Prediction of Pregnancy-induced Hypertension by Maternal Serum Beta Human Chorionic Gonadotropin Levels in Early Second Trimester of Pregnancy

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ABSTRACT

Objective: The study aims at testing the hypothesis that women with high serum beta human chorionic gonadotropin (β-hCG) in early second trimester have risk of developing pregnancy-induced hypertension and poor maternal and neonatal outcome. Early identification of at-risk women may help in taking timely preventive and curative management to prevent or delay complications associated with pregnancy-induced hypertension.

Materials and methods: Serum β-hCG was done in 400 antenatal women between 12 and 24 weeks of gestation and they were followed up till delivery and postpartum for 7 days. Assessment of serum β-hCG and its predictability for development of pregnancy-induced hypertension and its effect on maternal and fetal outcome were done.

Results: Women with high serum β-hCG levels at 12 to 24 weeks of gestation have 1.67 times more risk of developing pregnancy-induced hypertension (p = 0.035) and poor maternal and perinatal outcome.

Conclusion: Elevated maternal serum β-hCG at early second trimester is a good noninvasive predictor of pregnancy-induced hypertension. The maternal and perinatal outcome was directly proportional to levels of serum β-hCG.

Keywords: Beta human chorionic gonadotropin, Preeclampsia, Pregnancy-induced hypertension.

INTRODUCTION

Hypertensive disorder of pregnancy is an enigmatic condition despite exhaustive research and is associated with high maternal and perinatal mortality and morbidity. This remains a subject of great clinical relevance and intense interest and is a day-to-day problem for each and every obstetrician.

Pregnancy-induced hypertension occurs in approximately 3 to 5% of pregnancies and is still a major cause of both fetal and maternal morbidity and mortality worldwide. Overall, the incidence of preeclampsia ranges from 5 to 15%. In India, the incidence of preeclampsia is 8 to 10% of all the pregnancies. Incidence in primigravidae is 10% and in multigravidae, 5%.

Preeclampsia is best described as a pregnancy-specific syndrome unique to humans, which virtually affects every organ system. Although physicians for millennia have recognized preeclampsia, relatively little is known about its pathogenesis and prevention. The primary concern about elevated blood pressure relates to the potential harmful effects on both mother and fetus. These potential adverse effects range in severity from trivial to life threatening.

Preeclampsia is a multisystem disorder of unknown etiology that is unique to human pregnancy and is characterized by abnormal vascular response to placentation associated with increased systemic vascular resistance, enhanced platelet aggregation, activation of coagulation system, and endothelial dysfunction. Additionally, renal, hepatic, coagulation, and central nervous system can be affected.

Preeclampsia is associated with increased risk of maternal mortality and maternal morbidities like convulsions, abruptio placenta, acute renal failure, cerebrovascular complications, liver hemorrhage, and disseminated intravascular coagulation (DIC).

The infants of preeclamptic mothers have a significantly higher incidence of prematurity, somatic growth retardation, thrombocytopenia, delayed adaptation, patent ductus arteriosus, and gastrointestinal hypomotility.

Despite extensive research and improved technology in recent decades, the etiology and pathophysiology of...
the syndrome remain enigmatic. So, there are no rational preventive or therapeutic interventions available.

A careful consideration of various factors and individualization of cases is necessary for clinicians considering appropriate management. There is paucity of formulated guidelines for management of pregnancy-induced hypertension at term. So, such studies in low-resource settings will be of great value in synthesizing evidence regarding an ideal predictor and management of women with pregnancy-induced hypertension at term.

AIMS AND OBJECTIVES

- To estimate serum β-hCG levels between 12 and 24 weeks of pregnancy and to assess the predictive value of raised β-hCG levels in the development of pregnancy-induced hypertension in antenatal women.
- To study pregnancy outcome.
- To correlate the maternal and neonatal outcome with levels of serum β-hCG in pregnancy-induced hypertension.

MATERIALS AND METHODS

This hospital-based prospective cohort study, time-bound study of analysis of serum β-hCG in early second trimester as a predictor of pregnancy-induced hypertension, in 400 antenatal women admitted to obstetric ward and labor room of a rural, tertiary care hospital, was carried out in the Department of Obstetrics and Gynecology over 2 years from October 1, 2013 to October 31, 2015 after obtaining permission from the institutional ethics committee.

Selection of Subjects

Consecutive antenatal women with 12 to 24 weeks of gestation and willing to participate in the study and deliver at the tertiary care center were assessed and enrolled in the study as per the formulated inclusion and exclusion criteria.

Inclusion Criteria

- 18 to 30 years old primi-/multigravidae with singleton pregnancy with gestational age of 12 to 24 weeks as determined by last menstrual period or by ultrasound scan
- Antenatal women with first-trimester blood pressure record suggestive of normal blood pressure
- Women willing to participate in the study and ready to deliver in this hospital

Exclusion Criteria

- Antenatal women with chronic hypertension
- Antenatal women with diabetes mellitus
- Antenatal women with congenital anomalies
- Antenatal women with multiple gestations

EVALUATION

Particulars of all antenatal women attending outpatient department as well as women admitted to obstetric ward and labor room were noted, such as name, age, symptoms, menstrual history for menarche, last menstrual period, obstetrical history for gravidity, parity, abortions, preeclampsia in previous pregnancies, gestational diabetes mellitus, growth restriction, low birth weight, prematurity, late pregnancy losses, and neonatal deaths in previous pregnancies. Past medical history was asked for associated medical disorders like diabetes, thyroid, and autoimmune disorders. Significant surgical history, family history, and diet and nutrition history were also asked.

A thorough clinical examination including height, weight, pulse, pedal edema, thyroid enlargement, etc., was done.

Blood pressure was measured as per the guidelines for measuring blood pressure during pregnancy.

This was followed by systemic examination. In obstetrical examination, gestational age, presentation, and amount of liquor were noted and fetal heart sounds were auscultated with fetoscope.

All patients were critically evaluated for gestational age depending upon their last menstrual period, regularity of menstrual cycle, clinical examination details, or early ultrasound scan. Routine antenatal investigations like blood group and Rh typing, human immunodeficiency virus, hepatitis B surface antigen, Venereal Disease Research Laboratory test, sickling, serum thyroid-stimulating hormone, postglucose blood sugar, urine for albumin and microscopy were done, and specific investigation like serum β-hCG level done was sent between 12 and 24 weeks of gestation.

Ultrasoundography was done in

- First trimester: dating and viability.
- Second trimester: anomalies, fetal growth, and placental localization
- Third trimester: fetal growth, liquor, fetal well-being, placenta, and Doppler for intrauterine growth restriction and preeclampsia.

All antenatal women were followed up monthly till 28 weeks, biweekly till 28 to 36 weeks, and weekly after 36 weeks till delivery and postpartum for 7 days. During follow-up, blood pressure was monitored in every visit. The diagnosis of pregnancy-induced hypertension was done according to the criteria set by National High Blood Pressure Education Program. Women with preeclampsia were managed as per hospital protocol. Assessment of serum β-hCG and its predictability for development of
pregnancy-induced hypertension and its effect on maternal and fetal outcome was done. Furthermore, the maternal and neonatal outcomes were correlated with levels of serum β-hCG in pregnancy-induced hypertension.

**Statistical Analysis**

After data collection, it was entered in an Excel worksheet. All data analysis was done with the help of Statistical Package for the Social Sciences 15 version, EpiInfo software version 7. The continuous quantitative data were summarized as mean and standard deviation, while discrete (categorical) data in numbers and percentage (%).

The categorical variables were compared by chi-square (χ²) test. A p-value <0.05 was considered as significant and the value < 0.001 was considered highly significant.

**RESULTS**

The present study was undertaken to assess the predictability of raised serum β-hCG in second trimester (12–24 weeks) as a predictor of pregnancy-induced hypertension. A total of 400 antenatal women taken into the study were followed up till delivery and 7 days postpartum for development of pregnancy-induced hypertension and pregnancy and labor complications. The relative risk of raised serum β-hCG and development of pregnancy-induced hypertension was noted and the maternal and perinatal outcome in women with pregnancy-induced hypertension and normotensive women was analyzed and compared.

During the study period of 2 years, 400 antenatal women were taken into the study with serum β-hCG done at 12 to 24 weeks of gestation.

Of the 400 women, 80 women developed pregnancy-induced hypertension, giving the frequency of pregnancy-induced hypertension at a tertiary care center to be 20%.

Most of the women in pregnancy-induced hypertension group and normotensive group belonged to the age group of 22 to 25 years.

The mean age of women in pregnancy-induced hypertension group was 26.13 ± 3.4079 years and in normotensive group, it was 25.1875 ± 2.9726 years. As the age advances, incidence of pregnancy-induced hypertension increases.

Forty-seven (58.75%) antenatal women with pregnancy-induced hypertension were well educated as compared with 228 (71.24%) normotensive women. The difference between the two study groups was not found to be statistically significant (p = 0.4617). There is no correlation between the educational status of women and development of pregnancy-induced hypertension.

Fifty (62.5%) women had pregnancy-induced hypertension and 195 (60.9%) normotensive women belonged to the middle socioeconomic status. The p-value is 0.797, which was not significant. Hence, the groups were comparable.

The majority of the women in pregnancy-induced hypertension and normotensive groups were primigravida: 35 (43.75%) and 148 (46.25%) respectively.

Forty-nine (61.25%) women with pregnancy-induced hypertension were on mixed diet and 189 (59.06%) normotensive women were on vegetarian diet. The p-value was 0.001 by chi-square test.

Comparison was done of weight gain during pregnancy and body mass index (BMI) for both women with pregnancy-induced hypertension and normotensive women at the time of booking (12–24 weeks of gestation age) and at delivery. The p-value of weight gain during pregnancy (p = <0.001) and BMI (p = 0.0013) was found to be highly significant.

The family history of diabetes mellitus and hypertension was significant in women who developed pregnancy-induced hypertension as compared with normotensive women. The difference between the two groups was statistically significant (p = 0.0259).

Seventy-three (91.25 %) antenatal women with pregnancy-induced hypertension had pedal edema which in itself is a risk factor for pregnancy-induced hypertension; 219 (68.44%) normotensive women had no pedal edema. Both the groups were comparable as the p-value was <0.001.

Table 1 shows that the systolic and diastolic blood pressure at the time of booking (12–24 weeks of gestation age) and at delivery was statistically highly significant in women who developed pregnancy-induced hypertension as compared with normotensive women (p-value <0.001).

Table 2 shows that women with high serum β-hCG levels at 12 to 24 weeks of gestation have 1.67 times more

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**Table 1:** Comparison of systolic and diastolic blood pressure between pregnancy-induced hypertension and normotensive antenatal women at the time of booking (12–24 weeks of gestation age) and at delivery

<table>
<thead>
<tr>
<th>Blood pressure</th>
<th>Pregnancy-induced hypertension</th>
<th>Normotensive</th>
<th>t-test</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure</td>
<td>At booking (12–24 weeks)</td>
<td>112.85 ± 9.166</td>
<td>108.71 ± 9.7323</td>
<td>3.43</td>
</tr>
<tr>
<td></td>
<td>At delivery</td>
<td>143.9250 ± 12.0145</td>
<td>119.4625 ± 10.1752</td>
<td>18.52</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>At booking (12–24 weeks)</td>
<td>73.825 ± 6.546</td>
<td>71.6938 ± 10.94</td>
<td>1.67</td>
</tr>
<tr>
<td></td>
<td>At delivery</td>
<td>94.5250 ± 9.0609</td>
<td>76.7406 ± 7.4652</td>
<td>18.22</td>
</tr>
</tbody>
</table>
risk of developing pregnancy-induced hypertension \((p = 0.035)\), whereas low serum \(\beta\)-hCG has high value, but it was by chance, and there is no association between low serum \(\beta\)-hCG and pregnancy-induced hypertension \((p = 0.334)\). It was found that women with high \(\beta\)-hCG level had severe pregnancy-induced hypertension and poor maternal and perinatal outcome.

Table 3 shows that 9 (11.25\%) women had antepartum (accidental hemorrhage), intrapartum (DIC), and postpartum (atonic postpartum hemorrhage and acute renal failure) which were the maternal complications in women with pregnancy-induced hypertension as compared with 2 (5\%) normotensive women. The difference in the complications in both the groups was statistically significant.

Twenty-three (28.75\%) women delivered vaginally at term in women with pregnancy-induced hypertension as compared with 174 (54.375\%) normotensive women; 57 (71.25\%) women had cesarean sections in women with pregnancy-induced hypertension as compared with 146 (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.

Sixty-eight (85.00\%) women with pregnancy-induced hypertension delivered at term as compared with 302 (94.375\%) normotensive women. Preterm delivery was necessitated in 12 (15\%) women with pregnancy-induced hypertension as compared with 18 (5.625\%) normotensive women. The difference between the two study groups was found to be statistically significant \((p = 0.0075)\).

Forty-four (55\%) women with pregnancy-induced hypertension delivered low birth weight babies as compared with 84 (26.25\%) normotensive women. The mean birth weight in women with pregnancy-induced hypertension was 2.4072 ± 0.5470 kg as compared with 2.6222 ± 0.3280 kg in normotensive women. The difference in the two study groups was found to be highly statistically significant.

Table 4 shows that 24 (30\%) women with pregnancy-induced hypertension had adverse fetal outcomes as compared with 22 (6.812\%) normotensive women. The difference between the two study groups was highly statistically significant.

**DISCUSSION**

Hypertensive disorders of pregnancy are one of the most common complications of pregnancy and affects up to 8\% of all gestations. \(^5\) Pregnancy-induced hypertension,
hemorrhage, and infection form a deadly triad contributing greatly to maternal morbidity and mortality rates.

The exact mechanism of pregnancy-induced hypertension is unknown, no standards for prediction exist, and most facets of management are unclear, so management of pregnancy-induced hypertension remains challenging and controversial.

Reduction of maternal and perinatal mortality and morbidity due to pregnancy-induced hypertension is the high priority in international community, it being one of the millennium development goals.

Placenta is the known primary trigger of pregnancy-induced hypertension. Pathophysiological placental abnormalities are seen consistently to be associated with pregnancy-induced hypertension. Women with pregnancy-induced hypertension have hyperplacentosis or an abnormal placentation. Hypoxic placental damage caused by hypertensive disorders results in relative hyperplasia of cytotrophoblastic cell and increased hormone β-hCG.

Over the last decade, there has been enhanced awareness of predictors. Despite so many predictors, due to lack of larger randomized trials, the search is still on for an ideal predictor.

Since the etiology is obscure, controversies in management prevail, leaving the clinician in a quandary.

In the present study, the frequency of pregnancy-induced hypertension at a tertiary care center was found to be 20% (Table 5).

The frequency in our study is similar to studies by Vidyabati et al (17.68%), U Singh et al (21.48%), Kiran et al (17.5%), and Wander et al (23.636%).

In study by Vidyabati et al and Wander et al, the level of serum β-hCG was high: 45,103.45 ± 17,028.01 and 60,375 ± 38,843 respectively. In the study of Remzi et al (33,960 ± 4,048.74), it was comparable to our study (24,967.93 ± 24,021.36) (Table 6).

Maternal Outcome

In our study, 9 (11.25%) women had antepartum (accidental hemorrhage), intrapartum (DIC), postpartum (atonic postpartum hemorrhage and acute renal failure) which were the maternal complications in women with pregnancy-induced hypertension as compared with 2 (5%) normotensive women. The study conducted by Vrijkotte et al had pregnancy-induced hypertension in 4.9% and preeclampsia in 3.7% women. In the study by Wander et al (7.69%) had eclampsia and 18 (22.57%) women had preeclampsia.

Fetal Outcome

In the present study, 24 (30%) women with pregnancy-induced hypertension had adverse fetal outcomes as compared with 22 (6.812%) normotensive women. The indications for neonatal intensive care unit (NICU) admission were hyperbilirubinemia, intrauterine growth restriction, asphyxia, and low birth weight. Most common was asphyxia indicated by low Apgar. Twelve (15%) were preterm and 44 (55%) were low birth weight. The study conducted by Vrijkotte et al showed that there were 5.3% were preterm and 9.3% were small for gestational age.

CONCLUSION

Pregnancy-induced hypertension is still a little understood entity, despite the enormous impact of its complications on maternal and fetal outcomes.

The above study concludes that frequency of pregnancy-induced hypertension at a tertiary care hospital is 20%.

High serum β-hCG levels is a high-risk factor which helps us in the prediction of pregnancy-induced hypertension. Women with high serum β-hCG levels estimated at 12 to 24 weeks of gestation have 1.67 times (relative risk = 1.67) risk of developing pregnancy-induced hypertension. The maternal and perinatal outcome was directly proportional to levels of serum β-hCG.

Maternal and perinatal morbidity is directly related to diagnosis and management of pregnancy-induced hypertension. Serum β-hCG should be considered during risk-based counseling. Women at “increased risk” of pregnancy hypertension are most commonly identified by personal or family history of high diastolic pressure, chronic medical disease, and/or abnormal uterine Doppler before 24 weeks. Combining various clinical, biochemical, and/or ultrasonographic risk markers may

Table 5: Frequency of pregnancy-induced hypertension in various studies

<table>
<thead>
<tr>
<th>Studies</th>
<th>Frequency (%)</th>
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<tbody>
<tr>
<td>Vidyabati et al</td>
<td>17.68</td>
</tr>
<tr>
<td>U Singh et al</td>
<td>21.48</td>
</tr>
<tr>
<td>Ephraim et al</td>
<td>54.54</td>
</tr>
<tr>
<td>Yadav Kiran et al</td>
<td>17.5</td>
</tr>
<tr>
<td>Siddiqui et al</td>
<td>33.33</td>
</tr>
<tr>
<td>Remzi et al</td>
<td>38.23</td>
</tr>
<tr>
<td>Wander et al</td>
<td>23.636</td>
</tr>
<tr>
<td>Our study</td>
<td>20</td>
</tr>
</tbody>
</table>

Table 6: Serum β-hCG in different studies

<table>
<thead>
<tr>
<th>Studies</th>
<th>Pregnancy-induced hypertensive</th>
<th>Normotensive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vidyabati et al</td>
<td>45,103.45 ± 17,028.01</td>
<td>21,762.39 ± 6,133.92</td>
</tr>
<tr>
<td>Remzi et al</td>
<td>33,960 ± 4,048.74</td>
<td>18,634 ± 1,618.7</td>
</tr>
<tr>
<td>Wander et al</td>
<td>60,375 ± 38,843</td>
<td>21,260 ± 9,565</td>
</tr>
<tr>
<td>Our study</td>
<td>24,967.93 ± 24,021.36</td>
<td>21,044.13 ± 16,323.19</td>
</tr>
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</table>
better identify women at increased risk; however, no interventional trial has used such an approach to evaluate preventative therapy.

Art of good obstetric care involves balance between vaginal delivery and cesarean sections. Randomized controlled trials have concluded that planned births at 37 weeks of gestation improve maternal and perinatal outcomes, which are in accordance with our study. Hence, induction of labor and aggressive management are the cornerstone for management of pregnancy-induced hypertension.

Thus, imparting knowledge regarding healthy pregnancy during antenatal care, screening for at-risk women by predictors, and timely treatment may help in reducing maternal and perinatal complications.

REFERENCES