

# Serum beta human chorionic gonadotropin levels and preeclampsia

Zahra Basirat, MD, Shahnaz Barat, MD, Mahmood Hajiahmadi, PhD.

## ABSTRACT

**Objective:** Preeclampsia is one of the most common complications of pregnancy. It is a trophoblastic disorder. Since human chorionic gonadotropin (hCG) is secreted by trophoblast, the purpose of the study was to determine the levels of  $\beta$ - (hCG) in preeclampsia and normal cases.

**Methods:** This study was conducted on 40 term pregnant women with preeclampsia (case group) and 40 normal pregnant cases (control group) in the Department of Obstetrics and Gynecology, Medical University, Babol, Iran, from 2004 to 2005. Serum  $\beta$ -hCG in all cases were measured by radioimmunoassay. The mean  $\beta$ -hCG level in preeclampsia (mild and severe) was compared with normal cases.

**Results:** The maternal serum,  $\beta$ -hCG level in patients with preeclampsia ( $39840 \pm 24630$  IU/L) was higher than in the control group ( $27460 \pm 25862$  IU/L) ( $p=0.031$ ). In mild preeclampsia (34 cases), the mean serum  $\beta$ -hCG level was  $31991 \pm 16758$  IU/L while in severe preeclampsia (6 cases)  $84312 \pm 9257$  IU/L ( $p<0.0001$ ). The mean serum  $\beta$ -hCG level in mild and severe preeclampsia was higher compared to the normal cases.

**Conclusions:** The results of this study show that the levels of  $\beta$ -hCG in severe form of preeclampsia is higher compared to the milder ones.

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Preeclampsia is one of the most common and unknown complications of pregnancy found in 3-7% of pregnancies.<sup>1</sup> It is one of the deadly triad along with hemorrhage and infection.<sup>2</sup> Preeclampsia is best described as blood pressure (BP)  $\geq 140/90$  mm Hg after 20 weeks of gestation and proteinuria  $\geq 300$  mg/24 hour or  $\geq 1+$  dipstick.<sup>1</sup> Pathogenesis of preeclampsia has not been exactly known yet, but one of the most important factors is vasospasm, which causes vascular damage and local hypoxia leading to hemorrhage, necrosis and end organ damages.<sup>1</sup> In a normal pregnancy, resistance to vasopressor substances occurs which is decreased in preeclampsia. Besides, in preeclamptic women production of prostacyclin I<sub>2</sub> and nitric oxide (2 vasodilators) decrease greatly and at the same time secretion of thromboxane A<sub>2</sub>

increases. These changes are apparent as early as 22 weeks in women who later develop preeclampsia.<sup>3</sup> It seems that endothelial cells dysfunction is the main cause of preeclampsia. Pregnancy complicated by preeclampsia typically show reduced 30-50% reduction in uteroplacental blood flow. A typical response to reduced blood flow is an increase in villous capillary number to maximize blood flow, which causes acceleration of placental maturation.<sup>4</sup> Some risk factors for the development of preeclampsia are nulliparity, age  $>40$ , African-American race, family history of preeclampsia, chronic hypertension, chronic renal disease, diabetes mellitus, and multiple gestation.<sup>2</sup> The human chorionic gonadotropin (hCG) is a glycoprotein with lipid structure. Its best known biologic function is the maintenance of the corpus

From the Department of Obstetric and Gynecology (Basirat, Barat), Yahyanejad Hospital, and the Department of Biostatistics (Hajiahmadi), Babol Medical University, Babol, Iran.

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Address correspondence and reprint request to: Dr. Zahra Basirat, Department of Gynecology, Yahyanejad Hospital, Babol Medical University, Babol, Postal Code: 471365647, Iran. Tel. +98 (111) 2223594-7. Fax. +98 (111) 2225035. E-mail: Zahra\_Basirat@yahoo.com

luteum of pregnancy.<sup>1</sup> Other functions include the promotion of relaxin secretion by the corpus luteum. The leuteinizing hormone-hCG receptors are found in myometrium and in uterine vascular tissue. It has been hypothesized that hCG may act to promote uterine vascular vasodilatation and myometrial smooth muscle relaxation.<sup>5</sup> Some investigators showed that high serum hCG level can be a helpful marker in the diagnosis and clinical management of preeclampsia.<sup>6</sup> Also unexplained hCG elevation during the second trimester may be associated with a range of adverse pregnancy outcomes including fetal growth retardation and preeclampsia.<sup>7</sup> Elevation of hCG in preeclampsia are thought to be due to persistent uteroplacental ischemia.<sup>8</sup> Since preeclampsia is a prevalent problem in our society, and its pathogenesis is not clearly explained; any investigation in this field is valuable. Therefore, we performed this study to determine the relation of serum  $\beta$ -hCG levels in mild and severe form of preeclampsia and normal pregnancy.

**Methods.** This case-control study was conducted in 2 groups of nulligravida term pregnant women (with gestational age of 38-40 weeks) referred to the Obstetrics and Gynecology Department of Yahyanejad Hospital in Babol, Iran, Medical University from 2004 to 2005. Gestational age was calculated from the 1st day of last menstrual period unless ultrasonography before 16 weeks demonstrated a discrepancy of at least 10 days in which case ultrasonographic dating of pregnancy was used for calculations.<sup>9</sup>

The first group consisted of 40 preeclamptic patients and the second one, 40 pregnant women with normal BP, systolic blood pressure (SBP) of <130 mm Hg and diastolic blood pressure (DBP) of <90 mm Hg. After getting informed consent, 5 ml blood sample was obtained from each patient, all of the serum samples were kept in a refrigerator and then tested for  $\beta$ -hCG by radioimmunoassay (Kavoshyar IRMA). Inclusion criteria for preeclampsia were as follows: BP  $\geq$ 140/90 mm Hg on 2 occasions apart from 4 hours and urine protein  $\geq$ 1+. Preeclampsia was classified as mild and severe form. The exclusion criteria were: multiple pregnancy, diabetes mellitus, chronic hypertension, and other medical diseases. The control group included normal term pregnant women who were referred to the labor room for delivery. The study was approved by the ethical committee. Also noted was the age, gestational age, gravida, urine albumin, platelet, coagulation tests, serum creatinine, BP and symptoms of severe preeclampsia, such as headache, blurred vision, and epigastric pain for all cases. Data were analyzed using the Statistical Package for Social Sciences, T-test, Analysis of Variance, Kruskal-Wallis and Mann-Whitney test.

**Results.** The gestational age and age in both groups were equal. The mean age of women in the preeclamptic group was  $24.88 \pm 0.6$  years and in the normal pregnant group was  $25.2 \pm 5.0$  ( $p$ -value = 0.795). The mean SBP of the preeclamptic group was  $147.25 \pm 9.8$  mm Hg and in the normal group  $106.75 \pm 7.29$  mm Hg ( $p < 0.001$ ). The mean DBP of the preeclamptic was  $92.63 \pm 3.75$  mm Hg and in the normal group was  $68.13 \pm 8.2$  mm Hg ( $p < 0.001$ ). Among the cases, 34 (85%) had mild and 6 (15%) had severe disease. The mean serum,  $\beta$ -hCG levels in the case group was  $39840 \pm 24630$  IU/L and in the normal group  $27460 \pm 25862$  IU/L ( $p = 0.031$ ). In both mild and severe form of preeclampsia,  $\beta$ -hCG was higher than the normal cases ( $p < 0.0001$ ) (Table 1).

**Discussion.** Pathogenesis of preeclampsia are not exactly known yet. However, one of the most important factors is vasospasm, which causes vascular damage and local hypoxia.<sup>1</sup> Hermsteiner et al<sup>10</sup> believed that hCG appears to be an important embryonic signal, which could trigger adaptive cardiovascular changes in early pregnancy, simultaneously preserving a sufficient utero-placental perfusion during the entire gestation period by an endothelium-independent mechanism.

In the present study, we compared the relation between serum  $\beta$ -hCG levels in 80 preeclamptic and normal pregnant women. The mean age in these 2 groups did not differ significantly ( $p = 0.79$ ). The mean serum  $\beta$ -hCG level in preeclamptic cases was significantly higher than the normal pregnant cases ( $p = 0.031$ ). A study conducted by Gurbuz et al<sup>6</sup> showed that the mean serum  $\beta$ -hCG levels was 17361.31 mIU/ml in the mild preeclamptic group, 49817.59 mIU/ml in the severe preeclamptic group, 41101.09 in the superimposed preeclamptic group. The result of our study, such as the findings of Gurbuz<sup>6</sup>, showed that a high serum  $\beta$ -hCG level can be a helpful marker in the diagnosis and management of this disease. Also, previous study measured serum  $\beta$ -hCG levels of second trimester in preeclampsia and normal pregnant cases and found elevated levels of  $\beta$ -hCG in preeclamptic cases.<sup>11-13</sup>

Morssink et al<sup>14</sup> examined the association between hypertensive disorders of pregnancy and second trimester maternal serum alpha-fetoprotein (AFP) and hCG levels. Although a weak association cannot be excluded, the study found no clinically important increase in the risk of developing subsequent hypertensive disorders of pregnancy among women with abnormal second trimester levels of maternal serum AFP or hCG.

**Table 1** - Mean ± SD of beta-human chorionic gonadotropin (β-hCG) level in preeclamptic (mild and severe) and normal control cases.

Titer	Category Preeclampsia	Number	Mean ± SD	Range	Minimum	Maximum
β-hCG	*Mild	34	31991 ± 16758	56000	4800	60800
	†Severe	6	84312 ± 9257	26000	74000	100000
	‡Total	40	39840 ± 24630	95200	4800	100000
	Normal case	40	27460 ± 25862	85569	4431	90000
*β-hCG level in mild form of preeclampsia was higher than normal control cases ( $p < 0.0001$ ). †β-hCG level in severe form of preeclampsia was higher than mild form ( $p < 0.0001$ ). ‡β-hCG level in all cases of preeclampsia was higher than normal control cases ( $p = 0.031$ ).						

According to the study of Steier et al<sup>15</sup> in preeclamptic pregnancies, the maternal serum hCG levels were significantly higher than in uncomplicated pregnancies. Vaillant et al<sup>16</sup> conducted a study on 434 consecutive nulliparous with singleton pregnancies and found that the mean level of serum β-hCG was higher in pregnancy induced hypertension (PIH) than in controls. Casart et al<sup>9</sup> reviewed hCG levels in 30 women in their third trimester with preeclampsia and 30 normal pregnant women and showed higher immunoreactive level of β-hCG in preeclamptic patients. In a study conducted by Roiz-Hernandez et al,<sup>17</sup> β-hCG measured in 784 women between their 16th and 20th week of pregnancy. Preeclampsia prevalence was 7.1% among primigravidas and 4.6% among multigravida. The study showed measuring levels of β-hCG is useful in clinical practice to identify pregnant women who will develop preeclampsia. Hsu et al<sup>18</sup> studied 20 patients with mild and 12 with severe preeclampsia who were matched with 32 healthy normotensive women in the third trimester. They found the total hCG, β-hCG, and alpha-hCG were significantly higher in severely preeclamptic women, but not in those with mild preeclampsia, compared with those in their matched controls. Feng et al<sup>19</sup> also found higher level of β-hCG in mild, moderate, and severe form of preeclampsia versus in normal group.

In the study of Li et al<sup>20</sup> endothelin and serum β-hCG levels of patients with PIH and normal singleton pregnant women were determined by radioimmunoassay. The β-hCG levels were significantly higher in patients with PIH than in the control group, especially in moderate and severe PIH, but the difference was not significant between the mild form and normal cases. The increased level of β-hCG suggested that the dysfunction of the placental cells, which may be associated with the endothelial cell damage in PIH patients. In our study, the serum levels of β-hCG is elevated in all cases of preeclampsia, but

a few study demonstrated the difference between the levels of β-hCG in mild and severe preeclampsia. In this study, we showed that the level of β-hCG in severe form of preeclampsia is higher than the mild forms, and this level in mild form is significantly higher than the normal pregnancy. Heikkila et al<sup>21</sup> also showed that an elevated maternal serum hCG concentration is a marker of early-onset and severe disease with significant maternal and perinatal morbidity. This finding reinforces the association between elevated hCG concentrations and placental damage in early pregnancy. Elevated maternal serum hCG levels identify a subgroup of preeclamptic patients who needs intensive observation. Our finding shows that in both forms of preeclampsia (mild and severe forms), serum β-hCG is raised, this elevation was higher in severe than in mild form.

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