Fetal Outcome and Effectiveness of Highly Sensitive C-reactive Protein in Preeclampsia: A Tertiary Care Hospital Study

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ABSTRACT

Background: C-reactive protein (CRP) is an acutephase reactant and a frequently used marker of low-grade systemic inflammation. Its levels increase in response to both infectious and noninfectious exposures. Elevated CRP levels during pregnancy, as a marker of low-grade inflammation, have also been suggested to be associated with increased risks of fetal growth restriction and neonatal complications, such as preterm birth, low birthweight, and small size for gestational age (SGA). **Objective:** The aim of this study is to evaluate the impact of highly sensitive c- reactive protein in preeclampsia on fetal outcome. **Methods:** The cross-sectional observational study was conducted in the Department of Obstetrics & Gynecology of Dhaka Medical College Hospital, Dhaka, from January 2023 to December 2023. A total of 86 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, majority 42 (48.8%) of the patients were in 21 – 30 years age group and 26 (30.2%) patients were in >30 years age group, Mean±SD of age was 28.8 ± 5.1 years. Most of the patients 59 (68.6%) were housewife and 27 (31.4%) patients were service holder. About 28 (32.6%) patients were completed their graduation, 23 (26.7%) were completed higher secondary and 5 (5.8%) were illiterate. most of the patients 54 (62.8%) came from rural area and 31 (36.0%) patients came from urban area. Nullipara was found in 37 (43.0%) patients and multigravida was found in most of the patients 51 (59.3%). Antenatal care was found irregular in 48 (55.8%) patients. Preterm pregnancy was found in majority 63 (73.3%) of the patients. Mean±SD of systolic and diastolic blood pressure were found higher (167.67 ± 12.63 and 116.00 ± 7.21) and hsCRP was also found higher (13.80 ± 3.15). APGAR score was found less in 53 (61.6%) neonate at birth and APGAR score was found good in 59 (68.6%) neonate at 5 minutes. Average birth weight was found in 18 (20.9%) neonates, LBW was found in 52 (60.5%) neonates and very LBW was found in 16 (18.6%) neonates. Intrauterine growth retardation and prematurity were found in 36 (41.9%) and 35 (40.7%) neonates, admission to NICU was needed for 32 (37.2%) neonates, birth asphyxia was found in 18 (20.9%) neonates and stillbirth was occured in 7 (8.1) cases. **Conclusion:** Maternal CRP levels in preeclampsia are associated with fetal growth restriction and increased risks of neonatal complications.
Key words: hsCRP, Preeclampsia, Eclampsia, Fetal Outcome

I. INTRODUCTION:

The acute phase reactant c-reactive protein (CRP) is a commonly used indicator of low-grade systemic inflammation. In reaction to both viral and noninfectious stimuli, its levels rise [1]. Increased risks of common diseases like type 2 diabetes and cardiovascular disease are linked to elevated CRP levels [2,3].

It is still unclear, though, if these correlations represent causal pathways [4,5]. High levels of CRP, a low-grade inflammatory marker, have also been linked to a higher chance of fetal growth restriction and neonatal problems, including preterm delivery, low birthweight, and small size for gestational age (SGA) [6–8]. Endothelial failure is linked to low-grade inflammation, which can result in vascular dysfunction and inadequate placental development. An additional explanation for maternal systemic inflammation could be placental ischemia brought on by inadequate placentation [9, 10].

Consequently, inadequate placental development may put moms at higher risk for a range of pregnancy-related issues [11,12]. While multiple studies have linked elevated CRP levels to preterm birth, the findings on the relationship between CRP levels and fetal development measurements or neonatal problems are inconsistent [13,14]. Variations in research approaches and populations may account for discrepancies in the outcomes. The relationship between CRP levels and fetal growth measurements is unknown.

Pre-eclampsia (PE) is a characteristic disorder of pregnancy and endothelial dysfunction is likely to have a pivotal role in its pathophysiology. It is a complicated, multi-organ disease occurring in up to 6-8% of pregnancies, typically after 20 weeks of gestation in previously normotensive women [15,16].

High systemic blood pressure and proteinuria are two of the most prevalent symptoms of preeclampsia, which develops after 20 weeks of gestation [17]. It affects 2-8% of population globally and is linked to increased rates of neonatal and maternal morbidity and mortality [18, 19]. Every year, this illness claims the lives of 500,000 infants and 76,000 women worldwide [20]. In addition, compared to women in high resource nations, women in low resource countries had a higher chance of having preeclampsia [21].

Eclampsia, a consequence of preeclampsia, is linked to around 24% of maternal deaths in Bangladesh, where the frequency is concerningly high [22, 23]. 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 [24]. 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) in both fetuses and neonates [25].

Preeclampsia's etiology is yet unknown, although a number of variables appear to be involved in its development [26]. 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 [27]. It has been demonstrated that inflammation plays a significant role in the pathophysiology of many illnesses [28]. 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 [29]. 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 [30]. 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 [31].

C-reactive protein levels in normal human blood are less than 10 mg/L, and they rise with age without changing for gender [32]. Late pregnancy is associated with slightly greater levels [33]. 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 [34, 35]. 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 [36]. 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.

II. METHODOLOGY:

The cross-sectional observational study was conducted in the Department of Obstetrics & Gynecology of Dhaka Medical College Hospital, Dhaka, from January 2023 to December 2023. A total of 86 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).

III.   RESULT:

Table I: Distribution of the patients according to age (n = 86)
Table I shows that, majority 42 (48.8%) of the patients were in 21 – 30 years age group and 26 (30.2%) patients were in >30 years age group, Mean±SD of age was 28.8 ± 5.1 years

Age group	Frequency	%
≤20	18	20.9
21 - 30	42	48.8
>30	26	30.2
Total	86	100.0
Mean + SD: 28.8 ± 5.1 Years		

Table II: Distribution of the patients according to occupation (n = 86)
Table II shows that most of the patients 59 (68.6%) were housewife and 27 (31.4%) patients were service holder

Occupation	Frequency	%
Housewife	59	68.6
Service	27	31.4
Total	86	100.0

Table III: Distribution of the patients according to educational status (n = 86)
Table III shows that, 28 (32.6%) patients were completed their graduation, 23 (26.7%) were completed higher secondary and 5 (5.8%) were illiterate

Education	Frequency	%
Illiterate	5	5.8
Primary	12	14.0
Secondary	18	20.9
Higher Secondary	23	26.7
Graduate	28	32.6
Total	86	100.0

Table IV: Distribution of the patients according to residence (n = 86)
Table IV shows that, most of the patients 54 (62.8%) came from rural area and 31 (36.0%) patients came from urban area

Residence	Frequency	%
Urban	31	36.0
Rural	54	62.8
Total	86	100.0

Table V: Distribution of the patients according to obstetric parameters (n = 86)
Table V shows that, Nullipara was found in 37 (43.0%) patients and multigravida was found in most of the patients 51 (59.3%). Antenatal care was found irregular in 48 (55.8%) patients. Preterm pregnancy was found in majority 63 (73.3%) of the patients.

Obstetric Parameters		Frequency	Percent
Parity	Nullipara	37	43.0
	Primipara	18	20.9
	Multipara	31	36.0
Gravidity	Primigravida	35	40.7
	Multigravida	51	59.3
Antenatal care	Regular	26	30.2
	Irregular	48	55.8
	Not done	12	14.0
Gestational age	Preterm (<37 weeks)	63	73.3
	Term (≥37 weeks)	23	26.7

Table VI: Distribution of the patients according to clinical parameters (n = 86)
Table VI shows that, Mean±SD of systolic and diastolic blood pressure were found higher (167.67 ± 12.63 and 116.00 ± 7.21) and hsCRP was also found higher (13.80 ± 3.15).

Clinical Parameters			p-value
Blood pressures	Systolic BP (mmHg)	167.67 ± 12.63	<0.001
	Diastolic BP (mmHg)	116.00 ± 7.21	<0.001
hsCRP level	hsCRP	13.80 ± 3.15	<0.001

Table VII: Distribution of the patients according to APGAR score (n = 86)
Table VII shows that, APGAR score was found less in 53 (61.6%) neonate at birth and APGAR score was found good in 59 (68.6%) neonate at 5 minutes.

APGAR score		Frequency	Percent
At birth	Good (≥ 7)	33	38.4
	Low (Less than 7)	53	61.6
At 5 minutes	Good (≥ 7)	59	68.6
	Low (Less than 7)	27	31.4

Table VIII: Distribution of the patients according to birth weight (n = 86)
Table VIII shows that, Average birth weight was found in 18 (20.9%) neonates, LBW was found in 52 (60.5%) neonates and very LBW was found in 16 (18.6%) neonates

Birth weight	Frequency	%
Average birth weight	18	20.9
LBW	52	60.5
Very LBW	16	18.6
Total	**86**	**100.0**

Table IX: Distribution of the patients according to other fetal outcome (n = 86)
Table IX shows that, Intrauterine growth retardation and prematurity were found in 36 (41.9%) and 35 (40.7%) neonates, admission to NICU was needed for 32 (37.2%) neonates, birth asphyxia was found in 18 (20.9%) neonates and stillbirth was occured in 7 (8.1) cases

Fetal outcome	Frequency	%
Stillbirth (fresh)	7	8.1
Intrauterine growth retardation	36	41.9
Need admission to NICU	32	37.2
Birth Asphyxia	18	20.9
Prematurity	35	29.1

IV. 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) [37]. 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.

The cross-sectional observational study was conducted in the Department of Obstetrics & Gynecology of Dhaka Medical College Hospital, Dhaka, from January 2023 to December 2023. A total of 86 patients were enrolled and analyzed in this study.

In this study, majority 42 (48.8%) of the patients were in 21 – 30 years age group and 26 (30.2%) patients were in >30 years age group, Mean±SD of age was 28.8 ± 5.1 years. 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 [38]. Similar observations were made by Kara et al., (2019), Gharib et al. (2016) and Behboudi- Gandevani (2016) [39, 40, 41].

Most of the patients 59 (68.6%) were housewife and 27 (31.4%) patients were service holder. About 28 (32.6%) patients were completed their graduation, 23 (26.7%) were completed higher secondary and 5 (5.8%) were illiterate. most of the patients 54 (62.8%) came from rural area and 31 (36.0%) patients came from urban area. Nullipara was found in 37 (43.0%) patients and multigravida was found in most of the patients 51 (59.3%). Antenatal care was found irregular in 48 (55.8%) patients. Preterm pregnancy was found in majority 63 (73.3%) of the patients. 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 [37, 41].

Mean±SD of systolic and diastolic blood pressure were found higher (167.67 ± 12.63 and 116.00 ± 7.21) and hsCRP was also found higher (13.80 ± 3.15). 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 [42].

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 [38]. 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 [41]. 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) [42]. 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) [43]. 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) [44]. 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) [45].

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 [42].

APGAR score was found less in 53 (61.6%) neonate at birth and APGAR score was found good in 59 (68.6%) neonate at 5 minutes. 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) [45].

Average birth weight was found in 18 (20.9%) neonates, LBW was found in 52 (60.5%) neonates and very LBW was found in 16 (18.6%) neonates. Intrauterine growth retardation and prematurity were found in 36 (41.9%) and 35 (40.7%) neonates, admission to NICU was needed for 32 (37.2%) neonates, birth asphyxia was found in 18 (20.9%) neonates and stillbirth was occured in 7 (8.1) cases. 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. [46].

V.   CONCLUSION:

In conclusion, maternal low-grade inflammation in early pregnancy, as measured by CRP levels, was associated with fetal growth restriction and increased risks of neonatal complications. Further studies are needed to explore the underlying mechanisms and causality for these associations. Low birthweight, low APGAR score, fresh stillbirth, intrauterine growth retardation, birth asphyxia, and preterm cases were all associated with considerably higher hsCRP levels in preeclampsia.

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