

Serum Level of Beta Human Chorionic Gonadotropin in Pathogenesis of Pre-Eclampsia

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Abstract

Aims & Objective: To study the role of β -HCG in pathogenesis of preeclampsia and its association with severity of preeclampsia.

Materials and Methods: The prospective randomized study was conducted on 500 pregnant women of gestational age between 16-24 weeks with singleton pregnancy. Patients were classified into three groups, normal (N=250), mild pre-eclampsia (N=200) and severe pre-eclampsia (N=50). Quantitative determination of HCG by sandwich enzyme immunoassay. These values were compared by P value.

Results: The levels of serum urea, uric acid and β -HCG were found to be significantly increased in mild & severe ($P < 0.001$) pre-eclamptic women, as compared to normotensive controls. **Conclusion:** The maternal serum level of β -HCG plays one of the important role in pathogenesis of pre-eclampsia and its severity.

Keywords: β -HCG, mild pre-eclampsia, severe pre-eclampsia, Eclampsia

INTRODUCTION

Hypertension is the most common medical disorder in pregnancy. Hypertensive disorders of pregnancy are responsible for significant maternal and perinatal morbidity and are the third leading cause of pregnancy related deaths, superseded only by hemorrhage and embolism. [Coppage KH et al. 2005]. Pre-eclampsia, a condition prior to eclampsia (Greek word “eklampsis” meaning sudden flashing), is a systemic syndrome characterized by symptoms like hypertension, proteinuria and edema, often complicated by renal failure, pulmonary edema and coagulopathy. Consequences of these could be retarded growth of the fetus or mortality preceded by seizures and coma. Pre-eclampsia can occur in early pregnancy termed as “early onset pre-eclampsia” at <34 week gestation and late onset pre-eclampsia which occurs after 34 week of gestation. However, endothelial dysfunction is common in both early and late onset, responsible for the symptoms like proteinuria and hypertension. Failure to control these symptoms would result in fetal prematurity and premature delivery. Pre-eclampsia is a multisystem disorder, unique to pregnancy that is usually associated with raised blood pressure and proteinuria after 20 weeks of gestation. Eclampsia is one or more convulsions in association with syndrome of Pre-eclampsia. In Pre-eclampsia the systolic BP is ≥ 140 mmHg and diastolic BP ≥ 90 mmHg on 2 occasions at least 4hr apart after 20 weeks gestation in women with a previously normal blood pressure or ≥ 160 mmHg systolic or ≥ 110 mmHg diastolic, confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy and proteinuria ≥ 300 mg/24 hrs or a protein / creatinine ratio ≥ 0.3 mg/dl or a dipstick reading of $\geq 1+$. In the absence of proteinuria, preeclampsia is diagnosed as new-onset hypertension with the new onset of any of the following: thrombocytopenia, renal insufficiency, impaired liver function, pulmonary edema, or cerebral or visual symptoms. [ACOG, 2013] Human placenta synthesizes steroid, protein and glycoprotein hormones throughout gestation. Human chorionic gonadotropin (HCG) is a glycoprotein with a molecular weight of 47,000 Daltons. HCG produced by fetal yolk sac and syncytiotrophoblast (Gross SJ et al, 1994). Abnormally increased levels of HCG may be due to decreased placental perfusion with subsequent reduced oxygenation of syncytiotrophoblast (Fox H, 1970). The human chorionic gonadotropin (hCG) is composed of two non – covalently linked subunits, α and β , and is produced by syncytiotrophoblast cells of the placenta. Maternal serum hCG peaks at 8 – 10 wk of gestation and then declines to reach a plateau at 18 – 20 wk of gestation. The free β - subunit can derive from three sources, namely, direct trophoblast cell production, dissociation of hCG into free α and free β – subunits, and by macrophage or neutrophil enzymes nicking the hCG molecule (Cole LA et al 1993). The free β – hCG circulating in maternal serum corresponds to only about 0.3 – 4% of the total hCG (Spencer K 1991). The normal placenta differentiates during pregnancy with the cytotrophoblast dominant in early gestation and the syncytiotrophoblast dominant in late pregnancy. Placental vascular damage leading to

decreased oxygen supply might result in increased hCG production by hyperplastic cytotrophoblastic cells (Majumdar S et al 2005) There is a strict relationship between PIH and elevated serum β -HCG levels, indicating that there should be an abnormal placental secretory function in patients with severe pre-eclampsia . The aim of this present study was to find out the role of β -HCG in pathogenesis of pre-eclampsia and its association with severity of pre-eclampsia.

MATERIALS AND METHODS

The study was carried out at the Department of Obstetrics and Gynecology, R.N.T.Medical College,Udaipur, Rajasthan, India, after taking approval from ethical committee .The prospective randomized study was conducted on 500 pregnant women of gestational pregnancy 16-24 weeks with singleton pregnancy. Patients with chronic hypertension ,twin pregnancy ,molar pregnancy,chromosomally abnormal fetus ,diabetes,chronic renal disease ,autoimmune disorders ,thrombophelias ,family history of diabetes mellitus and cardiovascular diseases were excluded from the study. The patients were classified into three groups ,Normal (N=250), mild pre-eclampsia (N=200) and severe pre-eclampsia (N=50).The diagnosis of pre-eclampsia was established in according with the American college of Obstetrics and Gynecology definition.(ACOG,2013). The healthy pregnancy was diagnosed on the basis of clinical ,biochemical and ultrasound findings.Mild pre-eclampsia was considered having blood pressure ≥ 140 mmHg systolic and ≥ 90 mmHg diastolic ,on two occasion each 4 hours apart accompanied by proteinuria at least 1+on dipstick testing and severe pre-eclampsia was considered having blood pressure $\geq 160/110$ mmHg and proteinuria at least 3+on dipstick. Quantitative determination of HCG by sandwich enzyme immunoassay. Result are expressed as mean \pm standard error .The significance of the difference between the values from different groups is determined using one way analysis of variance (ANOVA).A level of $P < 0.05$ is defined as statistically significant.

RESULTS

Table1: Demographic characteristics of normal pregnancy and pre-eclampsia cases :

Sr. No.	Parameters	Normal Pregnancy (n = 250)	Mild Pre – eclampsia (n = 200)	Severe Preeclampsia (n = 50)	P- Value
1.	Means gestational age (weeks)	20.2 \pm 2.25	22.42 \pm 3.25	21.3 \pm 2.9	> 0.05
2.	Mean maternal age (years)	20.58 \pm 2.3	23.2 \pm 3.1	21.8 \pm 2.9	> 0.050
3.	Mean systolic blood pressure (mm Hg)	114.25 \pm 7.42	156.24 \pm 7.90	183.86 \pm 8.24	< 0.001
4.	Mean diastolic blood pressure (mm Hg)	76.61 \pm 8.67	99.51 \pm 4.87	113.06 \pm 5.11	< 0.001

Table 2:Laboratory data of Normal pregnancy, Mild and Severe pre-eclampsia

Sr. No.	Parameters	Normal Pregnancy (N = 250)	Mild Pre – eclampsia (N = 200)	Severe Preeclampsia (N = 50)	P-Value
1.	Urea (mg /dl)	15.50 ± 2.59	24.52 ± 3.99	35.46 ± 4.94	< 0.001
2.	Uric acid (mg /dl)	4.85 ± 1.31	5.83 ± 1.00	7.60 ± 0.77	< 0.001
3.	β -HCG (mIU /ml)	8091.44 ± 1493.68	15850.26 ± 789.53	19791.70 ± 987.02	< 0.001

Mild pre-eclampsia cases of those who showed ≥ 140 mmHg systolic or ≥ 90 mmHg diastolic one 2 occasions at least 4 hrs apart after 20wks gestation in women with a previously normal blood pressure . Severe pre-eclampsia cases of those who showed ≥ 160 mmHg systolic or ≥ 110 mmHg diastolic ,on 2 occasions 4 hours or more apart while the patients is an bed rest(ACOG,2013). Out of 250 pre eclampsia patients ,200 were mild pre-eclampsia and 50 were severe preeclampsia. Table:1 illustrates the Mean \pm SD levels of Systolic and diastolic blood pressure were significantly increased in mild and severe (P<0.001) pre-eclampsia women ,when compared with normotensive . Table 2 shows that the levels of serum urea, uric acid and β -HCG were found to be significantly increased in mild & severe (P<0.001) pre-eclamptic women ,as compared to normotensive controls.

DISCUSSION

Pre-eclampsia is well defined entity affecting pregnant women, the etiology of which remains uncertain. It may not be a single disease, but a syndrome of many possible origins. Pre-eclampsia is a syndrome which develops towards the end of pregnancy, there is no specific diagnostic tests for its prediction. Pre-eclampsia is a multisystem disorder of unknown etiology with hypertension, proteinuria or edema which predispose to potentially lethal complications such as eclampsia, acute renal failure, cerebral hemorrhage and circulatory collapse. β -HCG is selected from trophoblastic cells and in pre-eclampsia there is reactive hyperplasia of cells thus leading to raised levels. In pre-eclampsia the rise of blood pressure is due to vasoconstriction and impaired angiogenesis leading to hypoxia and hyperplasia of trophoblastic cells which causes hyper secretion of placental hormone ultimately leading to high level of circulating β -hCG. Human chorionic gonadotropin, a glycoprotein hormone is produced in excess by normal and neoplastic trophoblastic conditions like twin and molar pregnancies. High-level of circulating β -hCG are found in pre-eclampsia. As pre-eclampsia is probably a trophoblastic disorder, elevated β -hCG is thought to reflect early placental damage or dysfunction. Therefore, the study of pathologic changes and secretary reaction of the placenta may prove essential for understanding this disease. There is general agreement that the placenta remains the main source of

hCG in patients with pre-eclampsia, whether the cause of the high circulating levels of the hormone by placenta is still debated. Some advocate that hCG secretion may be increased as a consequence of abnormal placental invasion or placental immaturity. It may also be linked to the trophoblast response to hypoxia with the development of a hyper secretory state compared with normal pregnancies. It is well known that the cytotrophoblast is an undifferentiated stem cell, predominantly found in late trimester of pregnancy. The syncytiotrophoblast is a differentiated trophoblast found in early gestational period transformed from the cytotrophoblast. Although the mechanism of regulation of gestational hCG remains largely unknown, it is generally accepted that hCG, are only secreted by syncytiotrophoblasts. In pre-eclampsia the cytotrophoblast transformed into syncytiotrophoblast. Human placenta synthesizes steroid, protein, and glycoprotein hormones throughout gestation. [Shimar DT et al 2000] The production of hCG by the placenta in early pregnancy is critical for implantation and maintenance of the blastocyst. Since it is postulated that pre-eclampsia is likely a trophoblastic disorder [Robinson CJ et al 2001], Remzi Gokdeniz et al, found a strict relationship between severe pre-eclampsia and elevated serum β -HCG levels, indicating that should be an abnormal placental secretory function in patients with severe pre-eclampsia. In 1934 Smith et al talked about increasing HCG levels in severe preeclampsia for the first time.

CONCLUSION

The present study confirmed the elevated levels of β -HCG are associated with preeclampsia in second trimester. These findings suggest that severe pre-eclampsia women have higher hormonal changes than mild pre-eclampsia, and reflect the abnormal placentation in these patients.

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