and BMI in both groups were almost similar.

Table 1: Comparison of subjects.

	GH	Normal	P value
Age in years	27.08±4.5	26.8±3.9	0.87
BMI	24.5±2.08	23.9±2.6	0.42

Table 2 shows the comparison of blood pressure at the time of booking among PIH and normotensive group (14-20weeks) did not vary significantly. Blood pressure at the time of delivery for GH women was significantly higher in comparison to the BP of normotensive group (p value <0.001). This is true for both systolic and diastolic blood pressures.

Table 3 compares the beta HCG between two groups, shows that beta HCG is higher in GH group when compared to the normotensive group but not statistically significant.

Table 2: Comparison of systolic and diastolic blood pressure between GH and normal group.

	GH (n=12)	Normotensive (n=69)	P value
BP			
Systolic (mmHg)	118.1±8.1	114.80±7.3	0.15
Diastolic (mmHg)	78.3±3.8	75.9±6.7	0.19
At delivery			
Systolic (mmHg)	139.1±20.6	118.4±8.3	<0.001
Diastolic (mmHg)	90±7.3	77.8±4.8	<0.001

Table 3 Comparison of Mean±SD of serum beta hCG between GH and normotensive group.

Variable	PIH (n=12)	Normotensive (n=69)	P value
Serum beta Hcg (mIU/ml)	69808.66±54764.7	38126.49±97419.2	0.28

Table 4: Relation of beta hCG and hypertensive status.

Beta hCG (mIU/ml)	GH (n=12) (%)	Normotensive (n=69) (%)	No. of cases
<20000	3 (7.5)	37 (92.5)	40
20000-30000	-	10 (100)	10
30000-40000	1 (1)	9 (90)	10
40000-50000	-	3 (100)	3
50000-60000	2 (40)	3 (60)	5
60000-70000	3 (60)	2 (40)	5
70000-80000	-	-	-
80000-90000	-	2 (100)	2
90000-100000	-	2 (100)	2
>100000	3 (75)	1 (25)	4
Total	12	69	81

Table 5: Calculation of beta hCG median among GH and normotensive group.

	Mean	Maximum	Median	Minimum	Percentile 25	Percentile 75
Normotensive beta hCG	38126.5	808000.0	16700.0	2068.0	10000.0	34955.0
GH beta hCG	69808.7	160600.0	58763.0	12535.0	24454.0	108975.0

Table 6: Test statistics^a.

Statistics	beta hCG
Mann-Whitney U	186.000
Wilcoxon W	2601.000
Z	-3.033
P value	0.002

^aGrouping variable: GH.

The median values of beta hCG is higher in the GH group with a median of 58763.0 and normotensive group has a median of 16700.0 and this is statistically significant with

a Mann Whitney U value of 186 and p value of 0.002 (Table 5 and Table 6). Receptor operative curve analysis was performed to get a cut off value of beta hCG in predicting GH. Analysis showed that values <32729 had a sensitivity of 75% and specificity of 72.5%. Area under the curve is 0.775 which is an indicator of reasonable predictability.

ROC curve

Table 7 depicts the diagnostic accuracy of serum beta hCG in prediction of GH. Serum beta hCG (>32726

mIU/ml) has a sensitivity of 75% and specificity of 72.5%. The test and the gold standard agree on 59 out of 81 having a diagnostic accuracy of 72.8%. The Kappa value of 0.306 indicates moderate agreement with a p value of 0.003.

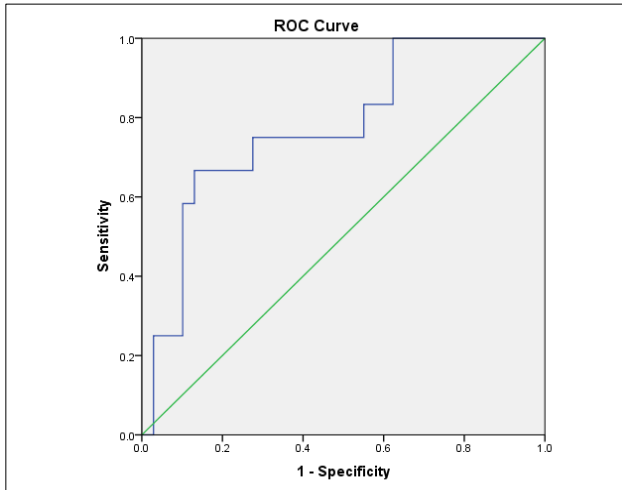


Figure 1: ROC curve.

Table 7: Sensitivity and specificity of beta hCG.

Study	Year	Sensitivity (%)	Specificity (%)	PPV (%)
Kaur gurumandeeep et al	2012	90.91	59	19
Satyanarayan et al	2001	14.29	87.93	12.5
Present study	2017	75	72.5	32.1

DISCUSSION

Among the 81 women who completed the study, 12 (14.8%) women subsequently developed GH and 69 women remained normotensive. In the study done by Vidyabati et al, 164 women at 14-20 weeks of gestation completed the study, 29 (17.7%) developed GH.⁷ In a study done by Satyanarayan et al, 200 women between 16-20 weeks of gestation were enrolled, 174 women completed the study out of which 21 (10.8%) developed GH.⁸ In the study done by Gurumandeeep et al, 178 women out of the 200 women enrolled completed the study. Out of which 22 (12.35%) developed GH and 156 remained normotensive.⁹

Age

In our study, mean age among the GH group was 27.08 years and among the normotensive group was 26.8 years. There was no significant difference between both the groups. In the study done by Vidyabati et al, the mean age was 27.17 years. It was observed that maximum GH was among the elderly primigravida’s belonging to the

age group of 31-35 years. In Satyanarayan et al, mean age group among GH group was 24.14 years and among the normotensive group was 24.27 years.

Blood pressure at booking

In our study, mean systolic blood pressure in GH group is 118.1 mmHg and diastolic BP is 78.3mmHg. In normotensive group it is 114.8 mmHg and 75.9 mmHg respectively. In Vidyabati et al, systolic blood pressure among the GH group was 120.7 mmHg and diastolic BP was 78.9 mmHg among the normotensive group. In Satyanarayan et al study, mean systolic blood pressure was 105 mmHg and mean diastolic blood pressure was 71.64 mmHg in normotensive group. Blood pressure at the time of booking between GH and normotensive group did not vary significantly.

Beta hCG

In the present study, incidence of GH with elevated beta hCG above 32726 mIU/ml was 32.1% when compared to women below 32726 mIU/ml was 5.7%.

The mean value of beta hCG was slightly higher in GH group than the normotensive group but was not statistically significant. Our study shows that maternal serum beta hCG has a sensitivity of 75% and specificity of 72.5% in predicting GH. In the study done by Vidyabati et al, 29 cases developed GH out of 164 women. Out of the 29 cases, 21 (72.4%) women had elevated beta hCG above 45000 mIU/ml. For every 1000 mIU/ml increase in serum beta hCG, 10.7% increase in chance of having GH. Study done by Kaur Gurumandeeep, 20 cases developed GH out of 24 women with beta hCG >2 multiples of median (MOM) as compared to 2 cases had GH out of 154 women with beta hCG ≤2 MOM which is statistically significant. Increasing beta hCG had direct association with the severity of GH. 1 out the 8 cases with <80000mIU/ml group had severe GH, while >80000mIU/ml group 12 out of 14 had severe GH with a significant p value <0.01.

The study conducted by Satyanarayn et al found no correlation between elevated serum beta hCG levels and GH. Mean hCG levels at mid trimester were non significantly higher in normotensive women (17112mIU/ml) when compared to those with GH (15666mIU/ml) women. 24 (12.3%) of the cases had elevated hCG levels on recruitment, out of which 21 (87.5%) remained normotensive and 3 (12.5%) developed GH. In study conducted by Desai et al, 62 out of the 90 cases had GH with beta hCG >2 MOM as compared to 21 out of 130 cases with beta hCG ≤2 MOM. It was also significant that 59 women out of 62 who developed GH had beta hCG >2 MOM before 32 weeks and on the other hand 18 out of 21 women with beta hCG <2 MOM developed GH after 32 weeks.¹⁰

CONCLUSION

Hypertensive disorders in pregnancy and its sequelae are a dreaded complication of pregnancy. There has been a constant attempt to identify the risk involved in pregnancy and its prediction. Prevention will follow if prediction is possible. Our study indicates an increased risk of GH in women with elevated beta hCG in second trimester. As yet there are no practical acceptable and reliable screening tests for gestational hypertension, serum beta hCG seems to be a very good noninvasive early predictor for the development of PIH.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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