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Original Article

Preeclampsia in Pregnant Women — Association with Disease Severity

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ABSTRACT

Introduction: *Preeclampsia commonly occurs after 20 weeks of pregnancy in consort with proteinuria and the absence of proteinuria, preeclampsia is known in associated with liver dysfunction, thrombocytopenia, and pulmonary oedema and causes severity, chronic disability, and even death or both mothers and babies. The study aimed to understand the severity of preeclampsia in pregnant women.* ***Methods and materials:*** *An observational case-control study was carried out in the Department of Obstetrics and Gynecology, Sir Salimullah Medical College Mitford Hospital, Dhaka from July 2020 to June 2021. A total number of fifty-six preeclampsia women (N=56) were enrolled in the study. Data were collected using the predesigned semi-structured questionnaire. Verbal & written consent was taken before recruiting the study population. Completed data forms were reviewed, edited, and processed for computer data entry. The data analysis was performed using Statistical Package for the Social Sciences (SPSS) Version 25.0.* ***Result:*** *Respondents' mean age was 27.35 ± 4.85 years. Most of the patients (23,41.1%) completed the primary level, majority of the patients (48,85.7%) were housewives. Respondents' mean systolic blood pressure (SBP) was 164.50 ± 18.13 mmHg and mean diastolic blood pressure (DBP) was 110.82 ± 14.86 mmHg and mean β -hCG concentration was 21301 ± 10102 mIU/ml.* ***Conclusion:*** *This finding suggests that preeclampsia women with severe features have developed levels of serum β-hCG. Maternal complications like eclampsia, PPH, and fetal complications like stillbirth, a higher number of NICU admission, and lower APGAR score were significant in PE with severe features than in PE without*

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severe features and controls.

Keywords: *Preeclampsia, Pregnancy, Placenta, β-hCG*

INTRODUCTION

Preeclampsia is one of the foremost reasons behind maternal death and illness across the universe and is characterized by the new start of hypertension and significant end-organ dysfunction with or without proteinuria in the midway of the prenatal period or post-delivery [1,2]. Preeclampsia is hypertension that usually occurs after 20 weeks of gestation in consort with proteinuria and the absence of proteinuria, preeclampsia is identified in association with liver dysfunction, thrombocytopenia, pulmonary oedema and causes severity, chronic disability, and even death of both mothers and babies [3,4]. According to the World Health Organization (WHO), the incidence is seven times lower in developed countries (0.4%) compared to developing countries (2.8%) [5]. In Bangladesh, the prevalence of preeclampsia is nearly 76,032 [6]. Pregnancy-related disorders may rise the occurrence of numerous cardiovascular disease risk factors, including metabolic syndrome, insulin resistance, microalbuminuria, endothelial dysfunction, inflammatory factors, and oxidative stress [7,8]. In the case of 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 eventually leading to a high level of circulating β-hCG [9]. The human chorionic gonadotropin (hCG) is classified into two non-covalently related subunits, α and β, and is produced by syncytiotrophoblast cells of the placenta and the normal placenta differentiates during pregnancy with the cytotrophoblast dominant in early gestation and the syncytiotrophoblast dominant in late pregnancy [10]. The relationship between increasing β-hCG levels and the severity of preeclampsia was first noted in 1934 [11]. Since then numerous studies have suggested that elevated maternal serum β-hCG levels may be associated with severe preeclampsia. Changed glycosylation patterns and/or the presence of Sialyl Lewis antigens on hCG have been associated with the pathogenesis of preeclampsia, which weakens the enrolment and/or development of tolerance–inducing immune cell types [12]. Preeclampsia and eclampsia are considered to be a likely trophoblastic disorders since β-hCG is secreted by trophoblastic cells. Its serum level may be essential in preeclampsia [13]. In our country, there has been little study on serum beta-human chorionic gonadotropin in preeclampsia. The study aimed to understand the severity of preeclampsia in pregnant women.

OBJECTIVES

- To evaluate the severity of preeclampsia in pregnant women.

METHODS AND MATERIALS

An observational study was carried out in the Department of Obstetrics and Gynecology, Sir Salimullah Medical College Mitford Hospital, Dhaka from July 2020 to June 2021. A total number of fifty-six preeclampsia women (N=56) were enrolled in the study and thirty-seven (n=37) were included as preeclampsia (PE) with severe features and another nineteen (n=19) were included as preeclampsia (PE) without severe features A purposive sampling technique was followed. All observations were noted in the clinical data sheet. Informed written & verbal consent of the study subjects were taken in easily understandable Bengali phrases. The results were calculated and interpreted through appropriate statistical analysis with the help of a statistician and

presented with a table with other illustrations. Ethical clearance was taken from the hospital. The information was kept confidential only to be used for the study purpose. As a baseline investigation, after 10 minutes of rest, BP was measured on both arms following the standard procedure. Korotkoff phase 1 (first beat heard) and phase 5 (disappearance of sound) was used to determine systolic (SBP) and diastolic blood pressure (DBP) with a sphygmomanometer. The BP was measured on the right arm with the patient sitting comfortably, legs uncrossed, and back and arm supported or lying on her back 45 degrees to horizontal. In both cases, the occluded brachial artery was kept at the level of the heart. When BP was found elevated on the initial assessment, the measurement was repeated at least 4 to 6 hours apart to confirm hypertension. After all aseptic precautions, 5 ml of venous blood sample was collected from the median cubital vein in a disposable plastic syringe from each study subject. The needle was detached from the nozzle and transferred blood immediately into a dry, clean, and plain test tube with a gentle push to avoid hemolysis. Then blood sample was allowed to clot at room temperature and then centrifuged at 3000 rpm for 20 minutes and the serum was separated for biochemical assay on the day of collection. The separated serum was collected in an Eppendorf tube labelled appropriately for biochemical assay. The human chorionic gonadotropin (hCG) is a glycoprotein composed of two noncovalently linked subunits, α and β, and is produced by syncytiotrophoblast cells of the placenta. The total β-hCG estimation was carried out by Vitros5600 Immunoassay Analyzer using enhanced chemiluminescence technology and sandwich ELISA method. Each laboratory should determine its reference interval for the diagnostic evaluation of patient results.

Data analysis

The study coordinators performed random checks to verify data collection processes. Completed data forms were reviewed, edited, and processed for computer data entry. Frequencies and percentages were used for descriptive analysis. The descriptive statistics of the study were presented in tables, figures or suitable graphs, frequency, percentage and mean ± SD as per the requirement of qualitative and quantitative variables. For statistical analysis Unpaired t-test, Chi-Square Test, and Fisher's Exact Test was done to see the difference between case and control. The data analysis was performed using Statistical Package for the Social Sciences (SPSS) Version 25.0. P values <0.05 was considered statistically significant.

Inclusion criteria:

- Age 18 - 35 years.
- 34 – 40 Weeks of Pregnancy
- Singleton pregnancy.

Exclusion criteria:

- Patients with multiple gestations
- Diagnosed case of gestational diabetes mellitus / Diabetes mellitus
- Pregnancy with chronic hypertension, chronic renal disease & autoimmune disease

RESULT

Among the preeclampsia (PE) patients (N=56), the mean age of the patients was 27.35 ± 4.85 years. Most of the patients (23,41.1%) completed the primary level, the majority of the patients (48,85.7%) were housewives, and around three-fourths of the patients (32,57.1%) had lower-middle income **[Table I].** About half of the patients' (29,51.8%) gestational age was less than 37 weeks, forty-five patients (45,80.4%) had multigravida, most of the patients (38,67.9%) had irregular antenatal checkups, mean SBP was 164.50 ± 18.13 mmHg and mean DBP was 110.82 ± 14.86 mmHg and mean B-hCG concentration

was 21301 ± 10102 mIU/ml ***[Table II].*** Among the preeclampsia patients, the mean β-hCG concentration with severe features was 23245±10761 mIU/ml and without severe features was 17514±7570 mIU/ml and the difference was statistically significant (p=0.043) among the two sections ***[Table III].*** Based on the maternal outcome, of thirty-seven PE patients (n=37) with severe features, one-fourth of the patients (9,24.3%) had a normal vaginal delivery (NVD), & of nineteen PE patients without severe features (n=19), around one-fifth of the PE patients (4,21.1%) had NVD and caesarean delivery was found significantly higher in PE without severe features than PE with severe features (p=0.001), postpartum haemorrhage (PPH) was non-significantly higher in PE with severe features than PE without severe features (p=.154), and eclampsia was found significantly higher in PE with severe features than PE without severe features (p=0.010). Based on the neonatal outcome, birth weight was found lower in PE with severe features than in PE without severe features but the difference was not statistically significant (p=0.162), stillbirth, IUGR and NICU admission were non-significantly higher in PE with severe features than PE without severe features (p=0.732, p=0.562 and p=0.507). APGAR score at 1 min and 5 min were found not statistically significantly lower in PE with severe features than PE without severe (p=0.190 in 1 min and p=0.371 in 5 min) ***[Table IV].***

Table I: Distribution of the preeclampsia patients based on Demographic profile (N=56)

Characteristics	(N,%)
Age (Years)	
Mean ± SD	27.35 ± 4.85
Educational status	
Illiterate	2 ,3.6%
Primary	23,41.1%
Secondary	17,30.4%
Higher secondary	11,19.6%
Graduate	3,5.4%
Occupation	
Housewife	48,85.7%
Service holder	6 (10.7%)
Student	2 (3.6%)
Monthly family income (BDT)	
Low-income (<6000)	20 (35.7%)
Lower-middle-income (6000-25000)	32 (57.1%)
Upper-middle-income (≥26000)	4 (7.1%)

Table II: Distribution of the preeclampsia patients based on Obstetric history (N=56)

Obstetric history	(N,%)
Gestational age (weeks)	
<37	29 (51.8%)
≥37	27 (48.2%)
Mean ± SD	36.28 ± 2.12
Gravida	
Primigravida	11 (19.6%)
Multigravida	45 (80.4%)
Antenatal checkup	
Irregular	38 (67.9%)
Regular	18 (32.1%)
Blood pressure	**Mean**±SD
Systolic BP (SBP) (mmHg)	164.50 ± 18.13 (135 - 210)
Diastolic BP (DBP) (mmHg)	110.82 ± 14.86 (90 - 175)
β-hCG concentration (mIU/ml)	21301 ± 10102 (8931 - 44530)

Table III: Distribution of the preeclampsia (PE) patients based on β-hCG concentration with and without severe features (N=56)

β-hCG concentration (mIU/ml)	**PE with severe features (n=37)**	**PE without severe features (n=19)**	
	Mean ± SD	**Mean ± SD**	***p-value***
	23245 ± 10761 (8931 - 44530)	17514 ± 7570 (9489 - 26233)	.043

Table IV: Distribution of the preeclampsia patients based on Maternal & Neonatal outcome with and without severe features (N=56)

Outcome	**PE with severe features (n=37)**	**PE without severe features (n=19)**	***p-value***
Maternal outcome			
Mode of delivery			.001
NVD	9,24.3%	4 (21.1)	
Cesarean section	28 (75.7)	15 (78.9)	
Maternal mortality	0 (0.0%)	0 (0.0%)	
Eclampsia	11 (29.7)	0 (0.0%)	.010
PPH	10 (27.0)	2 (10.5)	.154
Abruption placenta	3 (8.1)	2 (10.5)	1.000
Acute renal failure	0 (0.0%)	0 (0.0%)	
Hemolysis, elevated liver enzymes, and low platelets (HELLP)	2 (5.4)	0 (0.0%)	.544
Stroke	0 (0.0%)	0 (0.0%)	
Neonatal outcome			
Birth weight (kg)			.162
Below normal (<2.5)	22 (59.5)	8 (42.1)	
Normal (2.5 – 4.0)	14 (37.8)	11 (57.9)	
Macrosomia (>4.0)	1 (2.7)	0 (0.0)	
Mean ± SD	2.27 ± 0.85	2.58 ± 0.61	
Min-max	1.20 – 4.50	1.10 – 3.80	
Live birth	29 (78.4)	16 (84.2)	.732
Stillbirth	8 (21.6)	3 (15.8)	
IUGR	5 (13.5)	1 (5.3)	.562
NICU admission	10 (27.0)	3 (15.8)	.507
APGAR score (1 min)	7.40 ± 1.00	7.76 ± 0.56	.190
APGAR score (5min)	8.85 ± 1.70	9.29 ± 1.35	.371

DISCUSSION

Severe preeclampsia rarely develops during the second trimester of pregnancy. Preeclampsia patients may experience high blood pressure, protein in their urine, swelling, headaches and blurred vision. This state needs to be treated by a health care provider. This observational case-control study was conducted to evaluate maternal and perinatal outcomes in women suffering from preeclampsia.

In this current analysis, among the preeclampsia (PE) patients, the mean age of the patients was 27.35 ± 4.85 years. A

similar study found that the mean age of the preeclampsia patient was 23.3 years [14]. In another study, the author revealed that the mean age was 25.12 years [15]. In this extant series, most of the respondents completed the primary level of education (41.1%). Most of the study matters (85.7%) were housewives. Maximum respondents (57.1%) were from lower-middle-income families. Related socioeconomic status was found in the study conducted in Dhaka [14]. The current study revealed that the mean gestational age of the study subjects was 36.28 ± 2.12 weeks. A similar study showed that the mean gestational age was 33.3 ± 3.6 weeks [14]. In this present study, most of the participants had multigravida (80.4%). Another comparable result depicted that most women (77.6%) were multiparous [16]. This present analysis found that the respondents who were not under regular antenatal checkups were found significantly more (p= 0.004) in preeclampsia patients (67.9%) than that controls (41.1%). This current series described that maternal serum β-hCG concentration was maximum in cases (21301 ± 10102 mIU/ml) compared to the controls (12731 ± 4133 mIU/ml). The mean serum β-hCG was 29621±13299 mIU/ml in preeclampsia patients found in another contrary study [17]. Another associated examination found that high levels of β hCG in preeclamptic cases (16130 mIU/ml) than the normal pregnant group (4,621 mIU/ml) with a p-value < 0.001[18]. A related finding described that β-hCG levels in 30 preeclampsia cases in their 3rd trimester and 30 antenatal women with normal BP, showed a greater level of β-hCG values in preeclampsia [19]. β-hCG concentration was significantly higher in PE with severe features (23245 ± 10761 mIU/ml) than in PE without severe features (17514 ± 7570 mIU/ml) with p-value = 0.043, in this analysis. In this present content, there was a significant difference between the serum β-hCG level in the preeclamptic women compared to the healthy pregnant women and the severity of preeclampsia increases with a further rise of β-hCG level (p< 0.001) which differed significantly in another analysis [17]. The levels of β-hCG were found to be significantly increased in mild & severe (p< 0.001) [20]. The level of Serum β-hCG elevated in severe preeclampsia (19,793.40 ± 950 mIU/mL) mothers than in mild preeclampsia mothers (16,950.00 ± 1,709.22 mIU/ mL) (P < 0.001) [17].

International Journal of Biomedical and Healthcare Science included 500 pregnant women at 16– 24 weeks of gestation in which urea, uric acid, and β-hCG concentrations were evaluated, it was shown that all three variables were significantly higher in women with mild or severe PE than in normotensive women (p= 0.001) [21]. As regards the way of delivery, cesarean section was found considerably higher in PE patients (76.8%) than in controls (45.0%) and the difference was statistically significant (p< 0.001). PPH was significantly higher in women with preeclampsia (21.4%) than in controls (1.8%) and the difference was statistically significant (p=0.002). According to the present study, eclampsia was significantly higher in PE with severe features (29.7%) than in PE without severe features (0.0%). It was statistically significant (p=0.010). But there was no significant difference in the mode of delivery and PPH between PE with severe features and PE without severe features in this study (p>0.05). some authors believed that the highest rate (10%) of PPH was in the severe PE group, compared with 4% each in the mild PE and normotensive groups [16]. Abruption of the placenta was greater in PE patients (8.9%) compared to controls (0%) but the change was not statistically significant (p>0.05). This was nearly alike in PE with severe features (8.1%) and PE without severe features (10.5%) patients. HELLP syndrome was found in 2 (3.6%) cases in PE patients but none in controls. The

difference in complications like eclampsia, and PPH, were statistically significant (p=0.05). The authors found no significant difference in birth weight among the groups. According to the current findings, Stillbirth was significantly higher in cases (19.6%) than in controls (5.4%) with p-value = 0.042. There was no significant difference in stillbirth between patients with PE with and without severe features (p>0.05). The number of NICU admission was significantly higher in PE patients (23.2%) than in controls (3.6%) and it was statistically significant (p=0.004). But no significant difference was found in NICU admission between patients with PE with and without severe features (p>0.05). Similar findings found that NICU admission required a higher number in the severe PE group than in Mild PE and normotensive groups but the difference was not statistically significant [16]. In this current analysis, the APGAR score at 1 min and 5 min was significantly lower in PE patients than in controls (p=0.05). APGAR score in the first minute was significantly lower in the severe PE group comparing mild PE and controls. But there was no significant difference in APGAR score in the fifth minute in another contradictory analysis carried out in 2019 [16].

Limitations of the study

The study was conducted in a selected tertiary care hospital. The sample were taken purposively, so the biases may be arising which can impact the results. Sample size was short to analyze the accurate result. The study duration was too short so, the study findings cannot be generalized to the entire population.

CONCLUSION

The study findings suggest that preeclampsia women with severe features have higher levels of serum β-hCG. Maternal complications like eclampsia, PPH, and fetal complications like stillbirth, a higher number of NICU admission and lower APGAR score were significant in PE with severe features than in PE without severe features and controls. Thus, raised maternal serum β-hCG level is associated with preeclampsia.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

RECOMMENDATIONS

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 outcomes as well as decrease maternal morbidity and mortality. The study can be undertaken with a large sample size. Random sampling techniques can be used. Multicenter prospective studies can be done for a longer duration.

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