

ORIGINAL ARTICLE

COMPARISON OF D-DIMER LEVELS IN PREECLAMPSIA AND NORMAL PREGNANCY

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Background: Preeclampsia is associated with deposition of fibrin in microvasculature and maternal organ dysfunction. D-dimer is used as a marker of degradation and production of fibrin in the body. The objective of this study was to determine the mean plasma D-dimer levels among pregnant women and to compare mean plasma D-dimer levels between preeclamptic patients and women without preeclampsia. **Methods:** A cross sectional study was designed and conducted in the Obs/Gyn Department, Hayatabad Medical Complex, Peshawar. A total of 154 pregnant women fulfilling inclusion criteria were included. Non-probability consecutive sampling was used for collection of samples. Mean±SD was calculated for quantitative variables while qualitative variables were presented in the form of frequency and percentage. Independent sample *t*-test was used to compare mean plasma D-dimer levels between preeclampsia and normal patients. Stratification was done on the basis of age, gestational age, BMI, and booking status. Post-stratification *t*-test was applied and $p \leq 0.05$ was considered significant. **Results:** The mean age of patients was 27.73 ± 2.68 years (Range: 18–34 years). The mean gestational age was 37.43 ± 1.15 weeks (Range: 35–40 weeks). Preeclamptics were 58 (37.7%) while 96 (62.3%) were normotensive. The mean plasma D-dimer levels in total cases was 0.50 ± 0.41 ng/ml (Range: 0.115–1.156). The mean plasma D-dimer level in preeclamptics and normal cases was 1.02 ± 0.07 and 0.18 ± 0.04 (ng/ml) respectively ($p < 0.00$). **Conclusion:** Mean plasma D-dimer level was higher in preeclamptic patients as compared to normotensive pregnant women showing a significant correlation between preeclampsia and plasma D-dimer level in third trimester of pregnancy.

Keywords: Plasma D-dimer, preeclampsia, hypertensive disorders, pregnancy

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INTRODUCTION

D-dimer (DD) is a small portion of protein formed by fibrinolysis and significantly increases during pregnancy.^{1,2} Its concentrations in maternal blood increases throughout gestational period without any thromboembolic complication.³ A proper increase in blood coagulation is important for a pregnant female to reduce the risk of postpartum haemorrhage.⁴ D-dimer is one of the most valued indicators to diagnose and manage thrombotic states with venous thromboembolism, and atrial fibrillation.⁵

Globally, hypertensive disorders of pregnancy (HDP) complicate around 10% of pregnancies and are the second largest cause of maternal mortality but aetiologies and pathogenesis are not yet fully understood.⁶ HDP may lead to adverse events for foetus and mother, i.e., low birth weight, maternal stroke, mortalities, and neonatal intensive care needs.⁷ Preeclampsia (PE) is the most shared pregnancy complication of HDP, affecting 5–8% of pregnancies.⁸ It is diagnosed by arterial pressure of $>140/90$ mmHg measured on two occasions at more than 4 hours interval with higher than 300 mg of urinary protein in 24 hours after 20th week of gestation. About 5–7% of primigravida and 1–3% of multigravida get complicated by preeclampsia.⁹ World Health Organization (WHO)

estimates 50,000–75,000 annual deaths associated by complications of preeclampsia making it the leading cause of death during pregnancy.¹⁰

The higher levels of D-dimer indicate presence of high level of thrombus in blood.¹¹ This explains the mechanism of damage in preeclampsia where dissolution of fibrin clot plays a vital role in endothelial damage.¹² Therefore, more precautions must be implemented in high risk pregnancies to prevent development of preeclampsia and its complications.¹³ Recently, plasma D-dimer level is labelled as a biomarker for fibrinolytic and haematologic changes during preeclampsia. The studies conducted on various population has shown variations in its values therefore this study was designed to compare mean plasma D-dimer levels in preeclampsia and controls in our population.

MATERIAL AND METHODS

This cross-sectional study was conducted in Obs/Gyn Department of Hayatabad Medical Complex Peshawar, after approval from Institutional Ethical Committee, from 1st December 2018 to 31st May 2019. The sample size was calculated by using WHO sample size calculator. Sample size of pregnant women calculated was 154 (58 cases and 96 controls). Non-probability consecutive sampling was used for collection of samples.

There were 91 (59.1%) booked and 63 (40.9%) un-booked cases. The primigravidas of third trimester aged 20–40 years visiting Obs/Gyn Department for routine check-up or for hypertension were enrolled after their informed written consent. They underwent screening for preeclampsia and were grouped into primigravida with preeclampsia and normal pregnant females. Women with the history of coagulopathy, liver disease, or any inflammatory disorders were excluded.

About 3 ml of venous blood was collected in a container containing 3.2% tri-sodium citrate. The platelets poor plasma (PPP) was immediately prepared through centrifuge for 15 minutes at 3,000 rpm at room temperature. The plasma D-dimer levels were measured using (MISPA-i2 reagent, Switzerland).

The data were recorded on a pre-designed proforma and analysed using SPSS-16. Mean±SD were calculated for quantitative variables like, age, gestational age, plasma D-dimer level, weight, height, and BMI. Qualitative variables like education, rural, urban, booking status, status of blood pressure were presented as frequencies and percentages. Independent sample *t*-test was used to compare mean plasma D-dimer levels between preeclamptics and normal patients. Stratification was done on the basis of age, gestational age, BMI, and booking status. Post stratification *t*-test was applied, and $p \leq 0.05$ was considered as significant.

RESULTS

The mean age of cases was 27.73±2.68 (Range: 18–34) years. Mean height, mean weight, and BMI were 1.64±0.05 m, 67.71±9.86 Kg, and 25.02±3.19 Kg/m² respectively. Mean gestational age was 37.43±1.15 (Range: 35–40) weeks. Mean plasma D-dimer level was 0.59±0.41 (0.12–1.16) ng/ml. (Table-1).

Preeclamptic cases were 58 (37.7%), and 96 (62.3%) were normotensive. Mean plasma D-dimer level in preeclamptics was 1.02±0.07 and 0.18±0.04 ng/ml in normal cases ($p < 0.00$) (Table-2).

When data were stratified for age, period of gestation, BMI, and booking status, the mean plasma D-dimer levels in females with preeclampsia were statistically higher compared to normal females ($p < 0.05$) (Table-3).

Table-1: Age, height, weight, BMI, gestational age, and D-dimers in total cases

Parameters	Min	Max	Mean±SD
Age (Years)	20	34	27.73±2.68
Height (m)	1.55	1.75	1.64±0.05
Weight (Kg)	55	86	67.71±9.86
BMI (Kg/m ²)	20	31	25.02±3.19
Gestational age (Weeks)	35	40	37.43±1.15
D-dimers (ng/ml)	0.115	1.156	0.50±0.41

Table-2: Comparison of D-dimers in preeclamptics and normal females

Blood pressure Status	n	Plasma D-dimers level (ng/ml)		
		Mean	SD	<i>p</i>
Preeclamptics	58	1.02	0.07	<0.00
Normal females	96	0.18	0.04	

Table-3: Stratification of plasma D-dimers level in women with and without preeclampsia with respect to age, gestational age, BMI, and booking status

Parameters	Groups	Plasma D-dimers			
		n	Mean±SD	<i>p</i>	
Age (years)	20–28	Preeclampsia	35	1.02±0.07	<0.00
		Normal	49	0.18±0.04	
	29–40	Preeclampsia	23	1.03±0.06	<0.00
		Normal	47	0.18±0.05	
Gestational age (weeks)	<37	Preeclampsia	7	1.02±0.04	<0.00
		Normal	15	0.18±0.05	
	≥37	Preeclampsia	51	1.03±0.07	<0.00
		Normal	81	0.18±0.04	
BMI	Non-Obese	Preeclampsia	52	1.02±0.07	<0.00
		Normal	90	0.18±0.04	
	Obese	Preeclampsia	8	1.03±0.06	<0.00
		Normal	4	0.18±0.05	
Booking status	Un-booked	Preeclampsia	36	1.03±0.06	<0.00
		Normal	27	0.17±0.05	
	Booked	Preeclampsia	22	1.01±0.08	<0.00
		Normal	69	0.18±0.04	

DISCUSSION

The results of present study revealed that the mean plasma D-dimer level in preeclamptics were statistically higher than normotensive females ($p < 0.00$). This is in accordance with the study conducted by Khawaja *et al.* in 2019 who documented significant positive association between preeclampsia and high D-dimer levels.¹⁵ Similarly, a study conducted by Bozkurt *et al.* in 2015 also concluded that the levels of D-dimers in preeclamptics ($p = 0.03$) and eclamptics ($p = 0.02$) were significantly higher than the controls.¹⁶

An African study conducted in Sudan in 2017 also documented similar findings stating a statistically significant rise in plasma fibrinogen ($p = 0.00$) and D-dimer levels in preeclamptics compared to normotensive pregnant females ($p = 0.00$).¹⁴ However, Catarino *et al.* after studying a small sample size concluded that there is no significant difference in mean D-dimer level between preeclamptics and normotensive pregnant females.¹⁷ Contrarily, Kim *et al.*, reported a significantly higher D-dimer in hypertensive pregnant females ($p < 0.01$).²

Recently, Fazal S *et al.*, concluded that pregnant females having a tendency of developing gestational hypertensive complications have higher levels of D-dimer.¹⁸ A study conducted by Lefkou *et al.* also assessed biomarkers of hypercoagulability in females suffering from mild and severe preeclampsia. Only females with severe preeclampsia showed increase in D-dimer levels and consumption of natural coagulation inhibitors. This has also reflected the

tendency of prolonged PT and aPTT in severe preeclampsia.¹⁹ Similarly, Baboolall *et al*, in a retrospective observational cohort study reported obvious relationship between D-dimers concentration and severe preeclampsia.¹ A cross sectional study carried out in Dhaka Medical College Hospital, showed that the risk of having plasma D-dimer >0.5 µg/ml was 9 times more in preeclamptic women than normal pregnant women.²⁰

However a comparative cross sectional study conducted at King Edward Medical University Lahore, found fibrinogen, Platelet Distribution Width (PDW), platelet count and D-dimers changed in preeclampsia compared to normal pregnant females but were not statistically significant ($p>0.05$).²¹

CONCLUSION

The mean plasma D-dimer level was higher in preeclamptic patients as compared to normotensive pregnant women in our study population showing a significant correlation between preeclampsia and plasma D-dimer level in 3rd trimester of pregnancy. Monitoring D-dimer level can be used as a tool for early diagnosis and decision on management of complications of pregnancy induced hypertension.

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