

# Comparison of Serum Beta Human Chorionic Gonadotropin (S. $\beta$ -HCG) Level in Preeclamptic and Normal Pregnancy

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## Abstract

**Background:** Preeclampsia is a major cause of fetal maternal morbidity and mortality worldwide. WHO estimated the incidence to be seven times higher in developing countries than in developed countries (2.8% of live births versus 0.4%). Overall preeclampsia/eclampsia accounts for 10%–15% of maternal deaths. Exact etiology of the disease is unknown.

**Objective:** To compare the serum  $\beta$ -HCG levels in preeclamptic and normal pregnant women.

**Methods:** This case-control study was carried out in the Department of Obstetrics & Gynecology, Dhaka Medical College and Hospital, Dhaka, during July 2017 to June 2019 to evaluate the serum  $\beta$ -HCG level in preeclamptic and normal pregnant women. This study compares the  $\beta$ -HCG levels between the two groups as well as find out the association of serum  $\beta$ -HCG level with severity of preeclampsia. A total 80 women with  $\geq 37$  weeks of gestation admitted into the Department, who fulfilled the inclusion criteria were enrolled. Out of 80 pregnant women 40 with preeclampsia and rest 40 normal pregnant women were considered as case (Group I) and control (Group II) respectively. Serum  $\beta$ -HCG level of all the women were determined in the Departments of Biochemistry and Molecular Biology, Bangabandhu Sheikh Mujib Medical University. Statistical analysis of the results were obtained by using window based computer software devised with Statistical Packages for Social Sciences (SPSS-22.0).

**Result:** The mean systolic blood pressure was  $175.3 \pm 10.1$  mmHg in group I and  $113.1 \pm 14.0$  mmHg in group II. The mean diastolic blood pressure was  $106.75 \pm 10.47$  mmHg in group I and  $72.3 \pm 8.0$  mmHg in group II. The difference was statistically significant ( $p < 0.05$ ). The mean  $\beta$ -HCG was  $42235 \pm 34491$  IU/L in group I and  $29224 \pm 21022$  IU/L in group II. The difference was statistically significant ( $p < 0.05$ ). The mean  $\beta$ -HCG was  $27664.9 \pm 18076.4$  IU/L in mild preeclampsia and  $48474.7 \pm 31554.1$  IU/L in severe preeclampsia. The difference was also found statistically significant ( $p < 0.05$ ) between two groups. No difference in Serum  $\beta$ -hCG was found between mild preeclampsia and normal pregnancy.

**Conclusion:** Significantly high level of Serum  $\beta$ -hCG was found in the preeclamptic compared to the normal pregnant women. Serum  $\beta$ -hCG level also found raised according to the severity of preeclampsia due to hyperplastic trophoblastic cells of placenta. The maternal serum  $\beta$ -hCG plays one of the important role in the pathogenesis of preeclampsia and its severity.

**Keywords:** Serum  $\beta$ -HCG, preeclampsia, normal pregnancy

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**Introduction:**

Preeclampsia is a multisystemic disorder involving the placenta, liver, kidneys, blood, neurological and cardiovascular system. The symptoms of this multisystemic disorder appear during the second and third trimester of pregnancy and caused by the increased vasoconstriction which results in maternal hypertension, decreased utero placental circulation, edema, proteinuria, abnormal clotting, liver and renal dysfunctions<sup>1</sup>.

Proteinuria and increased blood pressure in preeclampsia are associated with a lower fetal birth weight, a lower APGAR score and an increased risk of adverse perinatal outcome<sup>2</sup>. It affects 3-8% of pregnancies and is a leading cause of maternal and perinatal mortality<sup>3</sup>. Approximately 10-15% of maternal deaths in developing countries are associated with preeclampsia leading to eclampsia<sup>2</sup>. Our neighboring country, India has the incidence of preeclampsia, as recorded from hospital statistics, varying widely from 5 to 15%<sup>2</sup>. The prevalence of Preeclampsia and Eclampsia was 46.8% and 35.4% respectively as per statistics of Obst & Gynae Department of Dhaka Medical College Hospital in 2018.

The human chorionic gonadotropin (hCG) is a glycoprotein composed of two non covalently linked subunits,  $\alpha$  and  $\beta$ , and is produced by syncytiotrophoblastic cells of the placenta. Maternal serum hCG peaks at 8 – 10 weeks of gestation and then decline to reach a plateau at 18-20 weeks of gestation. The free  $\beta$ -subunit can derive from three sources, namely, trophoblastic cell, dissociation of hCG into free  $\alpha$  and free  $\beta$ -subunits, and by macrophage or neutrophil enzymes nicking the  $\beta$ -hCG molecule<sup>8</sup>. Other study revealed that, in preeclampsia histological examination of placenta shows focal cellular necrosis in the syncytiotrophoblast and increased mitotic activity with cellular proliferation in the cytotrophoblast. In addition the proliferating trophoblast in severe preeclampsia is rapidly transformed into syncytiotrophoblast within 72 hours. The normal placenta differentiates during normal pregnancy with the cytotrophoblast dominant in early gestation and the syncytiotrophoblast dominant in late pregnancy<sup>1</sup>.

In preeclampsia 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  $\beta$ -hCG<sup>4</sup>. Preeclampsia and eclampsia are responsible for approximately 14.0% of maternal death per year<sup>5</sup>. Preeclampsia remains a major cause of prenatal morbidity and mortality worldwide. It is considered to be a trophoblastic disorder and since  $\beta$ -HCG is secreted by trophoblastic cells, it's serum level measurement may be or essential predictive factor in preeclampsia<sup>6</sup>. Preeclampsia is a common pregnancy related disorder in Bangladesh that originates in the placenta and causes variable maternal and fetal problems<sup>2</sup>. Normally serum  $\beta$ -HCG decreased at 18-20 week of gestation but assumed to be elevated in severely preeclamptic women which reflect a significantly pathologic change of hyperplastic cytotrophoblastic cells and abnormal secretory function of the placenta.

**Materials and Methods**

This case-control study was carried out in the Department of Obstetrics & Gynecology, Dhaka Medical College and Hospital, Dhaka, during July 2017 to June 2019 to evaluate the serum  $\beta$ -HCG level in preeclamptic and normal pregnant women. This study compare the  $\beta$ -HCG levels between the two groups as well as evaluated the association of raised serum  $\beta$ -HCG level with severity of preeclampsia. A total of 80 pregnant women  $\geq 37$  weeks of gestation admitted into the above mentioned Department, who fulfilled the inclusion criteria were enrolled. Out of 80 pregnant women 40 with preeclampsia and 40 normal pregnant women were considered as case (Group I) and control (Group II) respectively. Inclusion criteria for Group I were age: 18-40 years, women with preeclampsia, gestational age 37 weeks onwards, willing to participate in the study. Inclusion criteria for Group II were age: 18-40 years, women with no preeclampsia, gestational age 37 weeks onwards, willing to participate. Exclusion criteria for both Group I and II were patients with preexisting hypertension, twin pregnancy, malformed fetus, history of diabetes, chronic renal disease, immune diseases, family history of diabetes mellitus. Serum  $\beta$ -HCG was measured single time at gestational age 37 weeks onwards up to onset of labour. Serum  $\beta$ -HCG level was measured in the Department of Biochemistry and Molecular Biology, Bangabandhu Sheikh Mujib Medical University. Statistical analysis of the data

collected were obtained by using window based computer software devised with Statistical Packages for Social Sciences (SPSS-22.0).

### Result:

The results of this comparative study has been shown in table and scatter diagram. The demographic, anthropometric variables and obstetric variables are described in table I and II. Comparison of blood pressure and serum  $\beta$ -HCG between 2 groups are shown in table 3, 4 and 5.

The mean age was 27.1 $\pm$ 4.4 years in group I and 26.25 $\pm$ 5.3 years in group II. In group I, 25(62.5%) patients came from low socioeconomic status and 30(75.0%) in group II, 16(40.0%) patients were overweight in group I and 11(27.5%) in group II. The mean BMI was 23.53 $\pm$ 1.08 kg/m<sup>2</sup> in group I and 23.32 $\pm$ 0.86 kg/m<sup>2</sup> in group II. The difference was statistically not significant (p>0.05) between two groups. The mean gestational age was 37.89 $\pm$ 2.87 weeks in group I and 38.03 $\pm$ 4.23 weeks in group II. The mean systolic blood pressure was 175.3 $\pm$ 10.1 mmHg in group I and 113.1 $\pm$ 14.0 mmHg in group II. The mean diastolic blood pressure was 106.75 $\pm$ 10.47 mmHg in group I and 72.3 $\pm$ 8.0 mmHg in group II. The difference was statistically significant (p<0.05). In group I out of 40 preeclamptic patients 12 patients

had mild preeclampsia and 28 had severe preeclampsia. The mean systolic blood pressure was 150.5 $\pm$ 4.7 mmHg in mild preeclampsia and 181.7 $\pm$ 9.0 mmHg in severe preeclampsia. The mean diastolic blood pressure was 101.75 $\pm$ 6.0 mmHg in mild preeclampsia and 115.5 $\pm$ 3.5 mmHg in severe preeclampsia. The difference was statistically significant (p<0.05). The mean  $\beta$ -HCG was 42235 $\pm$ 34491 IU/L in group I and 29224 $\pm$ 21022 IU/L in group II. The difference was statistically significant (p<0.05). The mean  $\beta$ -HCG was 27664.9 $\pm$ 18076.4 IU/L in mild preeclampsia and 48474.7 $\pm$ 31554.1 IU/L in severe preeclampsia. The difference was also found statistically significant (p<0.05). There was no difference in serum  $\beta$ -HCG level in mild preeclampsia and normal pregnancy.

Table I shows the comparison of demographic and anthropometric variables between two groups, it was observed that the mean age was 27.1 $\pm$ 4.4 years in group I and 26.25 $\pm$ 5.3 years in group II. In group I, 25(62.5%) patients belonged to low socioeconomic status in and 30(75.0%) in group II came from low socio economic status. In group I, 16(40.0%) patients were overweight and 11(27.5%) in group II. The mean BMI was 23.53 $\pm$ 1.08 kg/m<sup>2</sup> in group I and 23.32 $\pm$ 0.86 kg/m<sup>2</sup> in group II. The difference was not statistically significant (p>0.05).

**Table I**  
Comparison of demographic and anthropometric variables between two groups (n=80)

	Group-I(n=40)		Group-II(n=40)		P-value
	Mean $\pm$ SD		Mean $\pm$ SD		
Age (in years)	27.1 $\pm$ 4.4		26.25 $\pm$ 5.3		<sup>a</sup> 0.437 <sup>ns</sup>
Range(min-max)	18-35		18-37		
Socioeconomic status	n	%	n	%	
Low income (BDT $\leq$ 81853.64) per year	25	62.5	30	75.0	<sup>b</sup> 0.227 <sup>ns</sup>
Lower- middle (BDT 81933.49-322223.82) per year	12	30.0	8	20.0	
Upper Middle (BDT 322303.68-996218.63) per year	3	7.5	2	5.0	
BMI (kg/m <sup>2</sup> )					
Normal (18.5-24.9 kg/m <sup>2</sup> )	24	60.0	29	72.5	
Overweight (25-34.9 kg/m <sup>2</sup> )	16	40.0	11	27.5	
Mean $\pm$ SD	23.53 $\pm$ 1.08		23.32 $\pm$ 0.86		<sup>a</sup> 0.339 <sup>ns</sup>
Range (min-max)	23.1-27.1		23.7-28		

ns= not significant

<sup>a</sup>p value reached from unpaired t test

<sup>b</sup>p value reached from Chi square test

Group I= Preeclamptic women

Group II= Normal pregnant women

Table II shows the comparison of obstetrical variables between two groups, it was observed that 28(70.0%) patients were primi gravida in group I and 22(55.0%) in group II. The mean gestational age was 37.89±2.87 weeks in group I and 38.03±4.23 weeks in group II. The difference is not statistically not significant ( $p>0.05$ ).

The mean systolic blood pressure was 175.3±10.1 mmHg in group I and 113.1±14.0 mmHg in group II. The mean diastolic blood pressure was 106.75±10.47 mmHg in group I and 72.3±8.0 mmHg in group II. The difference is statistically significant ( $p<0.05$ ) (Table-III).

The mean serum  $\beta$ -HCG was 42235±34491 IU/L in group I and 29224±21022 IU/L in group II. The difference

is statistically significant ( $p<0.05$ ) (Table-IV).

The mean serum  $\beta$ -HCG was 29224±21022 IU/L in normal pregnant women, 27664.9±18076.4 IU/L in mild preeclampsia and 48474.7±31554.1 IU/L in severe preeclampsia. The difference was statistically significant ( $p<0.05$ ) among three groups. The mean serum  $\beta$ -HCG was 27664.9±18076.4 in mild preeclampsia and 29224±21022 in normal pregnant women. There was no difference between mild preeclampsia and normal pregnancy (Table-V).

Figure 1 and 2 shows correlation between serum  $\beta$ -HCG with systolic and diastolic blood pressure. As the blood pressure rises, serum  $\beta$ -HCG also rises.

**Table-II**  
Comparison of obstetrical variables between two groups (n=80)

	Group-I (n=40)		Group-II (n=40)		P-value
	n	%	n	%	
Para					
Primi gravida	28	70.0	22	55.0	0.167 <sup>ns</sup>
Multi gravida	12	30.0	18	45.0	
	Mean±SD		Mean±SD		
Gestational age (weeks)	37.89±2.87		38.03±4.23		0.863 <sup>ns</sup>
Range (min-max)	37-40		37-40		

ns= not significant

<sup>a</sup>p value reached from unpaired t test

<sup>b</sup>p value reached from Chi square test

**Table-III**  
Comparison of the study groups by blood pressure (n=80)

Blood pressure (mmHg)	Group-I(n=40)	Group-II(n=40)	P-value
	Mean±SD	Mean±SD	
Systolic blood pressure	175.3±10.1	113.1±14.0	0.001 <sup>s</sup>
Range (min-max)	140-200	90-130	
Diastolic blood pressure	106.75±10.47	72.3±8.0	0.001 <sup>s</sup>
Range (min-max)	90-120	60-90	

s= significant

p value reached from unpaired t test

**Table-IV**  
Comparison of the study groups by serum  $\beta$ -HCG (IU/L) (n=80)

	Group-I(n=40)	Group-II(n=40)	P-value
	Mean±SD	Mean±SD	
Serum $\beta$ -HCG (IU/L)	42235±34491	29224±21022	0.045 <sup>s</sup>
Range (min-max)	6061.6-167234	1720-79454	

s=significant

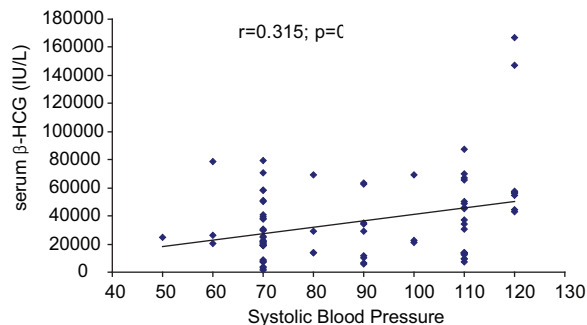
p value reached from unpaired t test

**Table-V**  
Distribution of the study population by serum  $\beta$ -HCG (IU/L) and severity of preeclampsia (n=80)

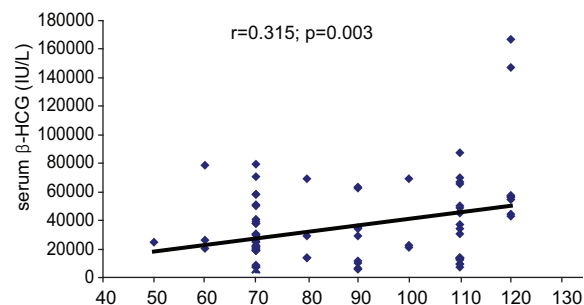
	Normal (n=40) Mean $\pm$ SD	Mild preeclampsia (n=12) Mean $\pm$ SD	Severe preeclampsia (n=28) Mean $\pm$ SD	P-value
Serum $\beta$ -HCG (IU/L)	29224 $\pm$ 21022	27664.9 $\pm$ 18076.4	48474.7 $\pm$ 31554.1	0.005 <sup>s</sup>
Range (min-max)	1720-79454	6061.6-63560	7577.0-167234.3	

s=significant

p value reached from ANOVA test



**Fig.-1:** Scatter diagram showing correlation of serum  $\beta$ -HCG (IU/L) and systolic Blood Pressure.



**Fig.-2:** Scatter diagram showing correlation of serum  $\beta$ -HCG (IU/L) and Diastolic Blood Pressure

### Discussion:

In this present study, the mean age was 27.1 $\pm$ 4.4 years in group I and 26.25 $\pm$ 5.3 years in group II. Similarly, the mean age was 23.3  $\pm$  6.7 years in case and 24.3 $\pm$ 5.2 years in control, in the study of Z. Begum et.al in 2014 at Dhaka Medical College Hospital, which are consistent with the current study<sup>7</sup>. Another study the mean age was 28.3  $\pm$  4.6 years in case and 27.3  $\pm$  4.8 years in control<sup>6</sup>.

It was observed that 70.0% patients were primi gravida in group I and 55.0% in group II. One of the

risk factor for preeclampsia is nulliparity because it is first time exposure to chorionic villi, often women have no preexisting comorbidities. As a result, regular antenatal check-up are advocated to detect hypertension and proteinuria until better widespread predictive tests are available, which may help stratify women into high- and low-risk groups. Another study found primigravida was 50.0% in case and 44.31% in control group respectively which are closely resembled with the present study<sup>7</sup>. Other study found that the maximum number of cases (75.0%) in case group and 50.0% in control group where primigravida, indicating that primigravida are at higher risk of developing preeclampsia compared to multigravida<sup>5</sup>.

In the present study, mean gestational age was 37.89 $\pm$ 2.87 weeks in case and 38.03 $\pm$ 4.23 weeks in control. On the other hand a study found the mean gestational age 35.7 $\pm$ 4.1 weeks in case and 36.6 $\pm$ 3.7 weeks in control, which is similar with the present study<sup>8</sup>. Nulliparity are known risk factors for preeclampsia among women with a high BMI (>35 kg/m<sup>2</sup>). In this current study, the mean BMI was 23.53 $\pm$ 1.08 kg/m<sup>2</sup> in group I and 23.32 $\pm$ 0.86 kg/m<sup>2</sup> in group II. The difference was statistically not significant (p>0.05). Another study observed that the mean BMI was 23.7 $\pm$  3.7 kg/m<sup>2</sup> in case and 24.0 $\pm$  2.5 kg/m<sup>2</sup> which is similar with the present study<sup>6</sup>.

In this current study, the mean systolic blood pressure was 175.3 $\pm$ 10.1 mmHg in group I and 113.1 $\pm$ 14.0 mmHg in group II. The mean diastolic blood pressure was 106.75 $\pm$ 10.47 mmHg in group I and 72.3 $\pm$ 8.0 mmHg in group II. The difference was statistically significant (p<0.05). Another study found the mean systolic blood pressure was 156.8 $\pm$ 21.2 mmHg in case and 111.6 $\pm$  12.2 mmHg in control<sup>8</sup>. Similar observation regarding the systolic blood pressure were also observed<sup>17,18</sup>. Another study showed the mean diastolic blood pressure was 101.8  $\pm$  11.1 mmHg in case and 75.0  $\pm$  8.3 in control<sup>8</sup>. In

this current study, it was observed that the mean systolic blood pressure was 150.5±4.7 mmHg in mild preeclampsia and 181.7±9.0 mmHg in severe preeclampsia. The mean diastolic blood pressure was 101.75±6.0 mmHg in mild preeclampsia and 115.5±3.5 mmHg in severe preeclampsia. The difference was statistically significant ( $p < 0.05$ ). Another study found that the mean diastolic blood pressure in severe preeclampsia 113.4± 84.87 mmHg and in the normal pregnancy was 67.7 ± 7.09 mmHg which closely resembled with the present study<sup>19</sup>.

In this present series, the mean serum  $\beta$ -HCG was 42235±34491 IU/L in group I and 29224±21022 IU/L in group II. The difference was statistically significant ( $p < 0.05$ ). Higher level of serum  $\beta$ -HCG was observed in preeclamptic group 34439.18 ± 28223.67 mIU/ml, range 2300.00-108735.00 mIU/ml than the normal group 20582.00 ± 17588.31 mIU/ml, range 2300.00-68961.00 mIU/ml<sup>6</sup>. Another study also showed the mean serum  $\beta$ -HCG level in preeclamptic women was 27802.51± 2324.46 mIU/ml which was significantly higher than normal pregnant women 12551.08± 1624.28 mIU/ml ( $p < 0.05$ )<sup>1</sup>. In this current study, it was observed that the mean serum  $\beta$ -HCG was 29224±21022 IU/L in normal pregnant women 27664.9±18076.4 IU/L in mild preeclampsia and 48474.7±31554.1 IU/L in severe preeclampsia. The difference was statistically significant ( $p < 0.05$ ) among three groups. The level of serum  $\beta$ -HCG markedly raised in severe preeclampsia (19793.40± 950 mIU/ml) than mild preeclampsia (16950.00 ± 1709.22 mIU/ml) ( $p < 0.001$ )<sup>4</sup>. It seems that high  $\beta$ -HCG level in case of preeclampsia, is due to placental perfusion disorder and severe damage to placental cells<sup>12</sup>.

In this study we found that serum  $\beta$ -hCG levels were significantly elevated in severe preeclampsia compared to mild preeclampsia and controls. There was no difference between mild preeclampsia and normal pregnancy.

### Conclusion:

This study suggest that the severity of preeclampsia is related with rise of serum  $\beta$ -HCG level due to hyperplastic trophoblast cells of placenta. The maternal serum  $\beta$ -HCG level has an important relation with preeclampsia and its severity.

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