

International Journal of Clinical Obstetrics and Gynaecology



ISSN (P): 2522-6614
ISSN (E): 2522-6622
© Gynaecology Journal
www.gynaecologyjournal.com
2024; 8(1): 106-111
Received: 23-12-2023
Accepted: 29-01-2024

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Association of Maternal Serum Human Chorionic Gonadotropin Level with Preeclampsia

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DOI: <https://doi.org/10.33545/gynae.2024.v8.i1b.1422>

Abstract

Introduction: Preeclampsia is a pregnancy specific disorder responsible for maternal and fetal morbidity and mortality. Every year approximately 70,000 women die due to preeclampsia and its complications. Exact etiology of this potentially fatal disorder remains poorly understood. Preeclampsia is a trophoblastic disorder where placental hypoxia causes hyperplasia of trophoblastic cells resulting increase hCG production. As hCG regulates the VEGF system, high serum hCG level may cause endothelial dysfunction and leads to the development of preeclampsia.

Objective: The study was designed to evaluate the association of maternal serum level of hCG with preeclampsia.

Methods: A case control study was conducted in the Department of Obstetrics and Gynecology, Institute of Child and Mother Health (ICMH), Dhaka, Bangladesh. A total of 62 pregnant women of preeclampsia and 62 pregnant women without preeclampsia were enrolled in this study. Pregnant women at 20-40 weeks of gestation diagnosed as preeclampsia were selected as cases. Normal pregnant women matching with cases by age and gestational age were selected as control in this study. Data was collected from the study subjects who were selected on the basis of eligibility criteria. Serum levels of β -hCG were measured and compared between case and control groups. Data analysis was carried out using SPSS version 22.0. P-value less than 0.05 was considered as statistically significant.

Results: In this study, the mean systolic pressure was higher in cases (148.7 \pm 19.4 mmHg) than in control (106.4 \pm 9.5 mmHg). Similarly, the mean diastolic pressure was higher in cases (96.4 \pm 11.8 mmHg) than in control (70.8 \pm 6.7 mmHg). The association of systolic and diastolic pressure between case and control was statistically significant ($p < 0.001$). Positive and significant correlation was observed between serum β -hCG compared with SBP ($r = 0.802$, $p < 0.001$) and DBP ($r = 0.773$, $p < 0.001$). Maternal serum β -hCG was higher in 20-28 weeks of gestation amongst the cases (57023.46 \pm 15970.9 IU/L) in relation to controls (21428.57 \pm 7841.8 IU/L) and slightly decreased in 29-40 weeks of gestation but still raised in cases (54224.69 \pm 18804.9 IU/L) compared to controls (13207.23 \pm 8483.3 IU/L). Overall, maternal serum beta hCG was higher in cases (54811.53 \pm 18159.3 IU/L) in comparison to the controls (15063.66 \pm 8975.7 IU/L) and was statistically significant ($p < 0.001$).

Conclusion: Serum β -hCG levels are significantly increased in patients with preeclampsia. So raised maternal serum hCG level is associated with preeclampsia.

Keywords: Maternal Serum Chorionic Gonadotropin, Preeclampsia

Introduction

Pregnancy can induce hypertension in normotensive women or aggravate already existing hypertension. Nearly one-tenth of maternal deaths in Asia and Africa and one-quarter of maternal deaths in Latin America are associated with hypertensive disorders of pregnancy. Among the hypertensive disorders, preeclampsia and eclampsia have the greatest impact on maternal and newborn morbidity and mortality [1]. Preeclampsia is a multisystem disorder that is primarily defined by the development of new-onset hypertension, persistent systolic blood pressure (SBP) of 140 mm Hg or higher, or diastolic blood pressure (DBP) of 90 mm Hg or higher measured on two separate occasion 4 hours apart after 20 weeks of gestation in a woman with previously normal blood pressure [2]. Although preeclampsia is usually accompanied by new-onset proteinuria, the American College of Obstetrics and Gynecology (ACOG) recently revised the diagnostic criteria for preeclampsia so that the presence of proteinuria for diagnosis is no longer required, stating that elevated blood pressure accompanied by other signs and symptoms is sufficient for diagnosis.

Other signs that are included by ACOG to identify cases with severe features are: high blood pressure $\geq 160/110$, thrombocytopenia, renal insufficiency, impaired liver function, pulmonary edema and cerebral or visual symptoms. The proportion of women who develop preeclampsia without proteinuria or who have proteinuria without hypertension preceding preeclampsia is unclear [3]. Preeclampsia is one of the leading causes of maternal and perinatal mortality and morbidity worldwide. Accurate incidence figures are difficult to obtain and the incidence varies between countries, but it is believed that preeclampsia has increased by 25% in the past 20 years worldwide and approximately 2-8% of pregnant women are affected [4]. Pre-eclampsia is responsible to contribute up to 20% of neonatal intensive care unit beds [5]. In Bangladesh, the incidence of preeclampsia is alarmingly high, about 20% of maternal death is associated with PE and eclampsia [6]. The risk factors for developing preeclampsia includes extremes of age (>35 or <17), nulliparity, pre-existing hypertension, vascular disorders, pre-existing gestational diabetes, family history of preeclampsia, poor socioeconomic status, PE or poor outcome in previous pregnancies, multifetal pregnancy, smoking, obesity, thrombotic disorder and other maternal, pregnancy associated and exogenous causes [7]. High blood pressure is an important sign of preeclampsia. The disease is sometimes referred to as a silent killer because most people can't feel their blood pressure going up and there is significant proteinuria in patients [8]. Preeclampsia can have an early onset (preeclampsia starting before 34 weeks of gestation) or late onset (preeclampsia starting after 34 weeks of gestation), can show mild or severe symptoms (systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 110 mmHg, proteinuria >5 g/24 hours, oliguria, neurological symptoms, other clinical symptoms such as altered liver function, thrombocytopenia $< 100,000$ /mm³, HELLP syndrome). Placental vascular damage leading to decreased oxygen supply might result in increased hCG production by hyperplastic cytotrophoblastic cells [9]. Evidences accumulated in the past 20 years indicates that in a large number of women with preeclampsia abnormal placentation is one of the initial events [10]; although it is not the only event that is the cause for preeclampsia. High circulating concentrations of human chorionic gonadotropin (hCG) in the second and third trimester of pregnancy have been associated with a range of adverse pregnancy outcomes including fetal growth retardation and preeclampsia [11]. Elevation of β -hCG in preeclampsia is thought to be due to persistent utero-placental ischemia. So, β -hCG may have role in the pathophysiology of preeclampsia. There are limited studies in the pathophysiology of preeclampsia. So, this study is an attempt to determine the associations of serum β -hCG with preeclampsia.

Materials and Methods

Study design: Case control study.

Place of study: This study was carried out in the Department of Obstetrics and Gynecology, Institute of Child and Mother Health (ICMH), Dhaka, Bangladesh.

Period of study: September 2018 to August 2019.

Study population

The study population includes the pregnant women between 20 to 40 weeks of gestation attending the outdoor and admitted in indoor of the Department of Obstetrics and Gynecology of ICMH. They were divided in to two groups:

Case: Pregnant women with gestational age between 20 to 40

weeks with preeclampsia (age - 18 to 35 years).

Control

Pregnant women with gestational age between 20 to 40 weeks without preeclampsia (age - 18 to 35 years).

Sample size determination

A total of 62 pregnant women of preeclampsia and 62 pregnant women without preeclampsia were enrolled in this study.

Inclusion criteria for case

- Pregnant women with gestational age between 20-40 weeks (age 18 to 35 years) with preeclampsia.

Inclusion criteria for control

- Pregnant women with gestational age between 20-40 weeks (age 18 to 35 years) without preeclampsia.

Exclusion criteria

- Patients with multiple pregnancies.
- Pregnancy with chronic hypertension.
- Pregnancy with diabetes mellitus.
- Pregnancy with chronic renal disease.

Study procedure

This case control study was conducted in ICMH, one year from IRB approval. Ethical committee clearance was obtained from the institution. The study populations were the pregnant women between 20-40 weeks of gestation attending in outdoor or admitted in the department of Obstetrics and Gynecology, ICMH. A total of 124 pregnant women were included in the study. The purpose and procedure of the study was discussed with the patients. Informed written consent was taken from those who agree to participate in the study. For each and every subject separate data collection sheet was prepared. Patient's blood pressure was recorded after 10 minutes of rest. Korotkoff phase - I (first beat heard) and phase - V (disappearance of sound) was used to determine systolic (SBP) and diastolic blood pressure (DBP). Proteinuria was distinguished by dipstick test. About 5 ml of midstream random urine sample was collected in a clean and dry test tube. The reagent strip was dipped into the urine for making sure that all the reagent areas have contacted the urine specimen. The strip was properly oriented near the appropriate color chart on the container label. Urinary protein changes the color of the reagent strip from yellow to green. Then 5ml of blood were drawn through venipuncture from ante-cubital vein and collected in a sterile test tube from the patients fulfilling the inclusion and exclusion criteria. Serum β -hCG level was measured by chemiluminescent immunometric assay by automated Atellica IM Analyzer (Details of the procedure is discussed in Appendices-VI). Data were collected from the patients on variables of interest using the structured questionnaire design by interview, observation, clinical examination and hematological investigation.

Data analysis: Statistical analyses were carried out by using Windows based Statistical Package for Social Sciences (SPSS-22). The descriptive statistics of the study was presented in tables, figures or suitable graphs, frequency, percentage, and mean \pm SD as per the requirement of qualitative and quantitative variables. Unpaired t test, Chi Square Test, Fisher's Exact Test was done to see the difference between case and control. Scatter plots in a graph was done to see the correlation between systolic-diastolic blood pressure and maternal hCG level. The p value <0.05 was considered as statistically significant.

Results

Table 1: Comparison of socio-demographic characteristics between cases and controls (case = 62, and control = 62)

Socio-demographic characteristics	Case	Control	Total	p- value
	N (%)	N (%)	N (%)	
Age in years				
≤20	13 (21.0)	13 (21.0)	26 (21.0)	0.802 ^a
21-30	33 (53.2)	36 (58.1)	69 (55.6)	
≥30	16 (25.8)	13 (21.0)	29 (23.4)	
Total	62 (100.0)	62 (100.0)	124 (100.0)	
Mean ± SD	25.65±4.43	25.13±4.41	25.39±4.41	0.766 ^b
Educational qualifications				
Up to primary	47 (75.8)	37 (59.7)	84 (67.7)	0.065 ^a
Secondary or higher	15 (24.2)	25 (40.3)	40 (32.3)	
Total	62 (100.0)	62 (100.0)	124 (100.0)	
Occupation				
Housewife	55 (88.7)	48 (77.4)	103 (83.0)	0.154 ^a
Student	5 (8.1)	5 (8.1)	10 (8.1)	
Service & others	2 (3.2)	9 (14.5)	11 (8.9)	
Total	62 (100.0)	62 (100.0)	124 (100.0)	
Monthly family income (BDT)				
Lower class	19 (30.6)	15 (24.2)	34 (27.4)	0.155 ^a
Lower middle class	30 (48.3)	27 (43.5)	57 (46.0)	
Upper middle class	13 (20.1)	20 (32.3)	33 (26.6)	
Total	62 (100.0)	62 (100.0)	124 (100.0)	
Mean ± SD	19193.55±6005.02	19645.16±7527.21	19419.35±6784.84	0.088 ^b

^aChi Square Test; ^bUnpaired t-test.

A total of 62 pregnant women of preeclampsia and 62 pregnant women without preeclampsia were enrolled in this study. Table 1 shows that, majority (55.6%) of the respondents were in the age group of 21-30 years. Most of the respondents were educated up to primary level (67.7%) and were housewives (83.0%). About 46% respondents from both group belongs to lower middle class. None of variables in each group statistically differed from one another.

Table 3 shows the maximum number of patients were from gestational age 29 -32 weeks (37.1%) in case and (32.3%) in control group. The mean gestational age was marginally higher in cases (32.44±3.5) than in control (31.97±4.7) but was not statistically significant (p=0.862).

Table 2: Comparison of parity between cases and controls (case = 62, and control = 62)

Parity	Case	Control	Total	p value
	N (%)	N (%)	N (%)	
Nulliparous	36 (58.1)	27 (43.5)	63 (50.8)	0.106 ^a
Multiparous	26 (41.9)	35 (56.5)	61 (49.2)	
Total	62 (100.0)	62 (100.0)	124 (100.0)	

^aChi Square Test

Table 2 shows that the proportion of nulliparous women was slightly higher in case group (58.1%) than in control group (43.5%), in contrast multiparous women were higher in control group (56.5%) than the case group (41.9%) which was not statistically significant (p=0.106).

Table 4: Comparison of previous history of preeclampsia between cases and controls (case = 62, and control = 62)

Previous history of preeclampsia	Case	Control	Total	p value
	N (%)	N (%)	N (%)	
Yes	6 (9.7)	0 (0.0)	6 (4.8)	0.028 ^a
No	56 (90.3)	62 (100.0)	118 (95.2)	
Total	62 (100.0)	62 (100.0)	124 (100.0)	

^aFisher's Exact Test

Table 4 illustrates that previous history of preeclampsia was present in 9.7% of cases and none (100.0%) in the controls but was statistically significant (p=0.028).

Table 5: Comparison of blood pressure between cases and controls (case = 62, and control = 62)

Blood pressure	Case (Mean±SD)	Control (Mean±SD)	p-value
Systolic BP (mmHg)	148.7±19.4	106.4±9.5	<0.001 ^a
Diastolic BP (mmHg)	96.4±11.8	70.8±6.7	<0.001 ^a

^aUnpaired t-test

Table 5 shows the mean systolic blood pressure was higher in cases (148.7±19.4 mmHg) than in controls (106.4±9.5 mmHg). Similarly, the mean diastolic blood pressure was higher in cases (96.4±11.8 mmHg) than in controls (70.8±6.7 mmHg). The association of systolic and diastolic blood pressure between case and control was statistically significant (p<0.001).

Table 3: Comparison of gestational age between cases and controls (case = 62, and control = 62)

Gestational age (weeks)	Case	Control	Total	p value
	N (%)	N (%)	N (%)	
≤ 28	13 (21.0)	14 (22.6)	27 (21.8)	0.862 ^a
29-32	23 (37.1)	20 (32.3)	43 (34.7)	
33-36	18 (29.0)	17 (27.4)	35 (28.2)	
≥ 37 (term)	8 (12.9)	11 (17.7)	19 (15.3)	
Mean	32.44±3.5	31.97±4.7	32.2±4.1	0.115 ^b
Total	62 (100.0)	62 (100.0)	124 (100.0)	

^aChi Square Test; ^bUnpaired t-test

Table 6: Comparison of serum β -hCG level between cases and controls (case = 62, and control = 62)

β -hCG level	Case (Mean \pm SD)	Control (Mean \pm SD)	p-value
Serum β -hCG	54811.53 \pm 18159.3	15063.66 \pm 8975.7	<0.001 ^a

^aUnpaired t-test

Table 6 shows that maternal serum beta hCG was higher in cases (54811.53 \pm 18159.3 IU/L) than the controls (15063.66 \pm 8975.7 IU/L). Unpaired t-test showed statistically significant ($p < 0.001$) values.

Table 7: Comparison of serum beta hCG level in study group according to gestational age (case = 62, and control = 62)

Gestational Age	Case (Mean \pm SD)	Control (Mean \pm SD)	p-value
20-28 weeks	57023.46 \pm 15970.9	21428.57 \pm 7841.8	<0.001 ^a
29-40 weeks	54224.69 \pm 18804.9	13207.23 \pm 8483.3	

^aUnpaired t-test

Table 7 shows that maternal serum β -hCG was higher in 20-28 weeks of gestation amongst the cases (57023.46 \pm 15970.9 IU/L) in comparison to the controls (21428.57 \pm 7841.8 IU/L) and in 29-40 weeks of gestation the mean maternal serum β -hCG level slightly decreased than 20-28 weeks but still raised in cases

(54224.69 \pm 18804.9 IU/L) compared to control group (13207.23 \pm 8483.3 IU/L). Unpaired t-test was done in both instances and this difference was statistically significant ($p < 0.001$).

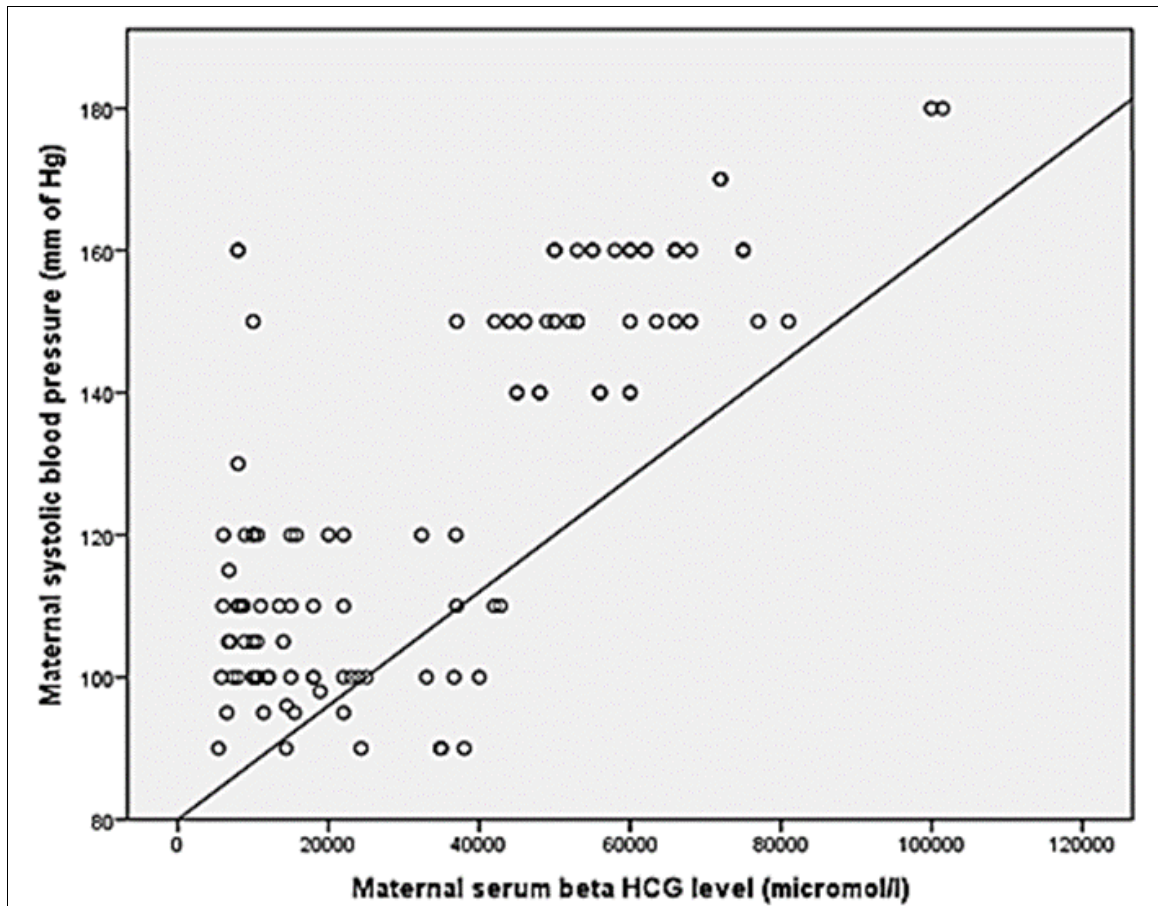


Fig 1: Correlation between serum β -hCG and SBP ($r=0.802$, $p < 0.001$).

Fig 1 shows the correlation between maternal serum beta hCG and maternal systolic blood pressure. Serum beta hCG level was positively correlated with maternal systolic blood pressure.

Maternal systolic blood pressure increased with increase in maternal serum beta hCG. This finding was statistically significant ($r=0.802$ and $p < 0.001$).

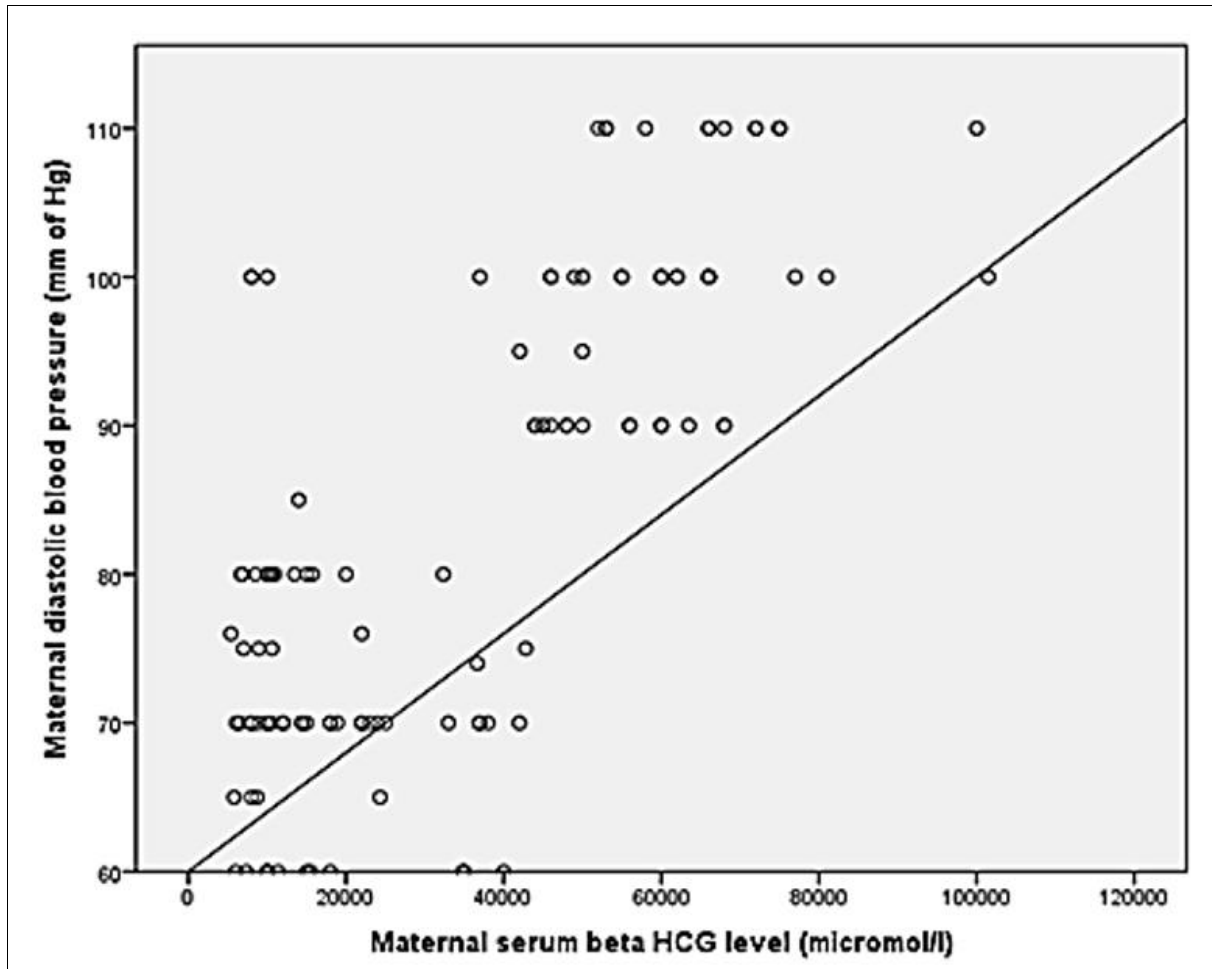


Fig 2: Correlation between serum β -hCG and DBP ($r=0.773$, $p<0.001$).

Fig 2 shows the correlation between maternal serum beta hCG and maternal diastolic blood pressure. Serum beta hCG level was positively correlated with maternal diastolic blood pressure. Maternal diastolic blood pressure increases with increased level of maternal serum beta hCG. This finding was statistically significant ($r=0.773$ and $p<0.001$).

Discussion

The current study was undertaken to determine the association of elevated serum β -hCG status in preeclampsia. The study included sixty-two (62) pregnant women with preeclampsia and sixty-two (62) normal pregnant women. There was no significant difference observed in respect of age distribution, educational level, occupation and economic condition between the preeclamptic cases and normotensive healthy pregnant controls in the present study ($p>0.05$). Whereas Mostafa *et al.*, recognized that there is association between level of education, home sanitation, family possessions, and economic status as an indicator for socioeconomic status and severity of preeclampsia [12]. In this study the mean SBP was higher in cases (148.7 ± 19.4 mmHg) than in controls (106.4 ± 9.5 mmHg). Similarly, the mean DBP was higher in cases (96.4 ± 11.8 mmHg) than in controls (70.8 ± 6.7 mmHg). The association of systolic and diastolic blood pressure between case and control was statistically significant ($p<0.001$). In a study by M. A. Jabbo demonstrated that the mean SBP and DBP was higher in the pre-eclamptic group compared to women with no features of pre-eclampsia and the difference was statistically significant ($p = 0.000$) [13]. In the present study positive correlation was found between maternal serum beta hCG and maternal arterial blood pressure. This study revealed maternal SBP increases with increased level

of maternal serum beta hCG which was statistically significant ($r=0.802$ & $p<0.001$) and maternal DBP also increases with increased level of maternal serum β -hCG and this finding was also statistically significant ($r=0.773$ & $p<0.001$). These observations and correlation between hCG and arterial blood pressure, support the findings of Sangeerani and Revathi's study [9]. In current study, maternal serum β -hCG was higher in 20-28 weeks of gestation amongst the cases (57023.46 ± 15970.9 IU/L) in relation to controls (21428.57 ± 7841.8 IU/L) and in 29-40 weeks of gestation mean serum β -hCG level slightly decreased but still raised in cases (54224.69 ± 18804.9 IU/L) compared to controls (13207.23 ± 8483.3 IU/L). In both the instances this difference was statistically significant ($p<0.001$). In a related study by Moslemizadeh *et al.*, also observed such significant relationship of hCG level with the gestational age [14]. The mean maternal serum β -hCG level in this study among the cases was higher (54811.53 ± 18159.3 IU/L) in comparison to the control groups (15063.66 ± 8975.7 IU/L). This finding was statically significant ($p<0.001$). Ayele and Zewde demonstrated mean serum levels of β -hCG in the case group was 34439.2 ± 28223.67 IU/ml and significantly higher than that of the control group, 20582 ± 17588.31 IU/ml [15]. Mujawar *et al.* also observed, patients with preeclampsia have significant increase in serum hCG concentrations in patients compared with normotensive control group [16]. Another study found the mean β -hCG concentration was $37,520.56$ IU/mL in women with severe PE, $16,487$ IU/mL in those with mild PE, and $11,699.82$ IU/mL in those who were normotensive ($p<0.001$) Taher and Alalaf *et al.* [17]. In a study the mean β -hCG of PIH group mothers was 54297.8 ± 22302.7 and that of normal group mothers was 27018.2 ± 11255.7 . The difference between the means was statistically significant ($p<0.001$) Victor and Jayalakshmi *et al.* [18] which is

similar to this study. From discussion, we can say that, socio-demographic variables are comparable in both groups. There is significant association and positive correlation between systolic and diastolic blood pressure with serum β hCG level. Serum β -hCG level is significantly higher in preeclamptic group than normal pregnant women. So, there is association between maternal serum hCG level with Preeclampsia.

Conclusions

The study finding suggest that patients with preeclampsia have higher serum β -hCG levels in comparison with normal pregnant women. High level of serum β -hCG is found to be a risk factor for development of preeclampsia. So raised maternal serum hCG level is associated with preeclampsia.

Limitations of the study

This study had some limitations:

- Study conducted in a selected tertiary hospital.
- The sample was not randomly selected.
- Sample size was small.
- Short study period.

So, the study findings cannot be generalized to the entire population.

Recommendations

1. Second or third trimester serum β -hCG measurement can be a cost-effective tool for identifying women who are at risk of developing preeclampsia. It will help in prevention or management before developing the overt disease to give better fetal outcome as well as decrease maternal morbidity and mortality.
2. Study can be undertaken with large sample size.
3. Random sampling techniques can be used.
4. Multicenter prospective studies can be done for longer duration.

Conflict of Interest

Not available.

Financial Support

Not available.

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How to Cite This Article

Ahmed RA, Hema SJ, Akter T, Hosne BA, Akhter SN, Akhter D, Akhter N. Association of maternal serum human chorionic gonadotropin level with preeclampsia. *International Journal of Clinical Obstetrics and Gynaecology* 2024;8(1):106-111

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