CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187
http://doi.org/10.5281/zenodo.3996180

Available online at: http://www.iajps.com *Research Article*

ASSOCIATION BETWEEN PRE-ECLAMPSIA AND HIGH D-DIMER LEVELS

Dr. Sara Fazal[1], Dr. Maida Naeem[2], Dr. Rameesha Shafiq[3]
[1]Pakistan Institute of Medical Sciences, Islamabad
[2]Civil Hospital Manawala, Sheikhupura
[3]Federal Medical and Dental College, Islamabad

Article Received: June 2020 **Accepted:** July 2020 **Published:** August 2020

Abstract:
Introduction: *Pregnancy is characterized by a hypercoagulable state due to a number of hormonal changes and alterations of clotting and fibrinolytic factors.* ***Objectives:*** *The main objective of the study is to analyse the association between pre-eclampsia and high D-Dimer levels.* ***Material and methods:*** *This cross sectional study was conducted in Holy Family/Benazir Bhutto Hospital, Rawalpindi during March 2019 to December 2019. GHD included gestational hypertension, PE, and superimposed PE. Their antepartum concentrations of d-dimer were measured as a part of routine evaluation for patients suspected with PE. The concentrations of d-dimer were determined by immunologic assay. 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:*** *Of the 90 pregnant women who met the inclusion criteria, 49 had severe GHD including severe PE or superimposed PE, and 41 had non-severe GHD. There were no statistical differences between the 2 groups in terms of maternal age, parity, or pre-pregnancy BMI. However, women with severe GHD has significantly earlier median gestational age at sampling, earlier median gestational age at delivery, lower median birth weight, and higher cesarean section rate compared with those with non-severe GHD. These differences may be attributed to the characteristics of severe PE.* ***Conclusion:*** *It is concluded that pregnant women with a tendency to develop gestational hypertensive complications tend to have higher concentrations of d-dimer.*

Corresponding author:
Dr Sara Fazal,
Pakistan Institute of Medical Sciences, Islamabad

QR code

Please cite this article in press Sara Fazal et al, ***Association Between Pre-Eclampsia And High D-Dimer Levels.,*** *Indo Am. J. P. Sci, 2020; 07(08).*

INTRODUCTION:

Pregnancy is characterized by a hypercoagulable state due to a number of hormonal changes and alterations of clotting and fibrinolytic factors. Probably, it helps to protect pregnant women from fatal hemorrhage during delivery, but it can also contribute to increase the thromboembolic risks during pregnancy and puerperium[1]. The patients with preeclampsia (PE) are known to have higher risk of thromboembolic complications than normal pregnant women. PE is associated with deposition of fibrin in microvasculature, which results in compromised placental perfusion, fetal growth restriction (FGR) and dysfunction in some maternal organs[2].

D-dimer is a plasma breakdown product of cross-linked fibrin and it is a widely used indicator for the exclusion of venous thromboembolism (VTE) with highly negative predictive value. However, the concentrations of d-dimer in maternal blood substantially increase physiologically throughout the gestational age without any thromboembolic complication because of continuous coagulation and fibrinolysis during the normal development of the placenta[3]. In a serial study, only 22% of women in mid-pregnancy and no women in the third trimester had a normal concentration of d-dimer (<0.50 mg/L)[4].

Increased baseline levels of d-dimer during pregnancy may be a kind of confounder in the interpretation of d-dimer results for the evaluation of thromboembolism, and d-dimer can be only useful in the limited cases with negative values during pregnancy. Previous studies suggested a higher threshold of d-dimer in pregnant women, or a gestational age-specific reference interval of d-dimer. Several studies showed that patients with PE had higher concentrations of d-dimer than normotensive controls. It may be associated with higher thromboembolic risk in patients with PE than normotensive controls[5].

D-dimer levels increase progressively during a normal pregnancy, which alters their clinical utility in the diagnosis of venous thromboembolism. This increase is proportional with gestational age. Some authors described higher levels of D-dimer in patients with IUGR, gestational hypertension, preeclampsia and *abruptio placentae* than in normal pregnancies[6]. The placenta growth could be a major determinant of the elevation of the D-dimer level during pregnancy but relation between placental volume and D-dimer levels has not been studied.

sEPCR (soluble endothelial protein C receptor) is an endothelial cell membrane glycoprotein that binds Protein C and activated Protein C (APC). sEPCR plays a critical role in foeto-maternal blood coagulation control and in preventing thrombosis at the maternal-embryonic interface[7].

Objectives

The main objective of the study is to analyse the association between pre-eclampsia and high D-Dimer levels.

MATERIAL AND METHODS:

This cross-sectional study was conducted in Holy Family/Benazir Bhutto Hospital, Rawalpindi during March 2019 to December 2019. GHD included gestational hypertension, PE, and superimposed PE. Their antepartum concentrations of d-dimer were measured as a part of routine evaluation for patients suspected with PE. The concentrations of d-dimer were determined by immunologic assay. 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. Statistical analysis was carried out using International Business Machines (IBM) Statistical Package for the Social Sciences (SPSS) statistics software ver. 20.0 (IBM Corp., Armonk, NY, USA). Nonparametric techniques were used for statistical analysis.

RESULTS:

Of the 90 pregnant women who met the inclusion criteria, 49 had severe GHD including severe PE or superimposed PE, and 41 had non-severe GHD. There were no statistical differences between the 2 groups in terms of maternal age, parity, or pre-pregnancy BMI. However, women with severe GHD has significantly earlier median gestational age at sampling, earlier median gestational age at delivery, lower median birth weight, and higher cesarean section rate compared with those with non-severe GHD. These differences may be attributed to the characteristics of severe PE.

Table 01: Comparison of D-dimer levels according to severity

	Non-severe (n=41)	Severe (n=49)	*P*	
			Unadjusted	Adjusted[a)]
D-dimer concentration (mg/L)	0.71 (0.09 to 5.39)	2.00 (0.11 to 7.49)	<0.01	0.008
Cases with abnormal d-dimer[b)]	22 (53.7)	44 (89.8)	<0.01	<0.01

Data are given as number of subject (percentage) or median (range).

[a)]Adjusted for gestational age at sampling (logistic regression analysis); [b)]Concentration of d-dimer >0.55 (mg/L).

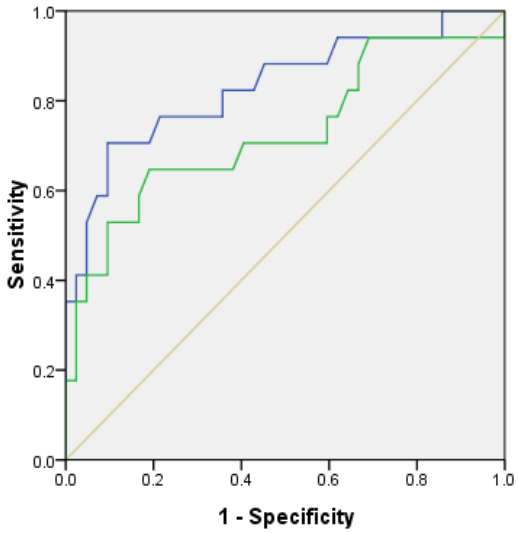

Figure 01: ROC curve of statin therapy in patients

Using ROC curve analysis, a cut-off value of 1.19 mg/L (ROC area under the curve, 0.71; 95% confidence interval, 0.60 to 0.82; *P*=0.001) for maternal concentration of d-dimer had 63.3% of sensitivity and 65.9% of specificity for the identification of severe GHD.

DISCUSSION:

Despite extensive research, diagnosis of preeclampsia remains a challenge. Although supplementary tests can aid in suspected preeclampsia, diagnosis is routinely assessed by blood pressure and determination of urinary protein concentration. The use of blood pressure measurement is unreliable, given the influence of body position, physical exertion and potential psychological complications, i.e., anxiety and stress[8]. Proteinuria is usually assessed by reagent dipsticks in a randomly collected urine sample. A 24-hour urine sample may provide more accurate results, but its collection is time consuming. Furthermore, reagent strip analysis can provide false positive results in the presence of vaginal discharge or if urine is too alkaline or contaminated, i.e., quaternary ammonium and chlorhexidine[9].

Identification of sensitive and specific biomarkers for precise diagnosis of preeclampsia is highly necessary in order to aid timely pregnancy intervention. Several laboratory markers have been proposed, but the reliability of these markers has been questioned. Although plasma D-Di has high negative predictive value for venous thromboembolism, its diagnostic value in preeclampsia has not been explored[10].

A variety of tests has been used for D-Di assessment, including ELISA, latex-based immunoassays and automated immunoturbidimetric assays. Because ELISA is a more sensitive assay, we decided to include only studies that used this methodology. As the hypercoagulable state increases in pregnancy, we included only women in their third trimester of gestation[11].

CONCLUSION:

It is concluded that pregnant women with a tendency to develop gestational hypertensive complications tend to have higher concentrations of d-dimer.

REFERENCES:

1. Jacobsen AF, Skjeldestad FE, Sandset PM. Incidence and risk patterns of venous thromboembolism in pregnancy and puerperium--a register-based case-control study. Am J Obstet Gynecol. 2008;198:233.e1–233.e7.
2. Chan LY, Tam WH, Lau TK. Venous thromboembolism in pregnant Chinese women. Obstet Gynecol. 2001;98:471–475
3. Lindqvist P, Dahlbäck B, Marŝál K. Thrombotic risk during pregnancy: a population study. Obstet Gynecol. 1999;94:595–599.
4. He S, Bremme K, Blombäck M. Acquired deficiency of antithrombin in association with a hypercoagulable state and impaired function of liver and/or kidney in preeclampsia. Blood Coagul Fibrinolysis. 1997;8:232–238.
5. Xiong Y, Zhou SF, Zhou R, Yang D, Xu ZF, Lou YT, et al. Alternations of maternal and cord plasma hemostasis in preeclampsia before and after delivery. Hypertens Pregnancy. 2011;30:347–358.
6. McKay DG. Hematologic evidence of disseminated intravascular coagulation in eclampsia. Obstet Gynecol Surv. 1972;27:399–417.
7. Reber G, Vissac AM, de Moerloose P, Bounameaux H, Amiral J. A new, semi-quantitative and individual ELISA for rapid measurement of plasma D-dimer in patients suspected of pulmonary embolism. Blood Coagul Fibrinolysis. 1995;6:460–463.
8. Szecsi PB, Jørgensen M, Klajnbard A, Andersen MR, Colov NP, Stender S. Haemostatic reference intervals in pregnancy. Thromb Haemost. 2010;103:718–727.
9. Francalanci I, Comeglio P, Alessandrello Liotta A, Cellai AP, Fedi S, Parretti E, et al. D-dimer plasma levels during normal pregnancy measured by specific ELISA. Int J Clin Lab Res. 1997;27:65–67.
10. Chabloz P, Reber G, Boehlen F, Hohlfeld P, de Moerloose P. TAFI antigen and D-dimer levels during normal pregnancy and at delivery. Br J Haematol. 2001;115:150–152.
11. Kline JA, Williams GW, Hernandez-Nino J. D-dimer concentrations in normal pregnancy: new diagnostic thresholds are needed. Clin Chem. 2005;51:825–829.