

Elevated serum β -hCG levels in severe preeclampsia

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Abstract

Background: Pregnancy induced hypertensive disorders are common complications responsible for fetal, neonatal and maternal morbidity. Current hypothesis regarding the pathophysiologic mechanisms of pregnancy induced hypertension point to early placental abnormalities.

Objective: To determine whether measurement of serum human chorionic gonadotropin might reflect a different secretory trophoblastic response of preeclampsia.

Study design: A prospective study.

Setting: Department of Obstetrics & Gynecology in Al-Kadimyia Teaching Hospital.

Patients and methods: A total of 80 pregnant women were studied during the period from October through July 2005. They included 40 patients with severe preeclampsia were matched with 40 healthy normotensive women in the third trimester with singleton pregnancies and without congenital malformations. Serum levels of β -hCG were measured by immunoenzymometric

assay before delivery and neonatal outcome was recorded.

Results: Serum β -hCG levels were found to be significantly higher in severe preeclamptic women compared with controls ($P < 0.05$). Elevated β -hCG levels in severe preeclampsia was associated with higher rate of preterm delivery (50% vs. 7.5%), higher rate of intrauterine growth restriction of birth weight $< 10^{\text{th}}$ centile (47.5% vs. 5%), higher rate of low birth weight of < 2500 gm (70.25% vs. 12.5%) and higher rate of fetal death (7.5% vs. 0).

Conclusion: Elevated serum β -hCG levels in severely preeclamptic women reflect a significantly pathologic change and abnormal secretory function of the placenta with subsequent pregnancy outcome.

Keywords: preeclampsia, Human chorionic gonadotrophin, pregnancy

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Introduction

Hypertensive disorders of pregnancy (HDP) are responsible for a significant amount of maternal and perinatal morbidity and mortality, they complicate about 7-10% of all pregnancies. Pregnancy induced hypertension (PIH) which includes preeclampsia-eclampsia is responsible for 70%, whereas chronic hypertension represents 30% of Hypertensive disorders in pregnancy⁽¹⁾.

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The development of preeclampsia usually occurs after 20 weeks gestation and typically ends within 48 hours of the postpartum period⁽²⁾.

Preeclampsia is a disease defined by hypertension, proteinuria and oedema in pregnancy; or as gestational hypertension with proteinuria. It is most commonly occurs during the last trimester of pregnancy, when it arises in the early second trimester (14-20 weeks), a hydatidiform mole should be considered⁽³⁾.

It is primarily a disease of primigravida, being twice as common as multigravida and is specific to pregnancy and immediate puerperium⁽⁴⁾. Preeclampsia subdivided into mild and severe forms⁽⁵⁾, the differentiation between them can be

misleading because apparently mild disease may progress rapidly to severe disease⁽⁶⁾.

Most current hypotheses regarding the pathophysiologic mechanisms of pregnancy induced hypertension point to early placental abnormalities. Human placenta synthesizes steroid, protein and glycoprotein hormones throughout gestation⁽⁷⁾.

Human chorionic gonadotrophin (hCG) is produced almost exclusively in the placenta but is synthesized in fetal kidney and a number of fetal tissues produce the β -subunit or intact hCG molecule⁽⁸⁾. It is secreted by trophoblast cells of the placenta and its production in early pregnancy is critical for implantation and maintenance of blastocyst⁽⁹⁾. HCG can be detected in the maternal blood as early as 6 days after ovulation and begins to decline a nadir being reached by about 20 weeks and is maintained at this lower level for the remainder of pregnancy⁽¹⁰⁾.

An association was reported between preeclampsia and elevated third trimester hCG levels⁽¹¹⁾. As preeclampsia is likely a trophoblastic disorder and hCG is secreted from the trophoblast⁽¹²⁾, we therefore investigated whether the level of serum hCG does correlate with the severity of preeclampsia and might reflect a different trophoblastic secretory response of this disease.

Patients and methods

A prospective study was conducted on 80 pregnant women attending the department of obstetrics and gynaecology in Al-Kadimyia Teaching

Hospital during the period from October through July 2005. Forty pregnant women with severe preeclampsia (group A) and forty healthy pregnant women as a control group (group B) with singleton pregnancies in the third trimester were matched for gestational age and maternal age. The patients were considered severe preeclamptic when systolic blood pressure ≥ 160 mm Hg or diastolic blood pressure ≥ 110 mm Hg, proteinuria > 5 gm in 24 hours, epigastric pain, cerebral or visual disturbance, pulmonary oedema, thrombocytopenia and abnormal liver function. All women were subjected to full physical and obstetrical examination and they were followed during their admission, delivery and postnatal period.

Venous blood samples were obtained from the subjects before delivery. The blood allowed to clot and sera were separated by centrifugation and stored frozen at -20°C until analysis. Serum levels of β -hCG levels were measured with enzymatic and immunometric assay Kits. Chi-square test and t-test were used for statistical analysis. P value < 0.05 was considered statistically significant.

Results

Table 1 shows no difference between group A and group B in terms of mean maternal age (30.57 ± 6.78 vs. 29.52 ± 6.59). Significant difference between the two groups was found regarding the gestational age (35.72 ± 1.93 vs. 37.11 ± 1.98) with P value < 0.05 .

Table 1: Maternal age and gestational age in preeclamptic and pregnant controls

Variables	Group A (n=40)	Group B (n=40)	P value
Age (years) Mean $\pm$ SD	30.57 $\pm$ 6.78	29.52 $\pm$ 6.59	0.484
Gestational age (weeks) Mean $\pm$ SD	35.72 $\pm$ 1.93	37.11 $\pm$ 1.98	0.001

Table 2 shows the mean systolic, diastolic blood pressure, serum uric acid and urea in group A and group B. statistical significant elevation was

found regarding systolic, diastolic blood pressure and serum uric acid P value <0.05. No significant difference was found in blood urea levels.

Table 2: The mean systolic and diastolic blood pressure, serum uric acid and urea values in both groups.

Variables	Group A (n=40)	Group B (n=40)	P value
Systolic BP(mmHg) Mean $\pm$ SD	165.8 $\pm$ 19.00	111.7 $\pm$ 7.4	< 0.0001
Diastolic BP(mmHg) Mean $\pm$ SD	114.2 $\pm$ 6.9	70.8 $\pm$ 7.6	< 0.0001
Serum uric acid(mg/dl) Mean $\pm$ SD	8.3 $\pm$ 1.8	4.0 $\pm$ 1.3	< 0.0001
Blood urea (mg/dl) Mean $\pm$ SD	28.1 $\pm$ 9.1	25.2 $\pm$ 7.1	0.1804

Table 3 shows the mean β -hCG levels in both groups. There was significant difference in the mean β -hCG value in

preeclamptic as compared to control (P value <0.05).

Table3: The mean β -hCG levels in preeclamptic and pregnant controls

	Group A n=40	Group B N=40	P value
β -hCG (mIU/ml) Mean $\pm$ SD	24685.000 $\pm$ 4465.53	16209.500 $\pm$ 2069.65	< 0.0001

Table 4 shows the neonatal outcome in group A and group B. The incidence of preterm delivery and intrauterine growth restriction were higher in severe preeclampsia (50%, 47.5%) as compared

to healthy pregnant. Furthermore, about 2/3 of preeclamptic pregnant have low birth weight infants in comparison to 12.5% of the control group. The fetal death rate in preeclamptic was 7.5%.

Table 4: The neonatal outcome in group A and group B

Neonatal outcome	Group A n (%)	Group B n (%)
Preterm delivery<37week	20(50%)	3(7.5%)
Intrauterine growth restriction	19(47.5%)	2(5%)
Low birth weight<2500gm	29(72.5%)	5(12.5%)
Fetal death	3(7.5%)	0(0%)

Discussion

In this study, we found that serum β -hCG levels were significantly elevated in severe preeclampsia, compared with the controls. The placenta seems to play a fundamental role in preeclampsia, as the condition improves rapidly after its removal. Examination of the placenta in pregnancies complicated by preeclampsia has revealed focal cellular necrosis in the syncytiotrophoblast and increased mitotic activity with cellular proliferation in the cytotrophoblast⁽¹³⁾. The proliferating syncytiotrophoblast in severe preeclampsia is rapidly transformed into syncytiotrophoblast within 72 hours⁽¹⁴⁾.

The normal placenta differentiates during pregnancy with the cytotrophoblast (undifferentiated stem cell) dominant in early gestation and the syncytiotrophoblast (differentiated trophoblast) dominant in late pregnancy⁽¹⁵⁾. Although the mechanism of regulation of gestational hCG remains largely unknown, it is generally accepted that hCG is only secreted by syncytiotrophoblast⁽¹⁰⁾. Barros et al.

found that the microdensitometric analysis of the section from normotensive and preeclamptic placenta indicated that there is statistically significant preeclampsia induced increased in immunohistochemical reaction intensity for hCG, which demonstrate that increase production of hCG by preeclamptic placenta is associated with strong hCG immunostaining of the syncytiotrophoblast⁽¹⁶⁾. Preeclampsia results at least in part from poor trophoblast invasion, thus Bahado et al.⁽¹⁷⁾ found that hCG may play a role in trophoblast invasion and measurement of this identifies women at high risk for developing preeclampsia. In preeclampsia early placental vascular damage leading to decreased oxygen supply might result in an increased hCG production by hyperplastic cytotrophoblast cells⁽¹⁸⁾. Also hCG productions has been shown to increase when normal placental villi in organ cultures were maintained under hypoxic conditions⁽¹⁹⁾.

In our study we found that serum β -hCG levels were significantly elevated in severe preeclampsia compared with the controls. This finding indicates that an abnormal secretory function exists in patients with severe preeclampsia. Many authors studied serum level of hCG in preeclampsia to define an abnormal placental secretory function or to predict development of preeclampsia before this disease is manifest.

Said et al.⁽²⁰⁾ found that serum β -hCG concentration were significantly higher in preeclamptic patient compared with normotensive women matched for age and gestation, and β -HCG level were found to rise before the clinical signs of preeclampsia appeared. Gurbu et al.⁽²¹⁾ found that the serum hCG level is especially significant in severe preeclampsia and superimposed preeclampsia.

Lee et al.⁽²²⁾ found that various molecular forms of hCG in serum and urine were significantly higher in preeclamptic than normotensive pregnancies. Similar results were obtained by Hsu CD et al.⁽¹¹⁾.

Jaiswar et al.⁽²³⁾ found that there is 100% correlation between high serum β -hCG level at early gestation and development of pregnancy induced hypertension later on during pregnancy. Similar results were obtained by Mullar F et al.⁽²⁴⁾.

An elevation in serum β -hCG levels in the second trimester has been linked with the development of later onset of preeclampsia⁽²⁵⁾.

Wenstorm et al.⁽²⁶⁾ found that an elevated hCG level is significantly associated with preterm delivery, fetal death, and fetal growth restriction.

Lieppman et al.⁽²⁷⁾ studied a cohort of 460 women and found a four fold increase in the risk of low birth weight

babies in women with high serum hCG levels. The risk of preterm delivery was 2.8 times more and risk of small for gestational age (IUGR) baby was 1.8 times more in these women.

In our study, low birth weight babies were significantly higher in hypertensive group (72.5%) than those in normotensive group (12.5%), also preterm delivery and fetal death appear to be higher in group A than in group B (50% versus 7.5%) and (7.5% versus 0%) respectively⁽²⁸⁾.

A higher incidence of preterm delivery was found among patients with severe preeclampsia in comparison to control group. This may be due to induction of labour or caesarean section because of maternal indications and complications of preeclampsia or due to fetal causes as severe intrauterine growth restriction and fetal distress. On the other hand preterm deliveries in the control group were mainly due to preterm premature rupture of membrane. This indicates that Serum β -hCG level was elevated in severe preeclamptic women and could be associated with adverse pregnancy outcome.

Conclusion

Serum β -hCG levels were found to be significantly elevated in severe preeclampsia compared with the controls and this may indicate an abnormal placental secretory function in patients with severe preeclampsia with subsequent adverse pregnancy outcome.

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