

Research/ Review

Implication of Thrombus Marker (D-Dimer) Levels in Preeclamptic Pregnant Women During the Third Trimester

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Abstract: Microvasculature fibrin deposition is implicated in preeclampsia. D-Dimer has emerged as a useful diagnostic tool for thrombotic conditions because its plasma concentration has a high negative implicative value for venous thromboembolism. Forty (40) consenting pregnant women were recruited from St. Philomina Catholic Hospital, Edo State, Nigeria. These subjects consisted of twenty (20) normotensive and twenty (20) preeclamptic pregnant women in their third trimester of pregnancy. Blood samples was spun in a bucket centrifuge at 2500 RPM (rounds per minute) for 10 minutes after which plasma was collected and stored frozen in plain sample bottles and was analyzed for thrombus marker (D- Dimer) levels by fluorescence immunoassay method. Data obtained from this study were analysed using Graph Pad Prism 9. Results generated were expressed as mean \pm SEM and a P-value of ≤ 0.05 were considered statistically significant. D- Dimer level statistically increased significantly ($p < 0.05$; < 0.0001) in pre-eclamptic women in their third trimester of pregnancy to 2.875 ± 0.043 U/L when compared to D- Dimer level 0.8320 ± 0.09836 U/L in Normotensive pregnant women. The present study showed that there was statistically significant increase in D-dimer in preeclamptic women compared to normotensive pregnant women, indicating various underlying pathophysiological processes such as thrombotic complications.

Keywords: D- Dimer, Microvasculature, Preeclampsia, Thrombus Marker

1. Introduction

Coagulation disorders have been implicated in the pathophysiology of preeclampsia, with elevated levels of thrombus markers observed in preeclamptic women [1]. D-Dimer is a thrombus marker that has been studied in the context of preeclampsia [1].

Preeclampsia is a complex and multifactorial pregnancy complication characterized by high blood pressure and damage to organs such as the kidneys, liver, and brain [2]. It affects approximately 2-8% of pregnancies worldwide, making it a leading cause of maternal and fetal morbidity and mortality [3]. Early detection and prediction of preeclampsia are crucial to prevent severe complications and ensure timely interventions [4].

This study aims to investigate the implication of thrombus marker (D-Dimer) levels in preeclamptic pregnant women in the third trimester of pregnancy. By analyzing D-Dimer levels, this research seeks to identify potential implication of D-Dimer in preeclampsia, enabling timely interventions and improving maternal and fetal outcomes.

2. Literature Review

D-dimer is a fibrin degradation product generated during fibrinolysis, the process by which the body breaks down clots. Its presence in the blood indicates the activation of coagulation and fibrinolysis pathways, making it a widely used biomarker for thrombotic conditions such as deep vein thrombosis, pulmonary embolism, and disseminated

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intravascular coagulation (DIC). In pregnancy, D-dimer levels naturally increase as gestation progresses, reflecting physiological hypercoagulability that protects against postpartum hemorrhage (9). Preeclampsia is a hypertensive disorder of pregnancy characterized by systemic endothelial dysfunction and a hypercoagulable state. Elevated D-dimer levels in preeclamptic pregnancies are well-documented, indicating excessive activation of the coagulation cascade and increased fibrin turnover. This rise in D-dimer is more pronounced in severe cases of preeclampsia and may correlate with the degree of maternal and placental vascular injury (10). Endothelial damage in preeclampsia promotes the release of tissue factor, which triggers coagulation. Simultaneously, impaired fibrinolysis due to altered plasminogen activator inhibitor-1 (PAI-1) activity exacerbates clot formation. The resulting imbalance between coagulation and fibrinolysis is reflected in elevated D-dimer levels, making it a potential biomarker for disease severity and progression (11). D-dimer measurement has gained interest as a diagnostic and prognostic tool in preeclampsia. Elevated D-dimer levels in early pregnancy may serve as a predictive marker for the development of preeclampsia, particularly in high-risk populations. Furthermore, persistently high or rapidly rising D-dimer levels during the third trimester may indicate severe disease or complications such as HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets) (12). The utility of D-dimer as a standalone marker is limited by its lack of specificity, as increased levels are also observed in normal pregnancy and other conditions. Combining D-dimer with other biomarkers, such as soluble fms-like tyrosine kinase-1 (sFlt-1) and placental growth factor (PlGF), may improve diagnostic accuracy and risk stratification in preeclampsia (13). Elevated D-dimer levels in preeclampsia underline the importance of monitoring coagulation status in affected pregnancies. Identifying women with significant coagulation abnormalities may guide therapeutic interventions, such as the use of low-dose aspirin or anticoagulants, to reduce maternal and fetal morbidity. Future research should explore the integration of D-dimer with other biomarkers in predictive models for preeclampsia and its complications (14).

3. Proposed Method

Geographical Description of the Study Area

This research was carried out among Third Trimester Pregnant women in St. Philomina Catholic Hospital, Edo State, Nigeria. It lies longitudinally at 04°E and 43°E and Latitude 05°44'N and 07°34'N. Its geopolitical location is the South South and it has a population of 3.5 million people. Oredo land, Benin City, the State capital, is 100 km long. Edo State, South-South, Nigeria. Oredo is a Local Government Area of Edo State, Nigeria. Its headquarters are in the town, Benin city. It has an area of 502 km² and a population of 500,000 at the 2006 census. Majority of which are civil servants, traders, businessmen/women, transporter, farmers, teachers/lecturers and students by occupation. Oredo, since after its designation as headquarters and as the host of Oba of Benin Palace, the town has grown into an urban center.

Research Design

Forty (40) consenting pregnant subjects were recruited from St. Philomina Catholic Hospital, Edo State. These subjects consisted of twenty (20) normotensive pregnant women in their third trimester of pregnancy with blood pressure between 120/80mmHg to 130/90 mm/Hg without presence of proteinuria and twenty (20) preeclamptic women in their third trimester of pregnancy classified as having preeclampsia according to their blood pressure measured was above 130/90 mm/Hg with the presence of proteinuria taken two consecutive times at presentation at the antenatal clinic of the hospital

Sample Size

The Population of study was determined using the formula;

$$N = Z^2pq/d^2$$

Where N= the desired sample size (when population is greater than 10,000)

Z= is a constant given as 1.96 (or more simply at 2.0) which corresponds to the 95% confidence level.

P= previous survey prevalence of 2.23%

q= 1.0-p

d= acceptable error 5%.

Where N= sample size, Z=1.96, p=0.1% (0.01) and d=5% (0.05)

N= 39.8 subject.

Therefore, the sample for this study is 40 respondents who are normotensive and preeclamptic pregnant women from Oredo town, Benin City.

Ethical Approval And Informed Consent

Ethical clearance (REC Approval No:RECC/10/2023(07)) was obtained from the Research Ethics Committee of St. Philomina Catholic Hospital, Edo State.

Written informed consent was obtained from subjects prior to commencement of the study.

Blood Sampling

10 milliliters (10 ml) of venous blood was drawn from consenting participants and placed in a lithium heparin sample bottles. Blood samples was spun in a bucket centrifuge at 2500 RPM (rounds per minute) for 10 minutes after which plasma was collected and stored frozen in plain sample bottles and was analyzed for thrombus marker (D- Dimer)

Experimental Protocols

After the subjects were identified and recruited into the study, they were taken to the lab where their vital signs was taken, after which blood samples were collected by venipuncture and taken to the chemistry laboratory for analysis.

Study Area/Population

The study were conducted for three months at St. Philomina Catholic Hospital, Edo State, Nigeria.

Inclusion Criteria

Normotensive and Preeclamptic pregnant women in the third trimester of pregnancy, within the age range of 25 to 35years was used for this study. Pregnant women were recruited for this study and women who had given birth before and were pregnant for the second time.

Exclusion Criteria

Normotensive and Preeclamptic pregnant women who were on drugs and with a known history of hyperlipidemia, gestational Diabetes and other comorbidity.

Biochemical Examination

Measurement of thrombus marker (D- Dimer) by Fluoresces Immunoassay

Principle :The D-Dimer Rapid Quantitative Test is a fluorescence immunoassay using a competitive method for quantitative analysis

Procedure

Step 1: Preparation

Allow the test cassette, detection buffer and specimen to equilibrate to room temperature prior to testing. Take out the ID chip, we make sure that the ID chip is consistent with the batch number of the test cassette and we inserted the ID chip into the chip port of the instrument.

Step 2: Sampling

Draw 75 μ L of whole blood or serum or plasma with a transfer pipette and it was added to the buffer tube.

Step 3: Mixing

Close The lid detection buffer tube was close and the sample mixture was mix thoroughly by shaking it well.

Step 4: Loading

Pipette 75 μ L of sample mixture was loaded into the sample well of the test cassette.

Step 5: Testing

There are two modes for FIA Meters, Standard Test mode and quick test mode. Standard Test mode was adapted in this experiment. For Standard Test mode: The test device was inserted onto the test cassette holder of FIA Meter right after adding sample mixture to the sample well. Press "Test" to start testing. The reaction time is 15 minutes.

Step 6: Reading result

Results are displayed on the main screen of meter and can be printed out by press "Print".

Step 7: Withdraw

The used test kit was discarded according to local regulations and procedure after released from the meter.

Data Analysis

Data obtained from this study were analysed using Graph Pad Prism 9. Results generated were expressed as mean \pm SEM and a P-value of ≤ 0.05 were considered statistically

significant. The significance of difference among the groups were used to assess the repeated-measures analysis of variance (ANOVA). Independent students' t-test were used to compare normotensive and preeclamptic pregnant women groups.

4. Results and Discussion

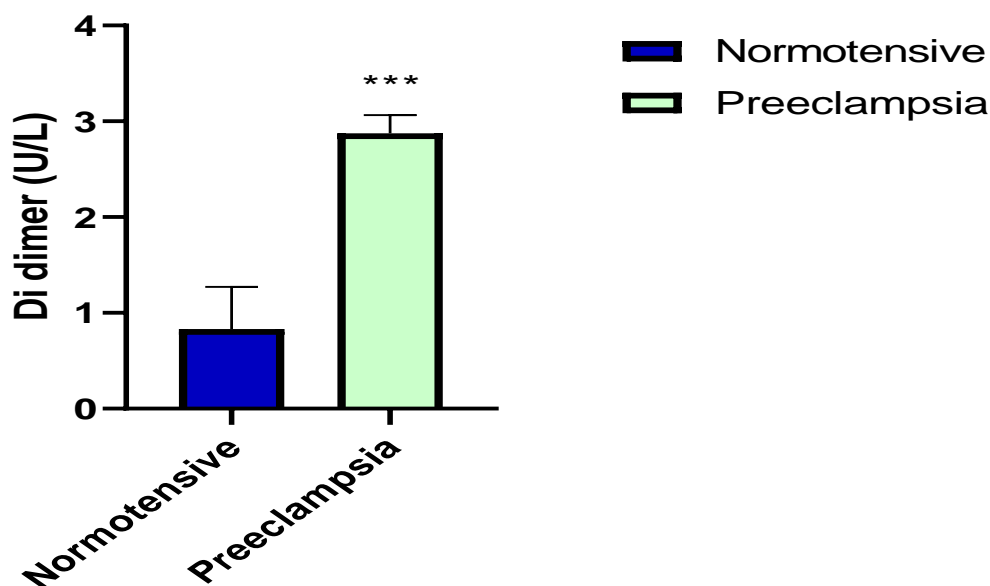


Figure 1: Mean \pm SEM of D- dimer level in normotensive (n=20) and preeclampsia (n=20). The t-test was carried out to access any significant difference. *** represents $p < 0.001$.

Figure 1 shows the levels of D-dimer in Normotensive and pre-eclamptic women in their third trimester of pregnancy. D- dimer level statistically increased significantly ($p < 0.05$; < 0.0001) in pre-eclamptic women in their third trimester of pregnancy to 2.875 ± 0.043 U/L when compared to d- dimer level 0.8320 ± 0.09836 U/L in Normotensive pregnant women.

Discussion

D-dimer is a fibrin degradation product that reflects ongoing coagulation and fibrinolysis [5]. Elevated D-dimer levels are associated with an increased risk of thrombosis and are often observed in preeclampsia due to endothelial dysfunction and activation of the coagulation cascade [6]. From Figure 1 in the present study shows significantly increase in D-dimer level in women with preeclampsia compared to normotensive pregnant women. Elevated D-dimer levels in preeclamptic women emphasis its implicative role as a biomarker for hypercoagulability and increased risk of thrombotic complications in preeclampsia. This present result agreed with the research of [7] Who studied the dynamic changes in perinatal coagulation function in patients with preeclampsia (PE). In their work, the general data and coagulation indexes of 290 PE patients during the perinatal period (prenatal and 1 and 3 days postpartum) and 256 healthy pregnant women in the third trimester of pregnancy were investigated, and the data were analyzed. Compared with healthy pregnant women D-dimer (DD), values increased before delivery ($P < .05$). The findings of [7] together with this present study and other research [6] further indicate the implication of D-Dimer in preeclampsia.

5. Conclusions

The present study showed that there was statistically significant increase in D-dimer in preeclamptic women compared to normotensive pregnant women, indicating various underlying pathophysiological processes such as thrombotic complications. This finding suggests the potential implication of D-Dimer in identifying and monitoring preeclampsia.

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