THE ASSOCIATION BETWEEN SERUM BETA-HUMAN CHORIONIC GONADOTROPIN AND PREECLAMPSIA

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Abstract:

Background: *Exact aetiology of this potentially fatal disorder remains poorly understood. A number of theories have been put forward where different biochemical markers have been implicated in the causal association of preeclampsia. This study was intended to find the association between serum β-hCG level and preclampsia*

Methods: *This cross-sectional, case-control study was conducted on 74 pregnant women with preeclampsia (cases) who were admitted in the Eclampsia ward of Dhaka Medical College Hospital, Dhaka between January and July of 2013. A total of 76 normotensive pregnant women were also taken from the Obstetrics & Gynaecology Out-patient Department of the same hospital as control. The study subjects were selected on the basis of predefined eligibility criteria. The serum levels of β-hCG were compared between case and control groups as well as between mild and severe preeclampsia.*

Result: *The case and control groups were almost similar in terms of all the baseline demographic and obstetric characteristics except past history of PET which was significantly higher in the former group than that in the latter group. Majority (97.1%) of the cases had severe hypertension (74.3%) with mean systolic and diastolic blood pressures being 162.6 and 110.8 mmHg respectively. The mean serum β-hCG was much higher in the case group than that in the control group ($p<0.001$). The mean serum β-hCG was the highest in severe preeclampsia and the lowest in the control group, while that in mild preeclampsia lie in between the two ($p<0.001$). The serum β-hCG exhibits a significantly linear correlation with systolic and diastolic blood pressures ($p<0.001$ respectively).*

Conclusion: *There was a significant difference between the β-hCG level in the preeclamptic women compared to the normotensive pregnant women and the severity of preeclamsia increases with further rise of β-hCG level.*

Key words: *preeclampsia, serum β-hCG.*

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Introduction:

Preeclampsia is a relatively common syndrome, dangerous for mother and infant, unpredictable in its onset and progression and untreatable except through termination of the pregnancy[1]. It affects up to 7% of pregnant women and is considered a leading cause of fetal growth restriction and perinatal morbidity and mortality. Despite many active researches for years, the exact aetiology of this potentially fatal disorder remains poorly understood. A number of theories have been put forward where different biochemical markers have been implicated in the causal association of preeclampsia. Several studies have reported an association between unexplained increases in maternal serum β-hCG levels in the second trimester of pregnancy and subsequent development of preeclampsia.[2]

Human β-hCG is a glycoprotein with lipid structure that is expressed in trophoblast and various malignant tumors. Human placenta

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synthesizes steroid, protein, and glycoprotein hormones throughout gestation[3]. The production of hCG by the placenta in early pregnancy is crucial for implantation and maintenance of the blastocyst. Since it is postulated that preeclampsia is a trophoblastic disorder[4], it has become essential to understand this disease, to investigate the pathologic and secretory reaction of the placenta. Twin pregnancies[5] and molar pregnancies[6] produce higher levels of hCG and they are associated with a higher incidence of preeclampsia than uncomplicated singleton pregnancies. An association has been reported between preeclampsia and elevated third trimester hCG levels[2]. Considerable evidence suggests an association between serum hCG levels and preclampsia[7-12]. Physiological concentrations of hCG is significantly increased in vitro capillary formation and migration of endothelial cells in a dose-dependant manner and has a novel function in ueterine adaptation to early pregnancy[13].

As the possible role hCG in the pathophysiology of preeclampsia is not well-understood and changes in its level can reflect the placental reaction to preeclampsia, we are encouraged to determine the association between serum â-hCG level and preclampsia after 20 weeks of pregnancy.

Methods:

In this cross-sectional case-control study, a total 74 pregnant women with preeclampsia who were admitted in the Eclampsia Ward of Dhaka Medical College Hospital, Dhaka, between January and July of 2013, were included in this study. Singleton pregnant women free from diabetes or trophoblastic disease or any other chronic disease were the criteria for inclusion in the study. Pregnant women with smoking habit were excluded from the study. A total of 76 normotensive pregnant women were taken from the Obstetrics & Gynaecology Out-patient Department of same hospital as control. Subjects of the two groups were compared for their baseline characteristics (age, socioeconomic status, BMI and gestational age). The criteria for severe preeclampsia were systolic blood pressure >160 mmHg and diastolic blood pressure >110 mmHg and proteinuria >5 g in 24 hours. In addition, any pregnant women with oliguria (urine output <30 ml per hour), cerebral or visual disturbance, epigastric pain, pulmonary oedema or abnormal platelet count or liver function profile was considered as severe preeclampsia. Subjects on inclusion into the study were tested for serum â-hCG. Serum levels of â-hCG were measured by immunochemistry (Imulite 1000, USA) and were compared between groups.

Statistical analysis was performed using Chi-square or Fisher's Exact Probability Test and Student's t-Test. Correlation between serum â-hCG and blood pressures were studied to see whether the two variables exhibit any linear correlation. The level of significance was set at 0.05 and $p<0.05$ was considered significant.

Result:

The case and control groups were almost similar in terms of age with mean age of the former and the latter groups being 23.3 and 24.3 years respectively (p=0.342). The groups were also identical with respect to their socioeconomic status (p=0.430). and BMI (p=0.291) (Table-I). Comparison of present and past obstetric history shows that there were no significant differences between the groups with respect to gestational age, gravida and or history abortion or MR (p=0.328, p=0.522 and p=0.847). However, the history of past PET was staggeringly higher in the case group compared to that in the control group ($p<0.001$) (Table-II).

Distribution of clinical variables among cases showed that majority (97.1%) of the cases had oedema and severe hypertension (74.3%) with mean systolic and diastolic blood pressures being 162.6 and 110.8 mmHg respectively. Over half (53.4%) of the cases had moderate proteinuria and 45.2% severe proteinuria (Table-III). The mean serum â-hCG was unusually higher in the case group than that in the control group ($p<0.001$) (Table-IV).

Association between severity of preeclampsia and serum â-hCG shows that mean serum â-hCG was the highest in severe preeclampsia and the lowest in the control group, while that in mild preeclampsia lie in between the two ($p<0.001$) (Table-V).

Table-I

Comparison of demographics and anthropometric variables between groups

Demographics and anthropometric variables	Group		P value
	Case(n = 74)	Control(n = 76)	
Age (years)	23.3 ± 6.7	24.3 ± 5.2	0.342
Socioeconomic status			
Lower	37 (50.0)	39 (52.7)	0.430
Middle class	26 (35.1)	29 (39.2)	
Rich	11 (14.9)	6 (8.1)	
BMI	23.6 ± 3.6	22.9 ± 2.6	0.291

Figures in the parentheses indicate corresponding %; Data were analyzed using Unpaired Student's 't' test and were presented as mean±SD. Chi-squared Test (χ^2) was done to analyze the data.

Table II

Comparison of obstetrical variables between groups

Obstetrical variables	Group		P
	Case (n = 74)	Control (n = 76)	value
Gestational age in weeks#	33.3 ± 3.6	32.7 ± 4.2	0.328
Gravida*			
Primigravida	35 (50.0)	28 (44.4)	0.522
Multigravida	35 (50.0)	35 (55.6)	
History of abortion/MR*	16 (23.5)	20 (26.3)	0.847
History of past PET*	34 (50.0)	2 (2.6)	<0.001

Figures in the parentheses indicate corresponding %; Data were analyzed using Unpaired Student's 't' test and were presented as mean±SD. Chi-squared Test (χ^2) was done to analyze the data.

Table-III

Distribution of cases by blood pressure and proteinuria

Clinical variables	Frequency (%)	Mean ± SD
Oedema	68 (97.1)	—
Systolic BP		
Mild (140–160 mmHg)	19 (25.7)	162.6±14.6
Severe (e"160) mmHg)	55 (74.3)	
Diastolic BP		
Mild (90–110 mmHg)	12 (16.2)	110.8±9.3
Severe (e"110 mmHg)	62 (83.8)	
Urine protein		
+	1 (1.4)	—
++	39 (53.4)	—
+++	33 (45.2)	—

Table IV

Comparison of obstetrical variables between groups

	Group		P
	Case (n = 74)	Control (n = 76)	value
Serum χ-hCG	45439.6±5003.6	4937.0±526.1	<0.001

Data were analyzed using Unpaired Student's 't' test and were presented as mean±SEM.

Table V

Association between serum χ-hCG and severity of preeclampsia

	Group			P
	Severe preclamsia (n = 65)	Mild preeclampsia (n = 8)	Control (n = 76)	value
Serum χ-hCG (mlu/ml)	47576.6±4804.6	43334.9±4894.3	4937.0±456.4	< 0.001

Figures in the parentheses indicate corresponding %; Data were analyzed using ANOVA statistics and were presented as mean±SD.

Discussion:

The present study showed that mean level of serum â-hCG was significantly higher in preclamptic women than that in their control counterpart. The mean level of of â-hCG also tends to be significantly higher in severe preeclamptic women than that in mild preeclamptic and normotensive controls. Our results are in concordance with most of the previous reports[14-18]. However, it is in contrast with some other studies[19,20]. As an indirect evidence of relationship between â-hCG and preclampsia, we studied the correlation between â-hCG and blood pressure and found that the former parameter exhibits a linear correlation with systolic and diastolic blood pressures ($p<0.001$) indicating that 25% of the rise in blood pressures could be explained by serum â-hCG. An even more pronounced relationship between the two variables was observed in a study, conducted in China on 142 normotensive and 43 preeclamptic women ($r = 0.677$, $p < 0.05$). The authors of the study concluded that the â-hCG level might reflect the degree of disordered activity of placental throphoblast in pregnancy induced hypertension (PIH) and could be utilized as a marker in determining PIH[16]. In another study, conducted on 32 women with PIH and 17 normotensive pregnant women, the relationship between Endothelin (ET) and hCG with preeclampsia was studied. The study concluded that ET and hCG are definitely higher in women with PIH than those in normotensive subjects. Therefore, their increases suggest a functional disorder in placental cells, which may result from damage to the endothelial cells[17].

In an attempt to measure the Urinary Gonadotropin Peptide (UGP) (the urinary metabolite of the hCG) in preeclamptic women, a case control study was conducted in Sweden in 1998. The study was carried out on 18 preeclamptic women and 20 normotensive pregnants in the third trimester of their pregnancy. A considerable increase in the UGP level was observed in preeclamptic patients than that in normotensive ones. These results suggest some placental hypoperfusion as a preeclamptic etiology[21]. A study conducted in Istanbul, Turkey, in 2004, compared â-hCG levels in 80 women suffering from mild preeclampsia, severe preeclampsia, superimposed hypertension and chronic hypertension with 25 normotensive pregnant women. The â-hCG level was reported to be 17000 mIu/mL in mild preeclamptic women, 49000 mIu/mL in severe preeclamptic women, about 41000 mIu mL/ml in women with superimposed hypertension, 12558 mIu/mL in

women with chronic hypertension and 9647 mIu/mL in normotensive women. The results indicated that the â-hCG level in women with severe preeclampsia was significantly more than those in other groups ($p<0.001$)[22].

The results of the present study showed that the â-hCG level in case of both mild and severe preeclampsia tends to increase due to disorder in the activity of placental cells leading to placental perfusion disorder and damaging to throphoblastic cells. Therefore, measuring the â-hCG level may help in the early diagnosis of the disease as well as may be an indicator of the severity of the disease.

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