Original Article

Association Between Pre-Eclampsia and High D-Dimer Levels

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Abstract

Objective: To determine the association between pre-eclampsia and high d-dimer levels.

Methodology: A total of 60 patients (30 pre-eclamptic and 30 normotensive) of age 18-40 years of any parity were included. Patients with chronic hypertension, smoking, alcoholic and renal disease were excluded. In all subjects, a blood sample was sent for measurement of plasma D-dimer levels. The report of each subject was assessed by the researcher herself and high levels of D-dimer (>0.5µg/ml) was noted as yes or no in both cases and controls.

Results: The mean age of women in the case group was 29.90 ± 4.89 years and in the control group was 30.08 ± 5.88 years. The mean gestational age was 26.67 ± 2.28 weeks. Mean parity was 2.82 ± 1.02. Frequency of high d-dimer levels in case group (pre-eclampsia) was seen in 14 (46.67%) while in control group (normotensive) was seen in 04 (13.33%) women which has shown p-value of 0.005 and odds ratio of 5.69 which is significant and shows a positive association between pre-eclampsia and high d-dimer levels (>0.5µg/ml).

Conclusion: An association between pre-eclampsia and high d-dimer levels (>0.5µg/ml) was found to be significant.

Keywords: Preeclampsia, D-dimer levels, Pregnancy.

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Introduction

D-dimer (D-Di) has been used as a marker of the production/degradation of fibrin in vivo. D-Di has emerged as a useful diagnostic tool for thrombotic conditions because its plasma concentration has a high negative predictive value for venous thromboembolism.6 D-dimer testing is of clinical use when there is a suspicion of deep venous thrombosis (DVT), pulmonary embolism (PE) or disseminated intravascular coagulation (DIC).

Preeclampsia is a hypertensive condition of pregnancy diagnosed when a woman with no history of hypertension develops hypertension and proteinuria after 20 weeks of gestation.[1] An important initiating event in the pathogenesis of preeclampsia is thought to be abnormal placentation with the shallow invasion of the placental cytotrophoblast and consequent compromised placental perfusion.[2] Preeclampsia (PE) is an intractable obstetric disorder that affects 6–8% of pregnancies worldwide. The abnormal invasion of placenta and the release of placenta-derived adverse factors during the first trimester is thought to be the main cause of the extensive damage to the maternal endothelium and systemic inflammatory response involving many systems and organs in late pregnancy.[3]

Preeclampsia is associated with microvasculature fibrin deposition and maternal organ dysfunction.

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In PE patients, the coagulation-fibrinolytic system is thought to be one of the most seriously affected systems by maternal inflammatory reactions and immune dysfunction.[4] The balance between coagulation and anticoagulation is vital to the regulation of utero-placental circulation and organ perfusion in a pregnant woman. An appropriate increase in blood coagulation is important for a normal pregnant woman to reduce postpartum hemorrhage and to limit other complications.[5] D-dimer (D-Di) has been used as a marker of production/degradation of fibrin in vivo. D-Di has emerged as a useful diagnostic tool for thrombotic conditions because its plasma concentration has a high negative predictive value for venous thromboembolism.[6] D-dimer testing is of clinical use when there is a suspicion of deep venous thrombosis (DVT), pulmonary embolism (PE) or disseminated intravascular coagulation (DIC).[7]

There was no data available locally regarding the role of D-dimer in determining coagulability status in pre-eclamptic women. Furthermore, study of this kind is required for establishing if pre-eclampsia affects vascular anatomy and physiology in pregnant patients. Through this study, we will be able to find the relation between pre-eclampsia and high levels of d-dimer as the main predictor of coagulability status, by comparing the frequency of high d-dimer levels of pre-eclamptic women with a control group of normotensive pregnant women. This study will provide a baseline and current local statistics of association between pre-eclampsia and high D-dimer levels (>0.5µg/ml). It will also help in deciding whether further recommendations, with regards to d-dimer screening, should be implemented in all pre-eclamptic women. Therefore, this study will be of clinical importance in planning prevention and therapeutic strategies.

Methodology

This case control study was done from January 2017 to December 2017, after approval from the local ethical committee. The sampling technique used was non-probability consecutive sampling. Sixty women (30 pre-eclamptic and 30 normotensive women) with singleton pregnancy either primiparous or multiparous of age 18-40 years, presented to the department of obstetrics & gynecology, PIMS Hospital, Islamabad, were selected. Patients with chronic hypertension, smoking, alcoholic and renal disease were excluded.

Informed consent of women was taken. In all subjects, the blood sample was sent to the Institutional Pathology laboratory for measurement of plasma d-dimer levels by consultant pathologist. The report of each subject was assessed by the researcher herself and high levels of d-dimer (>0.5µg/ml) was noted as yes or no in both cases and controls.

Data was entered and analyzed using SPSS-20. Descriptive statistics were applied to calculate mean and standard deviation for quantitative variables like age, gestational age, parity and BMI. Frequencies and percentages were calculated for qualitative variables like high levels of d-dimer (yes/no). Chi-square test was used to determine the association between pre-eclampsia and high d-dimer levels. $p \leq 0.05$) was considered as significant and the odds ratio was also calculated.

Results

The age range in this study was from 18 to 40 years with mean age of 29.98 ± 5.36 years. The mean age of women in case group was 29.90 ± 4.89 years and in control group was 30.08 ± 5.88 years. The majority of the patients 31 (51.67%) were between 31 to 40 years of age. The mean gestational age in case group was 26.60 ± 2.19 weeks and in control group was 26.73 ± 2.39 weeks. Mean parity was 2.82 ± 1.02.

Frequency of high D-dimer levels in case group (pre-eclampsia) was seen in 14 (46.67%) while in control group (normotensive) was seen in 04 (13.33%) women which has shown p-value of 0.005 and odds ratio of 5.69 which is significant and shows a positive association between pre-eclampsia and high d-dimer levels (>0.5µg/ml).(Table I)

Table I: Association between pre-eclampsia and high D-dimer levels (>0.5µg/ml).

		Cases (n=30)		Controls (n=30)	
		No. of Patients	%age	No. of Patients	%age
High D-Dimer Levels	**Yes**	14	46.67	04	13.33
	No	16	53.33	26	86.67

- *P value is 0.005 which is statistically significant.*
- *Odds ratio is 5.69 which is significant.*

Table II: Stratification of high D-dimer levels with respect to age, gestational age, parity and BMI.

		Cases (n=30)		Controls (n=30)		P-value	OR
		high D-dimer levels		high D-dimer levels			
		yes	no	yes	no		
Age of patients (years)	**18-30**	07 (46.67%)	08 (53.33%)	02 (14.29%)	12 (85.71%)	0.060	5.25
	31-40	07 (46.67%)	08 (53.33%)	02 (12.50%)	14 (87.50%)	0.036	6.12
GA (weeks)	**20-28**	10 (43.48%)	13 (56.52%)	03 (15.0%)	17 (85.0%)	0.043	4.36
	>28	04 (57.14%)	03 (42.86%)	01 (10.0%)	09 (90.0%)	0.036	12.0
Parity	**≤3**	10 (50.0%)	10 (50.0%)	03 (13.64%)	19 (86.36%)	0.011	6.33
	>3	04 (40.0%)	06 (60.0%)	01 (12.50%)	07 (87.50%)	0.196	4.67
BMI (kg/m^2)	**≤30**	09 (45.0%)	11 (55.0%)	03 (13.64%)	19 (86.36%)	0.025	5.18
	>30	05 (50.0%)	05 (50.0%)	01 (12.50%)	07 (87.50%)	0.094	7.00

Effect modifiers like age, gestational age, parity and BMI were controlled by stratification. Post stratification chi-square test was also applied and odds ratio was also calculated. P-value ≤0.05 was taken as significant. (Table II)

Discussion

Preeclampsia is a multifactorial disease characterized by hypertension and proteinuria after 20 weeks of gestation of the pregnancy. Preeclampsia is characterized by the deposition of fibrin in the walls of small blood vessels. D-dimer was used as a marker for degradation/synthesis of fibrin in vivo. D-dimer has emerged as a useful indicator in the diagnosis of thrombotic conditions because its plasma concentration has a high predictive value for the assessment of venous thromboembolism.[8] Manolov V et al.[8] found that elevated levels of D-dimer is associated with the development of pre-eclampsia in the third trimester of pregnancy compared with normal pregnancy. In a study, the average D-Di levels were 634 ± 228 ng/ml, 1426 ± 430 ng/ml, 2067 ± 580 ng/ml in the control group, preeclamptic and eclamptic patients, respectively. The levels of D-Di in preeclamptic and eclamptic patients were found significantly higher than the control groups (p = 0.034, p = 0.020).[9]

In a study[10], level of plasma D-dimer in 160 cases, including 106 normal pregnant women and 25 patients with mild and moderate PIH, 18 patients with preeclampsia and 11 patients with eclampsia were measured. The value (2.27 +/- 0.92 mg/L) of plasma D-dimer in mild and moderate PIH patients was markedly higher than that of normal third trimester pregnant women (1.45 +/- 0.38 mg/L, P < 0.01). The value (3.09 +/- 1.65 mg/L) of plasma D-dimer in preeclampsia patients was markedly higher than that of mild and moderate PIH patients (P < 0.01). The value (5.62 +/- 1.34 mg/L) of plasma D-dimer in eclampsia patients was markedly higher than that of preeclampsia patients. The author concluded that determination of plasma D-dimer level in second and third trimester pregnant women was of great significance in diagnosing early PIH and predicting the prognosis of PIH.[10]

Moreover, a cross sectional study[11] was carried out in the department of obstetrics and gynecology, Dhaka Medical College Hospital, Dhaka, Bangladesh. Pregnant women with pre-eclampsia were selected as cases. Healthy and uncomplicated pregnant women admitted in the same hospital were taken as controls. The study showed that 26-30 years and 21-25 years age category was higher in the case and control groups and the mean age was significantly higher in case group compared to control group (p=0.025). The study showed that 44% of case group had a significantly high level of plasma D-dimer (>0.5µg/ml) as opposed to the control group (8%) (p<0.001). Estimation of odds ratio demonstrates that pre-eclamptic women (case) had 9 times (95% of CI = 2.8 - 28.9) more risk of having plasma D-dimer >0.5µg/ml than that of normal pregnant women (control). The mean systolic and diastolic blood pressures in patients with plasma D-dimer >0.5µg/ml were considerably higher than those who had plasma D-dimer ≤0.5µg/ml (p<0.001). The study showed that majority (81.8%) of pre-eclamptic women with plasma D-dimer >0.5µg/ml had systolic blood pressure ≥ 160 mm Hg compared to 46.4% of those who had plasma D-dimer ≤0.5µg/ml (p=0.010). And ninety percent of pre-eclamptic women with plasma D-dimer >0.5µg/ml had exhibited severe proteinuria as opposed to 53.6% of those who had plasma D-dimer ≤0.5µg/ml (p=0.017). The study concludes that plasma D-dimer level can easily be used in

screening for the hypercoagulable state in pre-eclamptic patients which have preventive and therapeutic implications.[11]

A study in Sudanese preeclamptic women reported the statistically significant elevation of d-dimer levels in the woman with preeclampsia as compared to normotensive pregnant women (Mean ± SD1.016 ± 0.158 vs 0.168 ± 0.045 with P value 0.000).[12] Moreover, it was reported that concentrations of d-dimer were significantly elevated in patients with severe features than those without severe features among those with gestational hypertension.[13] Similarly, another study reported obvious relationship between d-dimers concentration and severe preeclampsia.[14]

We conducted this study to determine the association between pre-eclampsia and high d-dimer levels (>0.5µg/ml). Frequency of high d-dimer levels in case group (pre-eclampsia) was seen in 14 (46.67%) while in control group (normotensive) was seen in 04 (13.33%) women which has shown p-value of 0.005 and odds ratio of 5.69 which is significant and shows a positive association between pre-eclampsia and high d-dimer levels (>0.5µg/ml). In the current study, D-dimer levels of pre-eclamptic women as compared to normal controls were significantly high which correlates with the study conducted by Z Tacoosianet al.[15] Similar results were also reported by KucukgozGulec U et al where D-Dimer levels were significantly higher in study group than the control group and it was also significantly higher in the patients with severe pre-eclampsia than mild pre-eclampsia.[16]

Conclusion

Pregnant women with a tendency to develop gestational hypertensive complications tend to have higher concentrations of d-dimer. In this study, a significant association between pre-eclampsia and high d-dimer levels (>0.5µg/ml) was found. Further large-scale prospective cohort studies are needed, to clarify the exact diagnostic/prognostic role of serum d-dimer levels in pre-eclamptic women by doing prospective studies. This may play a pivotal role in the morbidity and mortality reduction of both mother and the fetus.

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