

## Original article

### D-dimer level in preeclampsia and normal pregnancy

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#### Abstract

Preeclampsia is a multifactorial disease characterized by high blood pressure and proteinuria after the 20th week of pregnancy. D-Dimer is a useful diagnostic tool for thrombotic conditions because its plasma concentration has a high negative predictive value for venous thromboembolism. This study aims to evaluate D-dimer level in preeclampsia and normotensive pregnant women. This cross sectional analytic study was conducted at the Obstetrics and Gynaecology department, Dhaka Medical College Hospital to evaluate the D-dimer level in preeclampsia and normal pregnancy, during July 2014 to June 2015. A total of 90 patients, out of them 45 were preeclamptic women considered as group A and 45 were normotensive pregnant women considered as group B. A P-value <0.05 was taken as minimum level of significance. Among 90 respondents, highest incidence was belonging to age 21-25 years. The mean age was found 25.84±4.7 which was higher in preeclampsia than normotensive pregnant women 23.80±2.8 years (p<0.05). Primigravida were significantly commoner in preeclampsia than that in normal pregnancy. The mean blood pressure was significantly higher in preeclamptic women than normotensive pregnant women (systolic 151.3+9.07 vs 114.0+8.36 mm Hg and diastolic 97.11+ 8.01 vs 73.55 +4.47 mm Hg, p<0.05). Plasma D-dimer level demonstrated their significant presence in preeclamptic women (44.4%) than that in the normotensive women (6.6%) p<0.05. Estimation of Odds Ratio demonstrates that preeclamptic women have 11-fold (95% of CI=3.0 – 41.5) higher risk of having plasma D-dimer >0.5 µg /ml than that of normal pregnant women. Correlation analysis found that D-dimer have positive correlation with both systolic (r= 0.571, p <0.001) and diastolic blood pressure (r= 0.514, p <0.05) of preeclamptic women. The study concludes that D-dimer level considered to be a potential bio-marker for hematologic and fibrinolytic changes occurs in preeclampsia.

**Keywords:** D dimer, pre-eclampsia, fibrinolysis, BMI.  
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#### Introduction

Preeclampsia is a multifactorial disease characterized by systolic blood pressure  $\geq 140$  mm Hg or diastolic  $\geq 90$  mm Hg at bed rest on at least two occasions 6 h apart, and with or without proteinuria  $\geq 0.3$  g/24 h, measured after the 20th week of pregnancy and remission of signs after delivery<sup>1,2</sup>. Preeclampsia can progress to eclampsia (characterized by seizures as a sign of affection of the cerebral vessels), syndrome HELLP (hemolysis, elevated liver enzyme, low platelets) or disseminated intravascular coagulation<sup>2</sup>. It is a serious complication of the second half of pregnancy and leading cause of neonatal mortality and morbidity, both directly via intrauterine growth restriction and indirectly through its association with the placental abruption and need for preterm delivery and also maternal death<sup>3,4</sup>. This study will help us to compare the D-dimer level between preeclamptic patients and normal pregnancy.

#### Methods

This cross sectional analytic study was conducted at the Obstetrics and Gynaecology department, Dhaka Medical College Hospital to evaluate the D-dimer level in preeclampsia and normal pregnancy, during July 2014 to June 2015. A total of 90 patients, out of them 45 were preeclamptic women considered as group A and 45 were normotensive pregnant women considered as group B. Inclusion criteria includes, age group from 17 – 35 years, parity less than 5, gestational age 28 to 40 weeks, singleton pregnancy, preeclampsia, diagnosed by blood pressure elevation, equal or more than 140/90 mm. Exclusion criteria includes, multiple pregnancy, polyhydramnios or oligohydramnios, known bleeding disorder, on anticoagulant therapy, abruptio placenta, intrauterine fetal death (IUD), suspected sepsis, history of essential hypertension, diabetes mellitus, chronic renal disease, hepatic disease, hypothyroidism or hyperthyroidism and other medical disease. Statistical analyses were carried out by using the SPSS (Statistical Package for Social Sciences) version 22.0 for windows

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(SPSS Inc., Chicago, Illinois, USA). Ethical clearance was taken from Ethical Review Committee (ERC), Dhaka Medical College (DMCH) Hospital.

**Result**

Twenty of 45 (44.4%) of preeclamptic women and 3 of 45 healthy pregnant women were found positive for D-dimer. In this study the D-dimer level was found significantly increased in preeclamptic women when compared with normotensive pregnant women.

**Table No 1: Distribution of the study subjects by demographic characteristics of (n= 90)**

Parameters	Group		p-value
	Group A (n=45)	Group B (n = 45)	
<b>Age</b>			
Mean ± SD	25.84 ± 4.719	23.80± 2.865	0.001
<b>Gestational age (weeks)</b>			
< 37	20(44.4)	15(33.3)	0.279
> 37	25(55.6)	30(66.7)	
<b>Socioeconomic condition</b>			
Lower	35(77.8)	33(73.3)	0.623
Middle	10(22.2)	12(26.7)	
<b>Gravida</b>			
Primi	31(68.9)	25(55.6)	0.192
Multi	14(31.1)	20(44.4)	
<b>Antenatal check up</b>			
Regular	9(20.0)	10(22.2)	0.965
Irregular	28(62.2)	27(60.0)	
None	8(17.8)	8(17.8)	

Table 1 Demographic characteristics between two groups did not show any significant difference in any of these parameters except age.

**Table No. 2: Distribution of the study subjects by plasma D-dimer of (n=90).**

D-dimer level	Group		OR	95% CI	p-value
	Group A (n=45)	Group B (n =45)			
D-dimer positive (>0.5 µg/ml)	20(44.4)	3(6.6)	11.1	3.0 -41.5	0.001
D-dimernegative (≤0.5 µg/ml)	25(55.5)	42(93.3)			

Table II shows that 44.4% of case group had a significantly high level of plasma D-dimer (> 0.5 µg/ml) as opposed to control group (6.6%) (p< 0.05). Estimation of odds Ratio demonstrates that preeclamptic women had 11 times (95% of CI = 3.0 - 41.5) more risk of having plasma D-dimer > 0.5 µg/ml than that of normal pregnant women.

**Table No. 3: Association of blood pressure and plasma D-dimer in preeclamptic women.**

Blood pressure	Plasma D-dimer level µg/ml		p-value
	> 0.5 (n=20)	≤0.5 (n = 25)	
<b>Systolic Blood Pressure</b>			
≥160 mmHg	15(33.3)	7(15.5)	p = 0.003
140-159 mmHg	5(11.1)	18(40.0)	
<b>Diastolic Blood Pressure</b>			
≥ 110 mmHg	5(11.1)	0(0.0)	0.001
< 100 mmHg	15(33.3)	25(55.6)	

Table No. 3 shows that majority (33.3%) of preeclamptic women with plasma D-dimer >0.5 µg/ml had systolic blood pressure ≥160 mmHg compared to (15.5%) of those who had plasma D-dimer ≤0.5 µg/ml. Association of blood pressure with plasma D-dimer level was statistically significant (p<0.05).

**Discussion**

The present study was conducted to evaluate the plasma D-dimer in preeclampsia and normal pregnancy for the prognosis and treatment of the disease. The preeclamptic women were significantly older (mean age=25.84±4.7) than the normotensive pregnant women (mean age=23.80±2.8 years). There was no significant difference in gestational weeks, gravida, parity, antenatal checkup and socioeconomic condition between two groups. Mean age was found statistically significant (p<0.05) between two groups. Ganai et al.<sup>4</sup> showed the mean age of control group 23.1±1.4 compared to study group 21.5±1.6, which shows that mean age of study group was significantly low(p<0.001). Mean age difference was statistically significant (p<0.05) between two groups which is comparable with the current study. Kumer et al.<sup>7</sup> showed the majority of the cases (55.3%) were in the age group of 26-30 years with mean of 25±3.02 which is comparable Vamsheedher et al.<sup>16</sup>, Shivakumer et al. and Prakash et al.<sup>12</sup> studied with the mean age of 24.57±3.46, 24.3 and 24.75±3.360 respectively, however in Onisai et al.<sup>17</sup> study he observed that the mean age of preeclampsia was 29.8 years.

In current study, it is observed that primigravida were significantly commoner in preeclamptic women that is 68.9% than in normotensive women which is 55.65%

( $p < 0.05$ ). Similarly, in another study, Kumer et al.<sup>7</sup> 61% of cases were of primigravida and 53% of cases were preeclampsia as compared to other studies like Prakash et al.<sup>12</sup> with 44% and Jahromi et al.<sup>13</sup> with 56% of cases. Similar observations were made by Chaware et al.<sup>14</sup> who showed 75 patients were primigravidae, 27 were second gravidae and 18 were third or more gravidae. As compared to mild and severe preeclampsia, eclampsia was more common in primigravidae.

The observation from the study has revealed that a staggeringly higher percentage of preeclamptic women had plasma D-dimer  $> 0.5 \mu\text{g/ml}$  (44.4%) compared to that observed in normotensive pregnant women (6.6%). The risk of developing plasma D-dimer  $> 0.5 \mu\text{g/ml}$  in preeclamptic women was estimated to be 11-fold (95% of CI=3.0 – 41.5) than that of normal counterparts. This observation is in accordance with the work of Abbas et al.<sup>9</sup> who showed D-dimer was significantly increased in preeclamptic women compared to normotensive pregnant women. Kovac et al.<sup>10</sup> mentioned the difference of D-dimer level between the first and the second and between the second and the third trimester is statistically significant  $p < 0.0001$  (student's t-test). In the present study, we found 3 patients of normotensive pregnant women out of 45 had D-dimer  $> 0.5 \mu\text{g/ml}$ . D-dimer as a marker of fibrinolysis increases to counter-balance the increased coagulation factors and reduces the incidence of venous thromboembolism in normal pregnancy. Several studies showed that D-dimer level progressively rise during the second and third trimesters of pregnancy.<sup>6,18</sup> Jeremiah et al.<sup>6</sup> also showed D-dimer values correlate significantly with gestation ( $r = 0.361$ ;  $P < 0.01$ ) and about 63.3% of the pregnant women had normal D-dimer values (0–200 ng/mL), 26.7% had elevated D-dimer levels (201–499 ng/mL), while 10.0% of the pregnant women were found to be at risk of thrombosis (D-dimer  $> 500$  ng/mL). A linear relationship was found to exist between D-dimer and gestation ( $y = 8.355x + 36.55$ ;  $R^2 = 0.130$ ;  $P < 0.005$ ). Similar observations were made by Abbas et al.<sup>9</sup> studied 60 preeclamptic women, where D-dimer showed significant positive correlation with the duration of hypertension appear ( $P = 0.000$ ). According to Kobayahi et al.<sup>15</sup> high level of D-dimer (D-dimer  $> 4 \mu\text{g/ml}$ ) which is useful bedside predictive marker together with a significant decrease of antithrombin is strongly indicative for termination of pregnancy. The findings of the present study is consistent with those described above with markedly raised plasma D-dimer level in patients with preeclampsia than in normal pregnant women. Thus preeclamptic coagulopathy can be assumed by the level of D-dimer.

In current study, correlation between blood pressure and D-dimer revealed, a high level of plasma D-dimer in preeclamptic patients with the increase in systolic and diastolic blood pressure. Plasma D-dimer has strong positive correlation with both systolic blood pressure ( $r =$

$0.571$ ,  $p < 0.001$ ) and diastolic blood pressure ( $r = 0.514$ ,  $p < 0.001$ ). Heilmann and his associates<sup>5</sup> also demonstrated similar correlation between D-dimer and diastolic blood pressure ( $r = 0.44$ ,  $p = 0.007$ ). The risk of developing coagulopathy in women with D-dimer  $> 0.5 \mu\text{g/ml}$  was estimated 11 times (95% of CI=3.0 – 41.5) higher in preeclamptic women than that of normal pregnancy. The mean blood pressures in patients with plasma D-dimer  $> 0.5 \mu\text{g/ml}$  were considerably higher than those who had plasma D-dimer  $< 0.5 \mu\text{g/ml}$  ( $p < 0.05$ ).

## Conclusion

Preeclamptic women are at risk of developing hypercoagulable state compared to the normotensive pregnant women. The study concludes that plasma D-dimer level can easily be used in screening for the hypercoagulable state in preeclampsia as D-dimer testing is quicker, relatively non-invasive, does not harm the fetus. Its role in pregnant women should be furthermore investigated in a larger prospective study.

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