



BETA HCG LEVELS AS A MARKER OF PRE ECLAMPSIA IN SECOND TRIMESTER (13-20 WEEKS) OF PREGNANCY

Obstetrics & Gynaecology

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ABSTRACT

Hypertensive disorders of pregnancy (HDP) include gestational hypertension, pre-eclampsia, eclampsia and chronic hypertension and they can complicate up to 10% of pregnancies. Early detection and management are crucial to improve outcomes for both mother and baby. In pre eclampsia, the insufficient trophoblast migration into the spiral arteries and subsequent placental hypoxia results in elevated hCG production by hyperplastic cytotrophoblastic cells of the placenta. Thus keeping in view the role of β hCG the present study was conducted to find correlation of β hCG with preeclampsia at 13-20 weeks of gestation.

KEYWORDS

Pre eclampsia, beta hCG, Markers of pre-eclampsia, predictor of pre-eclampsia, second trimester.

INTRODUCTION

Hypertensive disorders of pregnancy (HDP) include gestational hypertension, pre-eclampsia, eclampsia and chronic hypertension and they can complicate up to 10% of pregnancies.¹ Pre-eclampsia, either alone or superimposed on chronic hypertension is the most dangerous for both mother and fetus.¹ As per WHO estimation developing nations have a seven times higher incidence of pre-eclampsia (2.8% of live births) in comparison to the developed countries (0.4% of live births).²

Preeclampsia can be defined as gestational hypertension plus proteinuria (300mg/24 h or Urine protein: creatinine ratio ≥ 0.3 or Dipstick 1+ persistent) or:^{1,3,4}

- Thrombocytopenia (platelets $< 100,000 / \text{mm}^3$), or
- Renal insufficiency (Creatinine $> 1.1 \text{ mg/dL}$) or doubling of baseline, or
- Liver involvement (serum transaminase levels twice normal), or
- Cerebral symptoms (headache, visual disturbances, convulsions) or
- Pulmonary oedema.

Pre-eclampsia being a multisystem disorder occurs after 20 weeks gestation that results in increased risk of adverse maternal and foetal outcomes.

The pathogenesis of pre-eclampsia is not entirely understood, but it is believed to involve abnormal placentation, immune maladaptation, genetic factors, and endothelial dysfunction.^{5,6,7} Identifying reliable biomarkers that can predict the development of pre-eclampsia is of great importance in prenatal care.^{8,9}

During pregnancy, the normal placenta gets differentiated with the cytotrophoblastic cells domination in early pregnancy and the syncytiotrophoblastic cells domination in late pregnancy.¹⁰ In pre-eclampsia, focal cellular necrosis occurs in the syncytiotrophoblast and there is increased mitotic activity with proliferation of the cytotrophoblast.^{11,12} In severe pre-eclampsia, there is rapid transformation of the proliferating trophoblast into syncytiotrophoblast.¹³ The insufficient trophoblast migration into the spiral arteries and subsequent placental hypoxia results in elevated hCG production by hyperplastic cytotrophoblastic cells of the placenta.^{14,15}

Levels of hCG have a varied value between women with normal pregnancies. In the first trimester of pregnancy, concentrations of hCG rise exponentially in maternal serum and urine and doubling occurs about every 48 hours till the first 8 weeks. Beta hcg peaks usually at around 10 weeks of gestation and then levels decrease till the 16th week period of gestation where they remain fairly constant until term.¹⁶

Thus keeping in view the role of β hCG the present study was conducted to find correlation of β hCG with preeclampsia at 13-20 weeks of gestation.

MATERIAL AND METHODS

This was a prospective study. My study population included a total number of 100 antenatal women attending ANC clinic, department of obstetrics and gynecology, Government Medical College, Amritsar.

Inclusive Criteria:

Pregnant normotensive, non proteinuric women were randomly selected from the gestational age of 13 to 20 weeks of pregnancy irrespective of parity.

Exclusion Criteria

1. Multiple pregnancy
2. Congenital fetal malformations
3. Chromosomal disorders in fetus
4. Women with chronic hypertension
5. Diabetes mellitus complicating pregnancy
6. Heart disease complicating pregnancy
7. Women with renal disease.
8. Molar pregnancy
9. Gestational age < 13 and > 20 weeks

- A detailed history was taken about the name, age, address, height, pre-pregnancy weight, socioeconomic class, obstetric score, past history of preeclampsia and family history of preeclampsia.
- Thorough clinical examination was done including the Laboratory investigation those were basic hematological investigations (CBC, LFT, RFT, PT/PTI), urine albumin and maternal serum β -hCG was estimated by ELISA technique.
- Informed written consent was obtained from all subjects.
- Gestational age calculation was done by reliable menstrual history, dating scan/ first trimester USG with crown-rump length and urine for pregnancy test.
- Pre-eclampsia was observed in all subjects participating in the study by measuring the blood pressure during their antenatal visits (once a month till 28 weeks of gestation, once a fortnight till 36 weeks, and once a week till delivery).
- Subjects were followed by clinical examination and biochemical examination, blood pressure, urine for albumin, pedal edema and fetal wellbeing was assured by clinical examination/ USG.

RESULTS

A population based cohort study was done to study the role of maternal serum beta HCG for the prediction of pre-eclampsia at 13 - 20 weeks of gestation. My study population included total number of 100 antenatal women attending ANC clinic, Department Of Obstetrics & Gynaecology, Government Medical College, Amritsar. Patients were analysed on the basis of their beta HCG levels at 13-20 weeks and the following results were concluded from that—

- Mean age of study participants was 25.25 years with maximum number of pre eclamptic patients belonging to 21-25 years age group.
- 21 of the study participants were found to be hypertensive with mean systolic blood pressure of 115.97 mm of hg and mean diastolic blood pressure of 96.85 mm of hg.
- Out of these 21 study participants, 16 had pre-eclampsia with

mean systolic blood pressure of 158.12 mm hg and mean diastolic blood pressure of 98.6 mm of hg.

- Out of total 100 participants, 93 (97%) patients had normal creatinine levels whereas 7 (3%) patients had increased serum creatinine levels.
- In our study, out of 16 pre eclamptic patients, 3 patients (19%) had increased levels of serum creatinine.
- This shows serum creatinine levels are significantly higher in participants with pre-eclampsia compared to those without pre-eclampsia.
- In our study, out of 84 non- pre eclampsia patients, 6 had raised levels of SGOT and SGPT.
- Out of 16 Pre-eclamptic patients, 7 participants had raised SGOT and SGPT levels.
- The differences in SGOT and SGPT levels between participants with and without pre-eclampsia are statistically significant.
- In our study, out of 84 non- pre-eclampsia patients, 81 patients had normal platelet count whereas there was only 1 patient in each category of mild, moderate and severe thrombocytopenia.
- Out of 16 pre-eclampsia patients, 1 had mild, 2 had moderate and 1 had severe thrombocytopenia.
- Platelet counts showed significant variation between participants with and without pre-eclampsia. Lower platelet counts (indicative of thrombocytopenia) were more prevalent in participants with pre-eclampsia.
- Out of 100 study participants, 82 had normal beta HCG levels and 18 had increased levels of beta HCG.

Beta hCG of study participants					P-Value
Beta hCG	N	Percentage	Mean	Std Dev	
hCG normal 1400-52000	82	82%	22261.4	12408.9	0.001
Increased	18	18%	62282.56	5151.53	

- Out of 84 participants without pre-eclampsia, only 3 had increased levels of beta HCG whereas out of 16 pre eclamptic participants, 15 had increased levels of beta HCG.
- Elevated beta hCG levels were significantly associated with pre-eclampsia.
- In our study, it was found that maximum number of patients in the pre eclampsia group of participants were primigravida which was 50%.
- In our study, out of 84 participants without pre eclampsia, 50 had normal BMI, 38 were overweight and 11 were obese.
- Out of 16 pre-eclampsia participants, 6 were overweight and 7 were obese. Higher BMI categories (overweight, obese I) showed a statistically significant association with pre-eclampsia.
- In our study, out of 84 participants without pre eclampsia, only 10 participants had preterm birth.
- Out of 16 pre-eclampsia participants, 6 had preterm birth. Pre-eclamptic participants were more likely to have preterm births compared to non pre-eclamptic participants.

DISCUSSION

The aim of our study was to assess the role of beta HCG for the prediction of pre-eclampsia by measuring it at 13-20 weeks of gestation and correlation of levels of beta HCG with severity of pre-eclampsia. We analysed the patients on different parameters like age distribution, parity, BMI, systolic blood pressure and diastolic blood pressure, levels of serum creatinine, levels of SGOT and SGPT, platelet count and levels of beta HCG. A total of 100 pregnant women visiting the department were taken and analysed as per the different parameters.

All these 100 pregnant were analysed age wise. There were 4 participants in 15-20years age group, constituting 25% of the total sample of participants with pre-eclampsia. In 21-25 years of age group, there were 6 participants, accounting for 38% of the total sample of participants with pre-eclampsia. In 26-30 years of age group, there were 3 participants, making up 19% of the total sample of participants with pre-eclampsia. In 31-35 years age group, there were 3 participants, also comprising 19% of the total sample of participants with pre-eclampsia. There were no participants in 36-40 years age group with pre-eclampsia, represented as 0% of the total sample. Maximum number of participants belong to 21-25 years age group.

In a similar study conducted by Yadav BS et al¹⁷, 158 patients were randomly selected and matched by gestational age, consisting of 79 pre-eclampsia cases and 79 controls, all attending the ANC clinic at the Department of Obstetrics and Gynecology from March 2016 to August 2017.

The study found that pre-eclampsia was more common in young pregnant women of low socioeconomic status who engaged in strenuous activities. The mean age of participants was 24.51±3.707 years

In our study, all women were analysed on the basis of serum creatinine levels. In normal (less than 1.1 mg/dL) value category, there were 13 participants, comprising 81% of the total sample with pre-eclampsia. There were 3 participants in the increased creatinine value category, making up 19% of the total sample with pre-eclampsia.

In a similar hospital-based study conducted by Li XL et al¹⁸, data from 177 women with early or late preeclampsia with severe hypertension were collected and analyzed at a University Teaching Hospital between January 2010 and January 2011. The data included clinical parameters and laboratory biomarkers of liver and renal function. renal function markers, including blood urea nitrogen, creatinine, and uric acid, were significantly higher in early preeclampsia with severe hypertension.

In our study, there were 5 participants in the normal (less than 80 units/L) category, comprising 31% of the total sample with pre-eclampsia. The mean SGOT level was 22.5 units/L with a standard deviation of 4.509. There were 11 participants in the raised (more than 80 units/L) category, accounting for 69% of the total sample with pre-eclampsia. The mean SGOT level was 96.333 units/L with a standard deviation of 74.792.

The results of our study align with those of a study conducted by Munazza B et al in 2011¹⁹, which involved 100 pregnant women beyond 20 weeks of gestation admitted to the Obstetrics/Gynecology units of Ayub Teaching Hospital, Abbottabad. The participants were divided into two groups: Group A included 50 preeclampsia cases with blood pressure ≥140/90 mmHg, proteinuria ≥300 mg in 24 hours, and edema; Group B comprised 50 normal pregnant women beyond 20 weeks of gestation. The mean ALT levels in the preeclampsia cases were 55.81±31.93 U/L, compared to 15.22±3.30 U/L in the controls (p<0.001). The mean AST levels were 41.34±10.76 U/L in the cases and 24±2.54 U/L in the controls (p<0.001), demonstrating an association between increased liver enzyme levels and pregnancy-induced hypertension (PIH).

In our study, there were 12 participants with normal platelet count (>150,000 per microliter) comprising 12% of the total sample with pre-eclampsia. There were no participants in the mild thrombocytopenia category, representing 0% of the total sample with pre-eclampsia. There were 2 participants with moderate thrombocytopenia (50,000 - 100,000 per microliter) and 2 participants with severe thrombocytopenia (<50,000 per microliter) accounting for 2% and 12% of the total sample with pre-eclampsia respectively.

A study by Sultana R et al²⁰ assessed the association between platelet count and preeclampsia. Conducted as a case-control study in the Department of Biochemistry at Dhaka Medical College, Dhaka, from July 2010 to June 2011, it involved 100 pregnant women in their third trimester attending the Obstetrics & Gynecology Department of Dhaka Medical Hospital. Among them, 50 were diagnosed with preeclampsia (cases) and 50 were healthy pregnant women (controls). Platelet counts were measured for all participants. The mean platelet count for the cases was 144,260±96,472, while for the controls it was 198,100±51,219. The study demonstrated a significant difference in mean platelet count between the two groups, revealing that a low platelet count is associated with preeclampsia.

In our study, there was 1 participant with normal beta HCG, comprising 1% of the total sample with pre-eclampsia. The beta hCG level was 29,535 mIU/mL. Increased beta hCG levels were seen in 15 participants, accounting for 15% of the total sample with pre-eclampsia. The mean beta hCG level was 62,948.133 mIU/mL with a standard deviation of 4,928.163.

Similarly, in a study conducted by Said M E et al.²¹, maternal serum levels of beta-human chorionic gonadotrophin (β-hCG) were significantly higher in 41 primigravid patients with proteinuric pre-eclampsia compared to 41 primigravid normotensive women matched for age and gestation. β-hCG was also measured in serial serum samples from 13 women who experienced significant weight gain between 20 and 30 weeks of pregnancy. Of these, seven pregnancies were later complicated by pre-eclampsia, while the remaining six

remained normotensive. The study found that β -hCG levels increased before the clinical signs of pre-eclampsia appeared.

Similarly, in a prospective study conducted by Rathore N. et al.²², 200 women between 13 and 20 weeks of gestation were randomly selected. Serum beta-hCG levels were estimated using the Sandwich chemiluminescence immunoassay method and calculated as multiples of the median (MOM). The women were followed until delivery to monitor the development of gestational hypertension and preeclampsia, with results analyzed statistically. Of the 200 cases, 43 (21.5%) developed PIH. Beta-hCG levels were considered elevated if they were 2 MOM or higher. Among the 39 cases with beta-hCG levels at or above 2 MOM, 32 (82.1%) developed PIH, while 7 (17.9%) remained normotensive. Additionally, higher beta-hCG levels were associated with increased severity of PIH.

In our study among pre-eclamptic patients, 62.5% had term deliveries, while 37.5% had preterm deliveries. In contrast, among non pre-eclamptic patients, 88.09% had term deliveries, and only 11.90% had preterm deliveries. The observed and expected frequencies further illustrate this trend: pre-eclamptic patients had more preterm deliveries and fewer term deliveries than expected, while non pre-eclamptic patients had more term deliveries and fewer preterm deliveries than expected.

Similarly in a large population based case control study conducted by Davies E. L. et al.²³, used the Aberdeen Maternity and Neonatal Databank to analyze data on primiparous women with singleton pregnancies, who delivered between 1997 and 2012. Results showed a significant positive association between preeclampsia and preterm birth (adjusted odds ratio 4.43; 95% confidence interval 3.80–5.16).

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