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Original Research Article

Comparison between Highly Sensitive C - Reactive Protein in Subjects with Preeclampsia with Severe Features and Preeclampsia without Severe Features

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Abstract: ***Background*:** Preeclampsia (PE) develops in 4-5% of pregnancies in humans. It appears after 20 weeks of gestation and is defined by increased blood pressure and proteinuria. When convulsions occur or the hemolysis, high liver enzymes, and low platelet count (HELLP) condition materializes, PE can lead to eclampsia. It is well recognized that eclampsia and HELLP syndrome are linked to serious side effects include liver hemorrhage, lung edema, brain hemorrhage, and renal failure. ***Objective*:** The aim of this study is to compare between highly sensitive c- reactive protein in subjects with preeclampsia with severe features and preeclampsia without severe features. ***Methods*:** This case-control study was carried out in the Department of Obstetrics & Gynecology of Dhaka Medical College Hospital, Dhaka, from January 2023 to December 2023. A total of 68 patients were enrolled and analyzed in this study. The questionnaire was pretested, corrected and finalized. Data were collected by face-to-face interview and analyzed by appropriate computer based programmed software Statistical Package for the Social Sciences (SPSS), version 24. ***Results*:** In this study, maximum study subjects were in 21 – 30 years age group. Mean age of the study subjects was 26.12 ± 4.02 and 24.04 ± 4.32 years in PE with severe features and PE without severe features respectively. Majority of the patients 27(79.4%) and 25 (73.5%) were housewife in both cases. Illiterate 2 (5.9%), higher secondary 9(26.5%) and graduate 10(29.4%) were higher in PE with severe features than PE without severe features. Most of the patients 25 (73.5%) and 21 (61.8%) came from rural area. Nullipara was higher in PE with severe feature and multigravida was higher in PE without severe features. Antenatal care was found more irregular in PE patients with severe features subjects than PE without severe features. Preterm pregnancy was higher in PE with severe feature than PE without severe features. Systolic and diastolic blood pressure were found significantly higher in PE patients with severe features than without severe features. hsCRP was found significantly higher in PE with severe features than PE without severe features. APGAR score of the neonate was significantly better of PE patients without severe features than with

severe features patients both at birth and at 5 minutes. Average birth weight of the neonate was found higher of the PE patients without severe features than with severe features patients. There was 6(17.6%) very LBW of neonates of PE with severe features patients but none in PE without severe features patients. Intrauterine growth retardation, and prematurity were found higher in PE with severe features patients comparing PE without severe features. ***Conclusion*****:** Women with PE have higher serum hsCRP levels. Clinical and biochemical markers of PE are linked with elevated serum levels of hsCRP in preeclamptic women. Serum hsCRP levels can be measured to determine the severity of PE*.*

Keywords: Blood Pressure, hsCRP, Preeclampsia, Eclampsia, HELLP.

INTRODUCTION

High systemic blood pressure and proteinuria are two of the most prevalent symptoms of preeclampsia, which develops after 20 weeks of gestation [1]. It affects 2-8% of population globally and is linked to increased rates of neonatal and maternal morbidity and mortality [2, 3]. Every year, this illness claims the lives of 500,000 infants and 76,000 women worldwide [4]. In addition, compared to women in high resource nations, women in low resource countries had a higher chance of having preeclampsia [5].

Eclampsia, a consequence of preeclampsia, is linked to around 24% of maternal deaths in Bangladesh, where the frequency is concerningly high [6, 7]. Premature delivery and the NICU's inherent problems are two other important complications of preeclampsia. HELLP syndrome affects about 10% of women with preeclampsia/eclampsia [8]. The illness can range in severity from mild to severe enough to result in death or serious morbidity for the mother, including stroke, seizures, cerebral oedema, hepatic failure, renal failure, HELLP syndrome (low platelet count, elevated liver enzymes, and hemolysis), disseminated intravascular coagulation (DIC), and abruptio placentae. The effects of early pregnancy termination for maternal indications might result in severe prematurity, stillbirth, and intrauterine growth retardation (IUGR) [9].

The International Society for the Study of Hypertension in Pregnancy (ISSHP) defines preeclampsia, and FIGO uses this definition [5]. Preeclampsia, as defined by the ISSHP, is characterized by one or more of the following new onset conditions at or after 20 weeks of gestation and is accompanied by systolic blood pressure of at least 140 mmHg and/or diastolic blood pressure of at least 90 mmHg on at least two occasions measured 4 hours apart in previously normotensive women:

1. Proteinura (i.e., ≥30 mg/mol protein creatinine ratio; ≥300 mg/24 hours; or ≥2+ dipstick).
2. Evidence of other maternal organ dysfunction including acute kidney injury (creatinine ≥1 mg/dL). Liver involvement (elevated alanine aminotransferase or asparate aminotransferase more than 40 IU/L) with or without right upper quadrant or epigastric abdominal pain; neurological complication (e.g: eclampsia, altered mental status, blindness, stroke, clonus, severe headaches and persistent visual scotomata; or hematological complication (thrombocytopenia- intravascular coagulation, hemolysis) or
3. Uteroplacental dysfunction (such as fetal growth restriction, abnormal umbilical artery Doppler waveform analysis or stillbirth).

Preeclampsia's etiology is yet unknown, although a number of variables appear to be involved in its development [10]. Preeclampsia's precise pathophysiology is still unknown. Preeclampsia is thought to be caused by a toxic cocktail of angiogenic imbalance, hypoxia, weakened immunity, and inflammations [11]. It has been demonstrated that inflammation plays a significant role in the pathophysiology of many illnesses [12]. Endothelial dysfunction is linked to an increase in inflammatory markers, particularly C-reactive protein, which suggests that endothelial dysfunction may be the fundamental cause of this illness [13]. These observations are supported by clinical and biochemical evidence.

As an acute phase protein first synthesized in the liver in response to inflammatory stimuli, C-reactive protein is a crucial part of the innate immune system [14]. Acute phase protein C-reactive protein is frequently utilized as a diagnostic tool for inflammatory and infectious diseases. It has historically been employed as a disease activity marker and as an additional test for inflammation [15].

C-reactive protein levels in normal human blood are less than 10 mg/L, and they rise with age without changing for gender [16]. Late pregnancy is associated with slightly greater levels [17]. Elevations of 10–40 mg/L are caused by mild inflammation and viral infection, whereas 40–200 mg/L are produced by moderate inflammation and bacterial infection. Severe bacterial infections and burns are associated with levels exceeding 200 mg/L [18, 19]. According to Redman and colleagues, preeclampsia is a more widespread activation of intravascular leucocytes, the clotting and complement systems, and the mother's excessive reaction to pregnancy rather than an inherently distinct condition of pregnancy.

Accordingly, C-reactive protein may be a useful marker and contribute to the inflammatory response features of preeclampsia since it is a sensitive indicator of tissue damage and inflammation [20]. Therefore, the purpose of this research is to assess the relationship between elevated levels of C- reactive protein and the severity of preeclampsia as well as unfavorable fetal outcomes.

METHODOLOGY

This case-control study was carried out in the Department of Obstetrics & Gynecology of Dhaka Medical College Hospital, Dhaka, from January 2023 to December 2023. A total of 68 patients were enrolled and analyzed in this study. Patients who matched the inclusion and exclusion criteria were approached for participation in the study. Patients who were not willing to give consent were excluded. Purposive sampling was done according to the availability of the patients who fulfilled the selection criteria. Face to face interview was done to collect data with a semi-structured questionnaire. After collection, the data were checked and cleaned, followed by editing, compiling, coding, and categorizing according to the objectives and variable to detect errors and to maintain consistency, relevancy and quality control. Statistical evaluation of the results used to be obtained via the use of a window-based computer software program devised with Statistical Packages for Social Sciences (SPSS-24).

RESULT

Table I shows that, Maximum study subjects were in 21 – 30 years age group. Mean age of the study subjects was 26.12 ± 4.02 and 24.04 ± 4.32 years in PE with severe features and PE without severe features respectively.

Table I: Distribution of the patients according to age (n = 68)

Age (years)	PE with severe features (n=34)	PE without severe features (n=34)
≤20	4(11.8)	7 (20.5)
21 - 30	18(52.9)	19 (55.9)
>30	12(35.3)	8 (23.5)
Mean ± SD	**26.12 ± 4.02**	**24.04 ± 4.32**

Table II shows that, majority of the patients 27(79.4) and 25 (73.5) were housewife in both cases

Table II: Distribution of the patients according to occupation (n = 68)

Occupation	PE with severe features (n=34)	PE without severe features (n=34)
Housewife	27(79.4)	25 (73.5)
Service	7(20.6)	9 (26.4)

Table III shows that, Illiterate 2 (5.9%), higher secondary 9(26.5%) and graduate 10(29.4%) were higher in PE with severe features than PE without severe features.

Table III: Distribution of the patients according to educational status (n = 68)

Education	PE with severe features (n=34)	PE without severe features (n=34)
Illiterate	2 (5.9)	0 (0.0)
Primary	6 (17.6)	15 (44.1)
Secondary	7 (20.6)	12 (35.3)
Higher Secondary	9(26.5)	4 (11.8)
Graduate	10(29.4)	3 (8.8)

Table IV shows that, most of the patients 25 (73.5%) and 21 (61.8%) came from rural area

Table IV: Distribution of the patients according to residence (n = 68)

Residence	PE with severe features (n=34)	PE without severe features (n=34)
Urban	9(26.5)	13 (38.2)
Rural	25(73.5)	21 (61.8)

Table V shows that, Nullipara was higher in PE with severe feature and multigravida was higher in PE without severe features. Antenatal care was found more irregular in PE patients with severe features subjects than without severe features. Preterm pregnancy was higher in PE with severe feature than PE without severe features.

Table V: Distribution of the patients according to obstetric parameters (n = 68)

Obstetric Parameters		PE with severe features (n=34)	PE without severe features (n=34)
Parity	Nullipara	17(50.0)	13 (38.2)
	Primipara	6(17.6)	11 (32.4)
	Multipara	11(32.4)	10 (29.4)
Gravidity	Primigravida	15(44.1)	11 (32.4)
	Multigravida	19(55.9)	23 (67.6)
Antenatal care	Regular	11(32.4)	16 (47.1)
	Irregular	18(52.9)	14 (41.2)
	Not done	5(14.7)	4 (11.8)
Gestational age	Preterm (<37 weeks)	23(67.6)	20 (58.8)
	Term (≥37 weeks)	11(32.4)	14 (41.2)

Table VI shows that, Systolic and diastolic blood pressure were found significantly higher in PE patients with severe features than without severe features. hsCRP was found significantly higher in PE with severe features than PE without severe features.

Table VI: Distribution of the patients according to clinical parameters (n = 68)

Clinical Parameters	PE with severe features (n=34)	PE without severe features (n=34)	p-value
Systolic BP (mmHg)	169.67 ± 12.73	146.67 ± 7.11	<0.001
Diastolic BP (mmHg)	115.00 ± 7.31	96.33 ± 4.90	<0.001
hsCRP level	13.90 ± 3.16	7.59 ± 2.41	<0.001

Table VII shows that, APGAR score of the neonate was significantly better of PE patients without severe features than PE with severe features patients both at birth and at 5 minutes.

Table VII: Distribution of the patients according to APGAR score (n = 68)

	APGAR score	PE with severe features (n=34)	PE without severe features (n=34)
At birth	Good (≥ 7)	11(32.4)	19 (55.9)
	Low (Less than 7)	23(67.6)	15 (44.1)
At 5 minutes	Good (≥ 7)	21 (61.8)	29 (85.3)
	Low (Less than 7)	13(38.2)	5 (14.7)

Table VIII shows that, Average birth weight of the neonate was found higher of the PE patients without severe features than PE with severe features patients. There was 6(17.6%) very LBW of neonates of PE with severe features patients but none in PE without severe features patients.

Table VIII: Distribution of the patients according to birth weight (n = 68)

Birth weight	PE with severe features (n=34)	PE without severe features (n=34)
Average birth weight	13(38.2)	22 (64.7)
LBW	15(44.1)	12 (35.3)
Very LBW	6(17.6)	0 (0.0)

Table IX shows that, intrauterine growth retardation, and prematurity were found higher in PE with severe features patients comparing PE without severe features.

Table IX: Distribution of the patients according to other fetal outcome (n = 68)

Fetal outcome	PE with severe features (n=34)	PE without severe features (n=34)
Stillbirth (fresh)	3(8.8)	0 (0.0)
Intrauterine growth retardation	16(47.1)	7 (23.3)
Need admission to NICU	10(29.4)	8 (26.7)
Birth Asphyxia	8(23.5)	3 (10.0)
Prematurity	15(44.1)	3 (10.0)

DISCUSSION

The pregnancy illness known as preeclampsia is characterized by systemic inflammation. In 1930, Tillett and Francis found that individuals with an acute Pneumococcus infection had elevated serum levels of C-reactive protein (CRP) [21]. An acute phase protein called hsCRP proliferates in inflammatory areas. As a homopentameric protein, it is predominantly made in the liver, smooth muscle cells, macrophages, endothelial cells, lymphocytes, and adipocytes. This study set out to assess the relationship between hsCRP and preeclampsia severity as well as fetal fate in a tertiary care hospital.

This case-control study was carried out in the Department of Obstetrics & Gynecology of Dhaka Medical College Hospital, Dhaka, from January 2023 to December 2023. A total of 68 patients were enrolled and analyzed in this study.

In this study, maximum study subjects were in 21 – 30 years age group. Mean age of the study subjects was 26.12 ± 4.02 and 24.04 ± 4.32 years in PE with severe features and PE without severe features respectively. Similar age was observed in the study of Ertas *et al*., (2010) where mean age of PE without severe features and PE with severe features was 27.6 ± 3.6 and 25.4 ± 7.2 years respectively [22]. Similar observations were made by Kara *et al*., (2019), Gharib *et al*., (2016) and Behboudi-Gandevani (2016) [23-25].

Majority of the patients 27(79.4) and 25 (73.5) were housewife in both cases. Illiterate 2 (5.9%), higher secondary 9(26.5%) and graduate 10(29.4%) were higher in PE with severe features than PE without severe features. Most of the patients 25 (73.5%) and 21 (61.8%) came from rural area. Nullipara was higher in PE with severe feature and multigravida was higher in PE without severe features. Antenatal care was found more irregular in PE patients with severe features subjects than PE without severe features. Preterm pregnancy was higher in PE with severe feature than PE without severe features. Similar study was done by Sultana *et al*., (2015) which showed Irregular ANC was 27% in preeclampsia and 13 % in normal pregnant women. In the study of Ertas *et al*., (2010), nulliparity was 54.0% in PE without severe features and 71.0% in PE with severe features. Behboudi-Gandevani (2016) found nulliparity was 83.0% and 90.0% in PE without severe features and PE with severe features respectively [21-25].

Systolic and diastolic blood pressure were found significantly higher in PE patients with severe features than PE without severe features. Similar observation was also made by Gharib *et al*., (2016) [24]. In a similar study of Kumru *et al*., (2005), systolic and diastolic blood pressure were 172 ± 15 mm Hg and 108 ± 12 mm Hg respectively. There was significant positive correlation of hsCRP with systolic BP and diastolic BP in both PE with and without severe features [26].

hsCRP was found significantly higher in PE with severe features than PE without severe features. Similar observation was made by Ertas *et al*., (2010) who found mean hsCRP in PE without severe features was 9.6±7.1 mg/L and in PE with severe features was 23.4±16.5 mg/L [22]. Behboudi- Gandevani (2016) revealed hsCRP level in PE without severe features and PE with severe features was 7.2 ± 2.2mg/L and 9.4 ± 3.95 mg/L respectively [25]. In a similar study, Kumru *et al*., (2005) found significantly higher level of hsCRP in preeclampsia patients (9.5±0.8 mg/L) than normal pregnant women (3.9±2.5 mg/L) [26]. Jannesari and Kazemi (2017) also found significantly higher level of hsCRP in PE patients (7.71±6.19 ng/ml) than normal pregnant women (5.44±3.94ng/ml), they also revealed significantly higher level of hsCRP in pregnant women with PE with severe features (8.90±7.27 mg/L) than pregnant women with PE without severe features (6.70 ± 5.06 mg/L) [27]. Farzadnia *et al*., (2013) observed significantly higher hsCRP level in PE with severe features patients (12.8±7.3 mg/L) than PE without severe features (9.2±7.1 mg/L) [28]. Significantly higher hsCRP was observed in PE patients (23±4 mg /L) than normotensive patients (5±1 mg/L) in the study of Adali *et al*., (2011) [29].

Similar observation was also made by Gharib *et al*., (2016) [24]. In a similar study of Kumru *et al*., (2005), systolic and diastolic blood pressure were 172 ± 15 mm Hg and 108 ± 12 mm Hg respectively. There was significant positive correlation of hsCRP with systolic BP and diastolic BP in both PE with and without severe features [26].

APGAR score of the neonate was significantly better of PE patients without severe features then with severe features patients both at birth and at 5 minutes. Average birth weight of the neonate was found higher of the PE patients without severe features than with severe features patients. There was 6(17.6%) very LBW of neonates of PE with severe features patients but none in PE without severe features patients. According to Ertas *et al*., (2010), fetal birthweight was significantly higher in low hsCRP cases [22]. Kumru *et al*., (2005), in a similar study, found significantly lower birthweight in PE patients (2520±402.8 gm) than normal pregnant women (3125±735.5 gm), they also found elevated level of hsCRP was associated with low birth weight [26]. Farzadnia *et al*., (2013) observed significantly low birth weight in PE with severe fearures (2.1±0.97 kg) than Preeclampsia without severe features (2.3±0.68 kg) [28].

Intrauterine growth retardation, and prematurity were found higher in PE with severe features patients comparing PE without severe features. In cases of still birth, intrauterine growth retardation, birth asphyxia and prematurity, hsCRP levels were significantly higher. It is well known that PE increases the risks of intrauterine growth restriction and low birth weight by the study of Xiong *et al*., [30].

CONCLUSION

The results of this study demonstrated that compared to PE patients without severe features, those with preeclampsia with severe features had maternal hsCRP levels that were considerably higher. Low birthweight, low APGAR score, fresh stillbirth, intrauterine growth retardation, birth asphyxia, and preterm cases were all associated with considerably higher hsCRP levels.

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