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**Original Research Article**

# Association of D-Dimer with Severity of Preeclampsia and Their Feto-Maternal Outcome

Dr. Asma Akter[1*], Dr. Fatema Rahman[2], Dr. Rokon Ud Dowla[3], Dr. Saeedul Islam[4], Dr. Sazedul Islam[5], Saima Akter[6], Dr. Sumaiya Tazin[7]

[1]Medical Officer, Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital, Dhaka, Bangladesh
[2]Professor, Department of Gynaecology and Obstetrics, Head of Reproductive Endocrinology and Infertility, Dhaka Medical College Hospital, Dhaka, Bangladesh
[3]Registrar, Department of Neonatology, Sir Salimullah Medical College Hospital, Dhaka, Bangladesh
[4]Resident, Department of Anaesthesia, Analgesia and Intensive Care Medicine, BSMMU, Dhaka, Bangladesh
[5]Medical Officer, Holycare Hospital, Noakahali, Bangladesh
[6]Consultant Nutritionist, Holycare Hospital, Noakhali, Bangladesh
[7]Assistant Registrar, Department of Gynaecology and Obstetrics, Dhaka Medical College Hospital, Dhaka, Bangladesh

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***Corresponding author:** Dr. Asma Akter
Medical Officer, Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital, Dhaka, Bangladesh

## Abstract

***Background:*** Preeclampsia (PE) affects 2-8% of pregnancies worldwide, leading to maternal and fetal complications such as abruptio placentae, renal failure, and HELLP syndrome. ***Objective:*** To investigate the association between plasma D-dimer levels and the severity of preeclampsia, along with its impact on fetomaternal outcomes. ***Methods:*** A case-control study was conducted at Dhaka Medical College Hospital from June 2021 to May 2022, enrolling 100 preeclamptic patients (50 with severe features and 50 without severe features). Participants were between 29-40 weeks of gestation. Exclusion criteria included chronic hypertension, renal/hepatic disorders, diabetes, and fetal anomalies. D-dimer levels were measured from 3 mL venous blood samples. Maternal and fetal outcomes were documented and analyzed using SPSS software. ***Results:*** The mean age of patients was 26.62 ± 3.99 years (PE without severe feature) and 27.26 ± 5.45 years (PE with severe feature). D-dimer levels were significantly higher in the severe feature group (2.91 ± 2.14 µg/mL) compared to the non-severe feature group (0.79 ± 0.45 µg/mL; $p<0.005$). Severe PE was associated with higher rates of postpartum hemorrhage (58.0%), HELLP syndrome (12.0%), abruptio placentae (44.0%), and fetal growth restriction (46.0%). The severe PE group also had significantly lower APGAR scores and higher NICU admissions (42.0%). Elevated D-dimer levels were significantly correlated with maternal and fetal complications, including eclampsia ($p=0.020$), HELLP syndrome ($p=0.011$), and fetal growth restriction ($p=0.022$). ***Conclusion:*** Elevated plasma D-dimer levels are significantly associated with the severity of preeclampsia and adverse maternal and fetal outcomes.

**Keywords:** Preeclampsia, D-dimer, Maternal outcomes, Fetal outcomes, HELLP syndrome.



## INTRODUCTION

Preeclampsia (PE), a hypertensive disorder that complicates approximately 2-8% of pregnancies worldwide, remains a major contributor to maternal and neonatal morbidity and mortality [1]. Defined by new-onset hypertension and proteinuria after 20 weeks of gestation, it can evolve into more severe forms, such as eclampsia, HELLP syndrome, and disseminated intravascular coagulation (DIC), potentially leading to life-threatening complications for both mother and fetus. In addition to its global prevalence, the incidence of preeclampsia varies based on parity, being more frequent in nulliparous women (3-7%) and less so in multiparous women (1-3%) [2]. Although PE is a relatively common condition, it continues to pose significant challenges in terms of early identification, effective management, and prediction of maternal and fetal outcomes. The consequences of untreated or poorly managed preeclampsia are dire, resulting in significant adverse outcomes, including maternal stroke, seizures, hepatic

and renal failure, fetal growth restriction, and even stillbirth. Worldwide, preeclampsia is responsible for approximately 76,000 maternal deaths and 500,000 neonatal deaths annually and its prevalence is notably higher in low-resource settings, including Bangladesh, where 24% of maternal deaths are attributed to eclampsia [3]. The pathophysiology of preeclampsia remains incompletely understood, but a variety of factors contribute to its development, including impaired placental trophoblast invasion, endothelial dysfunction, oxidative stress, and abnormal angiogenesis. Preeclampsia often manifests in the third trimester of pregnancy, with its incidence notably higher among first-time pregnancies [4]. While the primary pathophysiologic mechanisms of preeclampsia are centered on placental dysfunction, it is clear that a complex interplay of genetic, immunologic, and environmental factors contribute to its progression and severity.

A key feature in the clinical diagnosis and management of preeclampsia is the assessment of coagulation markers, particularly D-dimer, a fibrin degradation product that can be measured in maternal blood. D-dimer levels are typically elevated in PE patients due to fibrin deposition in the microvasculature of both maternal and fetal circulations, leading to placental ischemia, maternal organ dysfunction, and fetal growth restriction [5]. Under normal pregnancy conditions, D-dimer levels naturally rise due to the physiological activation of coagulation and fibrinolysis as the placenta develops and grows. However, in women with preeclampsia, these levels are abnormally high, reflecting the extent of fibrin deposition and degradation occurring in the maternal and placental microcirculations. The role of D-dimer as a diagnostic tool in preeclampsia has garnered increasing interest, as elevated D-dimer levels are associated with several adverse outcomes, including increased risk of maternal complications such as eclampsia, HELLP syndrome, and DIC, as well as poor fetal outcomes such as intrauterine growth restriction, low birth weight, and preterm delivery [6]. D-dimer testing may therefore serve as a sensitive biomarker for distinguishing between severe and non-severe forms of preeclampsia, offering a potential strategy for early identification of at-risk patients, guiding treatment decisions, and improving patient management. Furthermore, the use of D-dimer testing to predict fetomaternal complications could lead to more timely interventions, such as early delivery or closer monitoring, which may significantly reduce maternal and neonatal morbidity.

The physiological basis for D-dimer elevation in preeclampsia lies in the pathogenesis of the disease, where impaired trophoblastic invasion of the uterine spiral arteries results in placental ischemia, inflammation, and oxidative stress [7]. These processes lead to the release of various pro-inflammatory cytokines and vasoactive factors, which in turn activate the coagulation cascade. The resulting formation of fibrin clots in the placental microvasculature and the maternal circulation leads to the production of D-dimer as the clots undergo fibrinolysis. Elevated D-dimer levels are thus reflective of ongoing fibrin deposition and degradation, indicating a heightened state of coagulation activation and fibrinolysis [8]. The clinical utility of D-dimer as a diagnostic marker in preeclampsia is further supported by studies showing that higher levels of D-dimer are associated with more severe disease features, including postpartum hemorrhage, HELLP syndrome, and abruptio placentae. The association between elevated D-dimer levels and adverse fetal outcomes, such as fetal growth restriction (FGR) and preterm birth, is also well-documented. In preeclamptic women, poor placental perfusion, as a result of impaired vascular remodeling, leads to reduced nutrient and oxygen delivery to the fetus, resulting in growth restriction and increased likelihood of preterm birth. D-dimer levels may serve as a predictive biomarker for fetal growth impairment, allowing for earlier interventions to prevent adverse outcomes. In addition, D-dimer has been found to correlate with lower APGAR scores, as well as an increased need for neonatal intensive care unit (NICU) admission, both of which are indicative of poor neonatal outcomes [9].

Despite the growing body of evidence supporting the clinical utility of D-dimer in preeclampsia, its use remains underutilized in many clinical settings. In Dhaka Medical College Hospital, where this study is being conducted, a well-established hematology and bone marrow transplant (BMT) department routinely conducts coagulation profiles, including D-dimer testing, for patients with preeclampsia. However, there is limited research specifically addressing the utility of D-dimer in distinguishing between preeclampsia with severe features and non-severe preeclampsia, as well as its predictive value for maternal and fetal outcomes in the Bangladeshi context. This gap in knowledge forms the basis of the current study, which seeks to evaluate the relationship between maternal D-dimer levels and the severity of preeclampsia, as well as the associated maternal and fetal outcomes. By elucidating the role of D-dimer in preeclampsia, this research aims to contribute to the development of more effective diagnostic and prognostic tools, ultimately improving the management and outcomes of preeclamptic pregnancies.

**Aims and Objective**

The general objective of this study is to assess the relationship between D-dimer levels and the severity of preeclampsia, as well as their association with feto-maternal outcomes. Specific objectives include comparing D-dimer levels in patients with severe and non-severe preeclampsia, exploring the correlation between D-dimer and disease severity, and analyzing D-dimer levels in relation to different feto-maternal outcomes.

# MATERIALS AND METHOD

**Inclusion criteria**

- Age between 18 -35
- Singleton pregnant
- Pregnant patient having gestational age 29 weeks to 40 weeks
- Patient of preeclampsia with or without severe features

**Exclusion criteria**

- Severe ill patient admitted in HDU and ICU
- Known case of chronic hypertension, chronic renal disease, hepatic disease and coagulation disorder
- Gestational diabetes mellitus
- Pregnancy with congenital anomaly.
- Intrauterine death
- BMI ≥30 kg/$m^2$

**Data collection**

Data were collected using a preformed data collection sheet. The relevant socio- demographic data of these women were collected and recorded. Data were collected by researcher herself.

**Data analysis**

Statistical analysis was performed using statistical package for social science (SPSS) software version 22.0. Qualitative data were presented as percentage with frequency and quantitative data as mean with standard deviation. Unpaired t-test, Mann-Whitney U test and Kruskal-Wallis test was performed for numerical data. Chi-Square test, Fisher exact test was performed to analyze the categorical variable shown with cross tabulation. Pearson's correlation test was done to see the association between two continuous data. A p values <0.05 was considered as statistically significant.

**Ethical Consideration**

Prior to the commencement of this study, the research protocol was approved by the Ethical Review Committee of Dhaka Medical College Hospital, Dhaka. The aims and objectives of the study along with its procedure, risks and benefits of this study were explained to the patients in easily understandable local language and then informed consent (appendix) was taken from each patient. It was assured that all information and records were kept confidential and the procedure would be helpful for both the obstetricians and the patients in making rational approach of the case management.

# MATERIAL AND METHODS

**Study Design**

This prospective case-control study was conducted at the Department of Gynecology and Obstetrics, Dhaka Medical College Hospital, from June 2021 to May 2022. The study aimed to evaluate the association of D-dimer levels with the severity of preeclampsia and feto-maternal outcomes among preeclamptic patients. It involved 100 pregnant women, aged between 18 and 35 years, who were diagnosed with preeclampsia, both with and without severe features, and had a gestational age between 29 and 40 weeks.

**Inclusion Criteria**

The study included pregnant women aged between 18 and 35 years, with a singleton pregnancy, and a gestational age between 29 to 40 weeks. Participants were diagnosed with preeclampsia with or without severe features, based on clinical presentation and laboratory results. The inclusion criteria aimed to ensure that the sample population was representative of women experiencing preeclampsia during the third trimester of pregnancy, minimizing confounding factors related to age, multiple gestation, or significant comorbidities.

**Exclusion Criteria**

Patients were excluded from the study if they had severe illness requiring intensive care unit (ICU) or high dependency unit (HDU) admission, or were known to have chronic hypertension, chronic renal disease, hepatic disorders, or coagulation disorders. Other exclusion criteria included gestational diabetes mellitus, pregnancy with congenital anomalies, intrauterine fetal death, and women with a BMI ≥30 kg/m². These criteria were established to avoid confounding by underlying chronic conditions or factors unrelated to preeclampsia.

**Data Collection**

Data were collected using a structured data collection sheet. Socio-demographic details, including age, parity, gestational age, and medical history, were recorded. Clinical data regarding preeclampsia severity and maternal complications were also documented. Blood samples for D-dimer testing were taken from all participants. The data were collected by the researcher, ensuring standardized procedures for each patient. Information was recorded accurately and analyzed to evaluate the association between D-dimer levels and feto-maternal outcomes.

**Data Analysis**

The collected data were analyzed using the Statistical Package for Social Sciences (SPSS) software version 26.0. Descriptive statistics were used to present qualitative data as percentages and frequencies, and quantitative data as means with standard deviations. The association between numerical data was assessed using unpaired t-tests, Mann-Whitney U tests, and Kruskal-Wallis tests. For categorical variables, Chi-square tests and Fisher's exact tests were applied. Pearson's correlation test was used to explore relationships between continuous variables. A p-value of <0.05 was considered statistically significant.

**Ethical Considerations**

Ethical approval for the study was obtained from the Ethical Review Committee of Dhaka Medical

College Hospital. Before participation, the research objectives, procedures, risks, and benefits were explained to all participants in a language they could easily understand. Written informed consent was obtained from each participant. Confidentiality of the patients' information was strictly maintained, ensuring that their personal details and medical data were securely stored. The study aimed to benefit both obstetricians and patients by providing insight into the management of preeclampsia.

## RESULTS

This Case control study was undertaken to assess the level of D-dimer with severity of preeclampsia in Dhaka Medical College Hospital. The results are as follows:

**Table 1: Demographic profile of the study subjects (N=100)**

| | PE without severe features | Pe with severe features | p-value |
|---|---|---|---|
| **Age (years)** | | | |
| ≤20 | 3 (6.0) | 4 (8.0) | |
| 21 - 25 | 13 (26.0) | 16 (32.0) | |
| 26 - 30 | 26 (52.0) | 20 (40.0) | |
| >30 | 8 (16.0) | 10 (20.0) | |
| Mean ± SD | 26.62 ± 3.99 | 27.26 ± 5.45 | [1]0.505 |
| **Educational status** | | | |
| Primary | 8 (16.0) | 6 (12.0) | [b]0.334 |
| Secondary | 30 (60.0) | 25 (50.0) | |
| Higher Secondary | 9 (18.0) | 17 (34.0) | |
| Graduate | 3 (6.0) | 2 (4.0) | |
| **Socio-economic status** | | | |
| Poor | 11 (22.0) | 13 (26.0) | b0.480 |
| Middle class | 34 (68.0) | 35 (70.0) | |
| Rich | 5 (10.0) | 2 (4.0) | |

Table 1 shows demographic profile of the study subjects. Maximum patients were in age group 26-30 years and 21-25 years age group in both groups. Mean age of the patients in PE without severe features group was 26.62 ± 3.99 years and PE with severe features group was 27.26 ± 5.45 years. There was no significant difference in age between two groups.

**Table 2: Obstetric characteristics of the study subjects (N=100)**

| Obstetric Parameter | PE without severes features(n=50) | PE with severe features(n=50) | p-value |
|---|---|---|---|
| Gestational age (weeks) <37 | 25 (50.0) | 42 (84.0) | [b]<0.00 1 |
| ≥37 | 25 (50.0) | 8 (16.0) | |
| Mean ± SD | 36.40 ± 1.60 | 34.32 ± 2.23 | [a]<0.00 1 |
| Antenatal checkup Regular | 20 (40.0) | 14 (28.0) | [b]0.444 |
| Irregular | 27 (54.0) | 32 (64.0) | |
| Not done | 3 (6.0) | 4 (8.0) | |
| Gravida Primigravida | 12 (24.0) | 13 (26.0) | [b]0.817 |
| Multigravia | 38 (76.0) | 37 (74.0) | |

[a]Unpaired t test and [b]Chi-Square test was done

Table 2 shows history of the study subjects. Gestational age was significantly higher in PE without severe features than PE with severe features

**Table 3: Blood pressure level of study (N=100)**

| | PE without severe features | PE with severe feature | p-value |
|---|---|---|---|
| Systolic blood pressure (mm Hg) | 150.96 ± 11.31 | 186.70 ± 14.41 | <0.00 1 |
| Diastolic blood pressure (mm Hg) | 93.24 ± 6.89 | 115.40 ± 7.20 | <0.00 1 |

Unpaired t test was done.

Table 3 shows blood pressure of the study subjects. Mean systolic blood pressure were 150.96 and 186.70 respectively in PE without severe features and PE with severe features. Mean diastolic blood pressure were 93.24 and 115.40 respectively in PE without severe features and PE with severe features. Both the systolic and diastolic blood pressure was significantly higher in PE with severe features than PE without severe features.

**Table 4: D-dimer level of the study subjects (N=100)**

| | PE without severe features | PE with severe features | p-value |
|---|---|---|---|
| D-dimer (µ/mL) | 0.79 ± 0.45 | 2.91 ± 2.14 | [a]<0.001 |

[b]Mann-Whitney U test was done

Table 4 shows D-dimer level of the study subjects. D-dimer was found significantly higher in PE with severe features than PE without severe features.

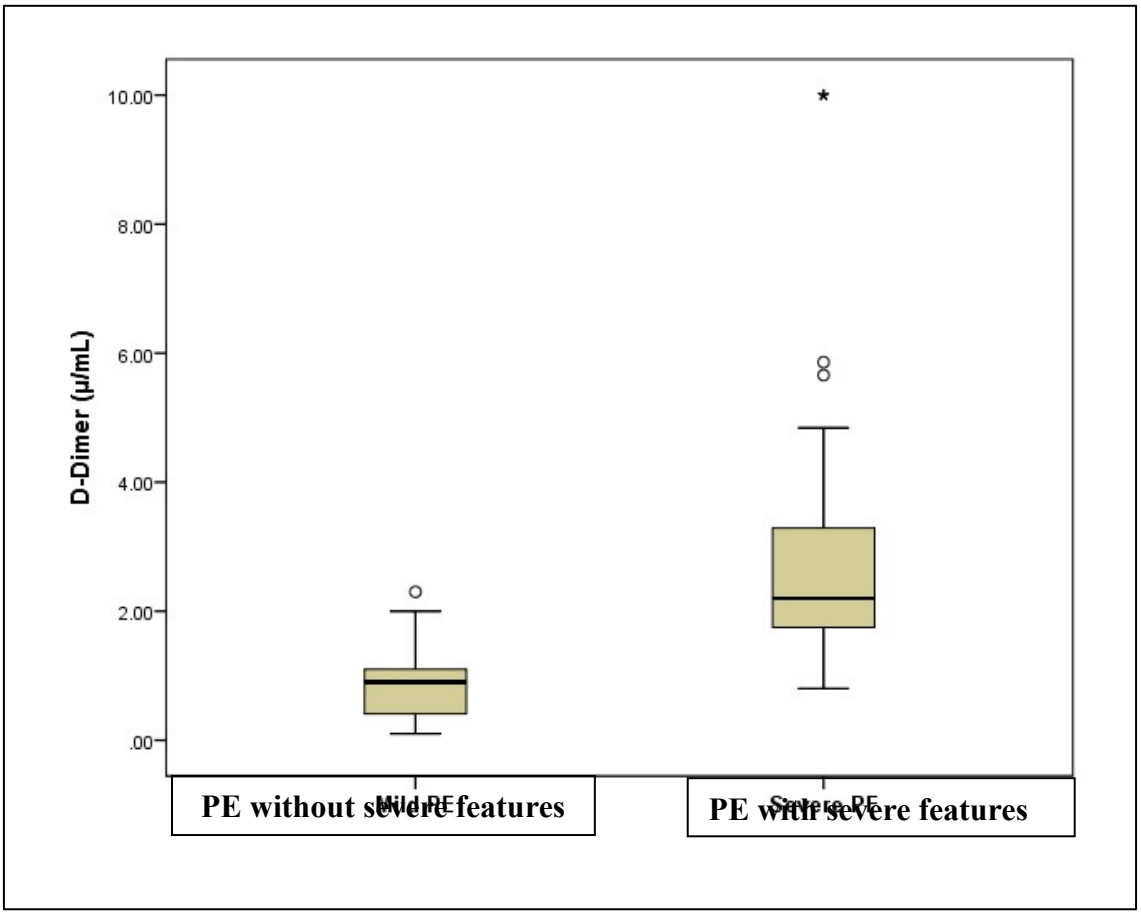


**Figure 1: Box plot showing D-dimer level in PE without severe feature and PE with severe feature patients**

**Table 5: Correlation of D-dimer with blood pressure (N=100)**

| Blood pressure | r | p-value |
|---|---|---|
| Systolic BP | 0.451 | <0.001 |
| Diastolic BP | 0.482 | <0.001 |

There was significant positive correlation of D-dimer with both systolic & diastolic blood pressure (p<0.001)

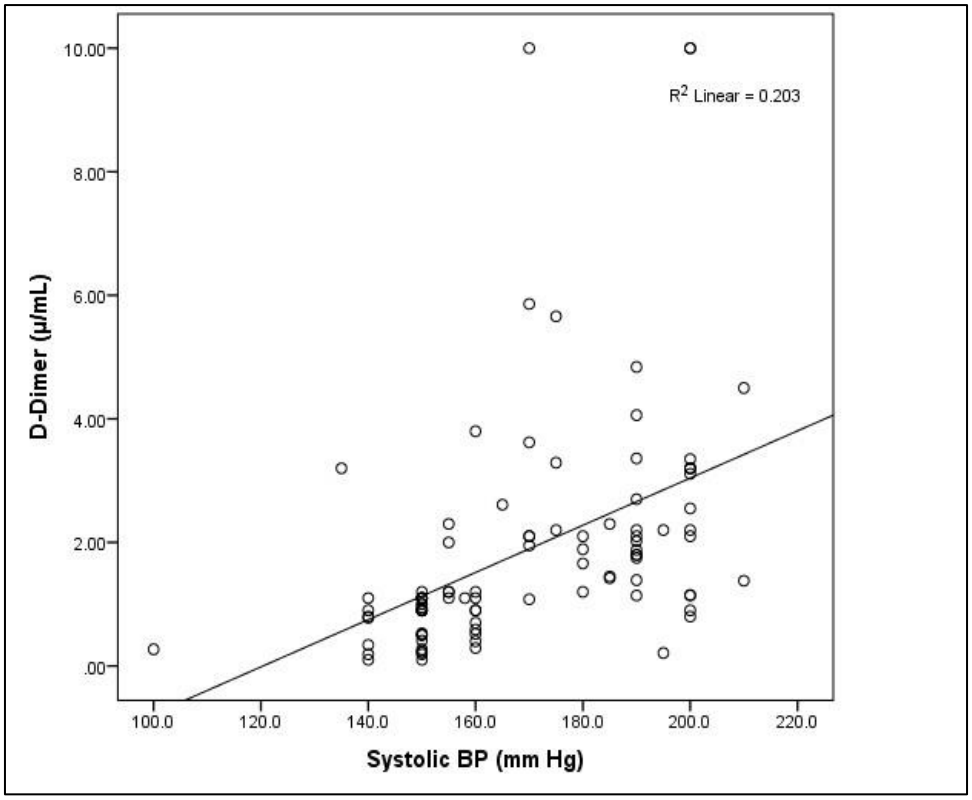


**Figure 2: Scattered diagram showing correlation of D-Dimer with systolic blood pressure**

There was significant positive correlation of D-Dimer with systolic blood pressure (r=+0.451; p<0.001)

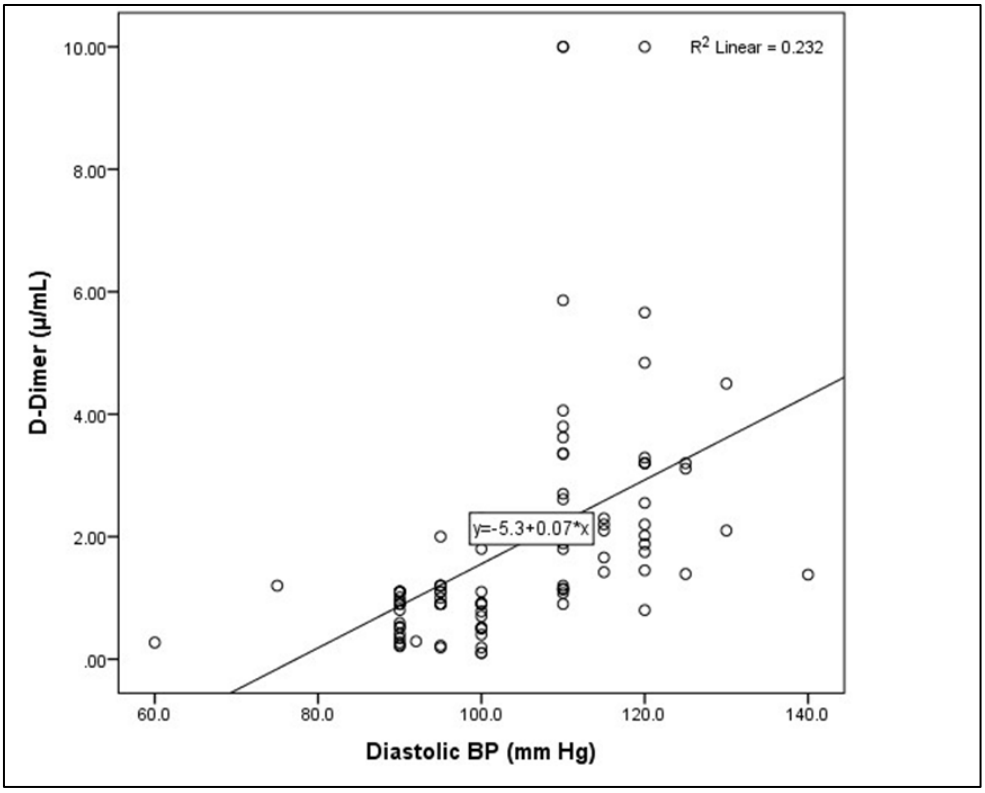


**Figure 3: Scattered diagram showing correlation of D-Dimer with diastolic blood pressure**

There was significant positive correlation of D-Dimer with diastolic blood pressure (r=+0.482; p<0.001)

**Table 5: Association of D-dimer with severity of preeclampsia (N=100)**

| D-Dimer (µg/mL) | PE without severe features | PE with severe feature | p-value |
|---|---|---|---|
| Normal (<0.5 µg/mL) | 13 (26.0) | 0 (0.0) | [a]<0.001 |
| Raised (≥0.5 µg/mL) | 37 (74.0) | 50 (100.0) | |
| Mean ± SD | 0.79 ± 0.45 | 2.91 ± 2.14 | [a]<0.001 |

[a]Chi-Square test and [b]Mann-Whitney U test was done

Table 5 shows association of D-dimer with severity of preeclampsia. Raised level of D-dimer was found all cases in PE with severe features patients. Difference was statistically significant.

**Table 6: Other lab findings of the study subjects (N=100)**

| | PE without severe features | PE with severe features | p-value |
|---|---|---|---|
| FDP (µ/mL) | 8.13 ± 4.96 | 29.56 ± 17.35 | [a]<0.001 |
| Hb% (g/dl) | 10.73 ± 1.24 | 10.37 ± 1.76 | [b]0.235 |
| Platelet count (x$10^3$ unit/ $mm^3$) | 224.7 ± 141.2 | 172.1 ± 176.3 | [a]<0.001 |
| PT (sec) | 12.89 ± 0.95 | 13.64 ± 1.83 | [b]0.012 |
| APTT (sec) | 29.77 ± 3.81 | 33.13 ± 6.71 | [b]0.003 |

[a]Mann-Whitney U test and [b]unpaired t test was done

Table 6 shows other lab findings of the study subjects. FDP, PT and APTT were found significantly higher in PE with severe features than PE without severe features patients.

**Table 7: Mode of delivery of Preeclamptic patient (N=100)**

| Mode of delivery | PE without severe features | PE with severe features | p-value |
|---|---|---|---|
| CS | 48 (96.0) | 41 (82.0) | [a]0.025 |
| VD | 2 (4.0) | 9 (18.0) | |

[a]Fisher Exact test was done

Table 7 shows mode of delivery. Mode of delivery in CS was significantly higher in PE without severe features than PE with severe features.

**Table 8: Other maternal outcome (N=100)**

| | PE without severe features | PE with severe features | p-value |
|---|---|---|---|
| Eclampsia | 1 (2.0) | 11 (22.0) | [a]0.002 |
| Postpartum hemorrhage | 1 (2.0) | 29 (58.0) | [a]<0.001 |
| Renal insufficiency | 0 (0.0) | 3 (6.0) | [a]0.242 |
| HELLP | 0 (0.0) | 6 (12.0) | [a]0.027 |
| Cerebrovascular disease | 0 (0.0) | 1 (2.0) | [a]1.000 |
| Disseminated intravascular disease | 1 (2.0) | 4 (8.0) | [a]0.169 |
| Abruptio placentae | 6 (12.0) | 22 (44.0) | [b]0.001 |
| Pulmonary edema | 1 (2.0) | 0 (0.0) | [a]1.000 |

[a]Fisher's Exact test and [b]Chi-Square test and was done

Table 8 shows others maternal outcome. Postpartum hemorrhage, HELLP and abruptio placentae were found significantly higher in PE with severe features than PE without severe features patients.

**Table X: Association of D-Dimer with mode of delivery in PE patients (N=100)**

| Mode of delivery | D-dimer (µg/mL) (mean ± SD) | p-value |
|---|---|---|
| CS | 1.83 ± 1.94 | 0.282 |
| VD | 1.99 ± 1.29 | |

Mann-Whitney U test was done

Table 9 shows D-Dimer level in different mode of delivery.

**Table 9: Association of D-Dimer with maternal outcome in PE patients (N=100)**

| | D-dimer (µg/mL) (mean ± SD) | p-value |
|---|---|---|
| Eclampsia | 3.20 ± 2.67 | 0.020 |
| No eclampsia | 1.67 ± 1.67 | |
| Postpartum hemorrhage | 3.25 ± 2.47 | <0.001 |
| No postpartum hemorrhage | 1.25 ± 1.12 | |
| Renal insufficiency | 1.91 ± 0.59 | 0.359 |
| Sufficient renal function | 1.85 ± 1.90 | |
| HELLP syndrome | 4.84 ± 4.06 | 0.011 |
| No HELLP syndrome | 1.66 ± 1.50 | |
| Cerebrovascular disease | 1.38 ± 0.00 | 0.900 |
| No cerebrovascular disease | 1.86 ± 1.88 | |
| Disseminated intravascular disease | 3.55 ± 3.72 | 0.150 |
| No disseminated intravascular disease | 1.76 ± 1.72 | |
| Abruptio placentae | 2.67 ± 2.31 | 0.001 |
| No abruptio placentae | 1.52 ± 1.57 | |

Mann-Whitney U test was done

Table 9 shows maternal outcome of the patients according to D-dimer level. Raised level of D-Dimer was significantly associated with eclampsia, postpartum hemorrhage, HELLP syndrome and abruptio placentae.

**Table 10: APGAR score and still birth according to severity of preeclampsia (N=100)**

| | PE without severe features | PE with severe features | p-value |
|---|---|---|---|
| APGAR score at birth (Low) | 11 (22.0) | 35 (70.0) | [a]**<0.001** |
| APGAR score at 5 minutes (Low) | 11 (22.0) | 33 (66.0) | [a]**<0.001** |
| Stillbirth | 0 (0.0) | 1 (2.0) | [b]1.000 |

[a]Chi-Square test and [b]Fisher's Exact test was done

Table 10 shows APGAR score and still birth according to severity of preeclampsia. APGAR score was found significantly low at birth and at 5 minutes in PE with severe features than PE without severe features group.

**Table 11: Foetal outcome according to severity of preeclampsia (N=100)**

| | PE without severe features | PE with severe features | p-value |
|---|---|---|---|
| Birth weight | 2350 ± 519 | 2017 ± 623 | **0.005** |
| Average | 26 (52.0) | 10 (20.0) | [a]**0.003** |
| Low | 20 (40.0) | 31 (62.0) | |
| Very low | 4 (8.0) | 9 (18.0) | |
| Fetal growth Restriction | 9 (18.0) | 23 (46.0) | [a]**0.003** |
| Admission to NICU | 8 (16.0) | 21 (42.0) | [a]**0.004** |
| Birth Asphyxia | 2 (4.0) | 11 (22.0) | [b]**0.007** |
| Prematurity | 3 (6.0) | 28 (56.0) | [b]**<0.001** |
| Resuscitation needed | 1 (2.0) | 15 (30.0) | [b]**<0.001** |

[a]Chi-Square test and [b]Fisher's Exact test was done

Table 11 shows foetal outcome according to severity of preeclampsia. Low and very low birth weight was found significantly higher in PE with severe features than PE without severes group. Fetal growth restriction, birth asphyxia and prematurity were found significantly higher in PE with severe features than PE without severe features group. NICU admission and resuscitation requirement was found significantly higher in PE with severe features than PE without severe features group.

**Table 12: Association of D-Dimer with APGAR score and stillbirth in PE patients (N=100)**

| | D-dimer (µg/mL) (mean ± SD) | |
|---|---|---|
| APGAR score at birth Good (≥7) | 1.14 ± 0.78 | <0.001 |
| Low (<7) | 2.69 ± 2.38 | |
| At 5 min Good (≥7) | 1.17 ± 0.79 | <0.001 |
| Low (<7) | 2.72 ± 2.43 | |
| Stillbirth | 4.06 ± 0.00 | 0.160 |
| Live birth | 1.83 ± 1.87 | |

Mann-Whitney U test was done

Table 12 shows association of D-Dimer with APGAR score and stillbirth. Raised level of D-Dimer was associated with low APGAR score.

**Table 13: Association of D-Dimer with foetal outcome in PE patients (N=100)**

| | D-dimer (µg/mL) (mean ± SD) | |
|---|---|---|
| Birth weight<br>Normal | 1.33 ± 1.08 | [b]0.084 |
| Low | 2.11 ± 2.05 | |
| Very low | 2.30 ± 2.60 | |
| FGR | 2.47 ± 2.34 | [a]0.007 |
| Non FGR | 1.56 ± 1.54 | |
| Need admission to NICU | 2.89 ± 2.92 | [a]0.024 |
| No need admission to NICU | 1.43 ± 0.96 | |
| Birth Asphyxia | 4.57 ± 3.48 | [a]<0.001 |
| Non birth asphyxia | 1.45 ± 1.03 | |
| Prematurity | 3.09 ± 2.62 | [a]<0.001 |
| Maturity | 1.30 ± 1.03 | |
| Resuscitation needed | 3.84 ± 2.87 | [a]<0.001 |
| No resuscitation needed | 1.47 ± 1.34 | |

[a]Mann -Whitney U test and [b]Kruskal -Wallis test was done

Table 13 shows association of D-Dimer with foetal outcome. Raised level of D-Dimer was associated with FGR, NICU admission, birth asphyxia, prematurity, resuscitation need.

**Table 14: True positive, false positive, false negative and true negative value of D-dimer in diagnosis of severity of preeclampsia at a cutoff point (0.5 µg/ml)**

| D-dimer | PE with severe features | PE without severe features | p-value |
|---|---|---|---|
| ≥0.5 µg/ml | 50 (100.0) | 37 (74.0) | <0.001 |
| <0.5 µg/ml | 0 (0.0) | 13 (26.0) | |

Fisher Exact test was done

## DISCUSSION

Preeclampsia (PE) is a hypertensive disorder of pregnancy that is marked by the onset of hypertension and the presence of organ dysfunction, typically after 20 weeks of gestation. The severity of PE can range from mild to severe, with the latter being associated with a higher risk of adverse maternal and fetal outcomes [10]. This study aimed to explore the relationship between serum D-dimer levels and the severity of preeclampsia, focusing on the association of elevated D-dimer with various maternal and fetal outcomes in patients with severe and non-severe PE. The results of this study are discussed in comparison with other findings in the literature.

### *Demographic Characteristics*

In this study, the majority of participants in both the PE without severe features and PE with severe features groups were aged between 21 and 30 years, with the peak age range being 26-30 years. The mean age of the patients in the PE without severe features group was 26.62 ± 3.99 years, while in the PE with severe features group, it was 27.26 ± 5.45 years. The difference in mean age was not statistically significant, which is consistent with findings from studies by Yuan *et al.*, where no significant age differences were noted between the two groups [11]. Similarly, Asghar *et al.* reported that most cases of PE were in the 26-30 years age group [12]. These findings suggest that PE can affect women across a wide age range, with no specific age group being predominantly at risk for severe manifestations of the disease.

### *D-Dimer Levels and Severity of Preeclampsia*

One of the most significant findings in this study is the marked difference in D-dimer levels between patients with PE without severe features and those with severe features. The mean D-dimer levels were significantly higher in the PE with severe features group (2.91 ± 2.14 µg/mL) compared to the PE without severe features group (0.79 ± 0.45 µg/mL; p<0.005). These results are in line with the findings of previous studies, including Duan *et al*., Belay Tolu *et al.*, Kim *et al*., all of whom observed significantly elevated D-dimer levels in patients with severe PE [13-15]. The results of this study support the hypothesis that D-dimer could serve as a useful biomarker for the severity of PE, potentially aiding in the identification of high-risk patients who may require more intensive monitoring and intervention. D-dimer is a fibrin degradation product that is typically elevated in conditions involving thrombosis, such as PE, which is known to have an increased risk of coagulation abnormalities. Elevated D-dimer levels in PE are thought to reflect the extent of vascular damage, endothelial dysfunction, and increased fibrinolysis. In this study, the significant elevation in D-dimer levels among those with

severe PE highlights its potential role in assessing the severity of the disease and possibly predicting the risk of complications such as thrombosis, postpartum hemorrhage, and organ failure.

***Gestational Age and Preeclampsia Severity***

In contrast to previous studies, which have reported that women with severe PE tend to have longer gestational ages than those with non-severe PE, this study found that gestational age was significantly lower in the PE with severe features group (34.32 ± 2.23 weeks) compared to the PE without severe features group (36.40 ± 1.60 weeks) [16]. This discrepancy may be due to differences in study populations, with some studies including a broader range of PE cases, including those diagnosed earlier in pregnancy, or due to variations in the severity of disease at diagnosis. The association between severe PE and lower gestational age may suggest that severe manifestations of the disease are more likely to occur earlier in pregnancy, potentially leading to earlier delivery due to fetal or maternal distress. This observation is also consistent with the increased risk of preterm delivery associated with severe forms of PE.

***Maternal Outcomes and Complications***

Several maternal outcomes were significantly more common in the PE with severe features group compared to the PE without severe features group. Postpartum hemorrhage (PPH) was found in 58.0% of severe PE cases, compared to only 2.0% in the non-severe PE group ($p<0.001$). This finding aligns with the results of Kongwattanakul *et al.*, who found that women with severe PE were more likely to experience PPH [17]. A similar study also highlighted the association between elevated D-dimer levels and an increased risk of PPH in preeclamptic women. The increased incidence of PPH in severe PE is thought to be related to endothelial dysfunction, platelet aggregation, and coagulopathy, which are common in severe PE and can lead to significant bleeding complications during delivery. Additionally, HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome was observed in 12.0% of the severe PE cases in this study, which is consistent with the findings of a similar study who reported a significantly higher prevalence of HELLP syndrome in women with severe PE. HELLP syndrome is a serious complication of severe PE that is associated with a high risk of maternal morbidity and mortality, and the findings from this study highlight the importance of early identification and management of patients with severe PE to prevent such adverse outcomes. Furthermore, the incidence of abruptio placentae was significantly higher in the severe PE group (44.0%) compared to the non-severe PE group (12.0%), which is consistent with the findings of Belay Tolu *et al*., [18]. Abruptio placentae, or placental abruption, is a serious complication of PE that is associated with significant maternal and fetal morbidity. The increased risk of abruption in severe PE is thought to be related to the vascular changes and endothelial dysfunction that occur in the disease.

***Fetal Outcomes***

Fetal outcomes were also significantly worse in the severe PE group. The PE with severe features group had a considerably lower APGAR score at 1 minute (70.0% vs. 22.0%) and 5 minutes (66.0% vs. 22.0%) after birth compared to the PE without severe features group. These findings align with the results of a similar study, who reported significantly lower APGAR scores in severe PE cases. The lower APGAR scores in the severe PE group reflect the greater risk of fetal distress, hypoxia, and intrauterine growth restriction (IUGR) in these patients. In fact, fetal growth restriction was significantly more common in the severe PE group (46.0%) compared to the non-severe PE group (18.0%; $p=0.003$), a finding consistent with the study by Khawaja *et al*., [19]. IUGR occurs in PE due to placental insufficiency, and it is a known risk factor for adverse fetal outcomes, including low birth weight and increased risk of neonatal morbidity and mortality. In this study, birth weight was significantly lower in the severe PE group (80.0%) compared to the non-severe PE group (48.0%; $p=0.003$), which is consistent with the findings of a similar study. Low birth weight is a well-established consequence of severe PE, as the impaired placental blood flow and nutrient transfer in severe forms of the disease contribute to fetal underdevelopment. These findings emphasize the importance of closely monitoring fetal growth and development in women with severe PE, as well as the need for early intervention to optimize outcomes for both mother and child.

***Mode of Delivery***

In this study, the mode of delivery was found to differ between the two groups. The severe PE group had fewer caesarean section (CS) deliveries compared to the non-severe PE group (82.0% vs. 96.0%), which is contrary to the findings of Çintesun *et al*., who found that women with severe PE were more likely to have a CS delivery [20]. The lower rate of CS in the severe PE group in this study may be attributed to a variety of factors, including the timing of delivery, the clinical management approach, and the presence of other complicating factors such as fetal distress or IUGR. Additionally, the clinical decision for mode of delivery in severe PE cases often depends on the assessment of maternal and fetal well-being, with CS being the preferred option in cases of fetal distress or maternal complications.

***Comparison of Study Findings***

In this study, we observed significantly higher D-dimer levels in patients with severe preeclampsia (PE) compared to those with non-severe PE, which aligns with findings from previous studies. For instance, Jin *et al*. both reported significantly elevated D-dimer levels in patients with severe PE, suggesting that D-dimer could serve as a reliable biomarker for disease severity [21].

Similarly, Dong *et al*., highlighted the relationship between elevated D-dimer levels and adverse maternal outcomes, such as postpartum hemorrhage (PPH) and HELLP syndrome, which were also more common in our study's severe PE group [22]. Regarding maternal complications, our findings of a higher incidence of PPH and abruptio placentae in the severe PE group are consistent with the results of a smililar study. Both studies reported a stronger association between severe PE and these complications, reinforcing the notion that severe PE is a high-risk condition for maternal morbidity. Fetal outcomes in our study, such as lower birth weight and increased rates of fetal growth restriction (IUGR) in the severe PE group, also mirror the results of previous studies, including Gutiérrez García *et al*., which found a higher prevalence of IUGR and low birth weight in women with severe PE [23]. The significantly lower APGAR scores at 1 and 5 minutes in the severe PE group, found in our study, were similarly observed in studies by a similar study, reflecting the impact of severe PE on neonatal health. Overall, our results are consistent with the literature, further supporting D-dimer's role as a marker for assessing the severity of PE and predicting associated maternal and fetal complications [24-30].

## CONCLUSION

Preeclamptic pregnant women with severe features tend to have higher plasma concentrations of D-dimer than those without severe features. In our study, there is significant association of D-dimer with severity of preeclampsia. Raised plasma D-dimer level is also associated with adverse maternal outcomes including post partum hemorrhage, HEELP syndrome, abruptio placentae as well as adverse fetal outcome including Low birth weight, Fetal growth restriction, Low APGAR score, birth asphyxia and requirement of NICU admission.

### Recommendations

- Further studies on a larger sample and multiple time points can be done.
- To provide a more precise result, a longitudinal prospective study on women seeking antenatal care from the start of their pregnancy can be conducted.
- Plasma D-dimer levels can be used as a screening tool for monitoring the disease activity of preeclampsia.
- Further update procedure to measure D-dimer level is needed.

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### Abbreviations

| | |
|---|---|
| ACOG | American College of Obstetrics & Gynaecology |
| ANC | Antenatal Care |
| DBP | Diastolic Blood Pressure |
| DMCH | Dhaka Medical College Hospital |
| DIC | Disseminated intravascular coagulation |
| ERC | Ethical review committee |
| ELISA | Enzyme-linked immunosorbent assay |
| FIGO | International Federation of Gynecology & Obstetrics |
| FGR | Fetal growth restriction |
| HDU | High dependency unit |
| HELLP | Hemolysis, Elevated liver enzyme, low platelet count |
| HTN | Hypertension |
| ICU | Intensive care unit |
| NICU | Neonatal intensive care unit |
| PE | Preeclampsia |
| PIH | Pregnancy induced hypertension |
| SB | Still birth |
| SBP | Systolic Blood Pressure |
| SPSS | Statistical Package for the social science |
| VTE | Venous thromboembolism |

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