Evaluation of plasma fibrinogen and plasma D-dimer Levels among Sudanese preeclamptic pregnant women in Omdurman Maternity Hospital

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Abstract

Background: Preeclampsia is multisystem disease specified by high blood pressure and proteinuria after the 20th week of pregnancy. Preeclampsia is associated with microvasculature fibrin deposition and maternal organ dysfunction. Materials and methods: This is a case control study conducted in Omdurman maternity hospital during January 2016 to April 2016, the objectives of this study was to evaluate plasma D-dimer and plasma fibrinogen in preeclampsia and compared this value with normal pregnant women. Study included fifty pregnant women with preeclampsia in third trimester they (18-39) years and those pregnant women do not suffer from any conditions that could have altered the coagulation tests such as: preeclamptic women with previous clinical history of renal disease, gestational diabetes, liver disease, pregnant women on anticoagulant or aspirin, placental abruption, sepsis, stillborn or heavy vaginal bleeding and any chronic disease. Blood sample 1.8ml was collected from preeclamptic pregnant women and normal pregnant women by clean vein puncture. 1.8 ml will be collected in a tube containing 200µl of 3.2% sodium citrate and was centrifuged at 2000 rpm for 15 minutes. Plasma fibrinogen was estimated by Clauss method using Siemens multifibrin analyzer. The levels of D-dimer was estimated using Nycocard D-dimer. The results were expressed as mean ± SD. Statistical analysis was carried out by using SPSS software, version 21. The level of significance was set at < 0.05. Results: Preeclampsia and normal pregnancy groups were compared for fibrinogen and D-dimer. The mean levels of plasma fibrinogen (358.30±138.6 vs. 280.00±72.8 mg/dL, P.value <0.001) and plasma D-dimer (0.364±0.38 vs 0.148±0.06 mg/L, P.value < 0.000) were significantly higher in the preeclampsia group as compared to normal pregnancy. The percentage of high D-dimer was found in (48%) and (6%), while high fibrinogen was found in (48%) and (18%) in patients and control respectively. Conclusion: D-dimer and fibrinogen reported at high level in preeclamptic women when compared with normal pregnant women.

Keywords: preeclampsia, pregnancy, D-dimer, fibrinogen, Sudanese.
Introduction

Preeclampsia is a systemic disease specified by systolic blood pressure ≥ 140 mm Hg or diastolic ≥ 90 mm Hg, and proteinuria ≥ 0.3 g/24 h measured after the 20th week of pregnancy [1,2]. Many laboratory tests such as platelet count and liver enzymes can be used to monitor the risk of preeclampsia, but the diagnosis established by blood pressure and proteinuria measurement [2]. This disease can progress to Eclampsia (characterized by seizures as a sign of affection of the cerebral vessels), HELLP syndrome (hemolysis, elevated liver enzyme, low platelets) or disseminated intravascular coagulation (DIC) [2]. The symptoms of preeclampsia begin as early as the 20th gestational week and last for 6 weeks after delivery. Furthermore, Preeclampsia has high morbidity and mortality rates [3]. The pathogenesis of Preeclampsia is unknown, and the many theories related to the etiology of Preeclampsia pose great challenges for future investigation. The abnormal invasion of placenta and the release of placenta-derived adverse factors during the first trimester are thought to be the main cause of the extensive damage to the maternal endothelium and systemic inflammatory response involving some systems and organs in late pregnancy [4]. To date, there is no effective treatment for preeclampsia. Therefore, a reliable predictor for Preeclampsia would play an important role in early prevention and intervention. Preeclampsia can be classified into two degrees, mild Preeclampsia and severe Preeclampsia, and there are different treatments and clinical outcomes for each degree [5], it is necessary to predict the severity of Preeclampsia for rational gestational management [6]. Normal pregnancy is associated with impressive changes in the haemostatic mechanism and is a hypercoagulable state associated with increase in some coagulation factors. Coagulation and fibrinolytic systems undergo major alteration associated with reduced fibrinolytic activity. Some studies reported increased levels of fibrinogen and Fibrin Degradation Products (FDP) in normal pregnancy [7,8]. Fibrinogen is the major coagulation heterogeneous protein and it is symmetrical glycoprotein of 340 KD molecular weight. Some earlier studies showed that in preeclampsia the level of plasma fibrinogen was higher as compared to normal pregnancy [9,10]. In the early stages of fibrin clot formation, activated thrombin cleaves fibrinogen. Molecular polymerization is observed due to the formation of soluble fibrin, which is subsequently stabilized by covalent cross-linking with factor XIII—producing an insoluble fibrin matrix. Degradation is immediately initiated by plasmin, resulting in a variety of relatively stable dimeric fragments or fibrin degradation products. The smallest fragment, D-dimer, is resistant to plasmin degradation. D-dimer specifically reflects both fibrin polymerization and breakdown [11,12,13,14].
In Preeclampsia patients, the coagulation-fibrinolytic system is thought to be one of the most seriously affected systems by maternal inflammatory reactions and immune dysfunction [15]. The balance between coagulation and anticoagulation is vital to the regulation of utero-placental circulation and organ perfusion in pregnant woman. An appropriate increase in blood coagulation is important for normal pregnant woman to reduce postpartum hemorrhage and to limit other complications [16]. When this balance is upset in Preeclampsia patients, the bloodstream of the placenta and many organs is blocked by micro thrombosis [17]. Preeclampsia is associated dysfunction of some maternal organs [18].

Materials and methods

Study design: This is a case control hospitalize base study.

Study area: The study was conducted in Omdurman Maternity Hospital, Khartoum state in the period of January 2016 to April 2016.

Study population: The study was conducted on preeclamptic pregnant women as test group and normotensive pregnant women as control group.

Inclusion criteria: Pregnant women with confirmed diagnosis of preeclampsia.

Exclusion criteria: Preeclamptic pregnant women with clinical history of renal disease, diabetes mellitus, hypothrodism, liver disease, and pregnant women on anticoagulant or aspirin, placental abruption, sepsis, stillborn or heavy vaginal bleeding, non-hypertensive pregnant women and any chronic disease had been excluded.

Sample size: The study sample size was 100 samples (50 preeclamptic as test group and 50 normotensive pregnant as control) were enrolled in this study.

Data collection: The clinical data was obtained from history; clinical examination and hospital follow up records and were recorded in questionnaire sheet.

Blood sampling: Blood sample 1.8ml was collected from preeclamptic pregnant women and normal pregnant women by clean vein puncture. 1.8 ml will be collected in a tube containing 200µl of 3.2% sodium citrate and was centrifuged at 2000 rpm for 15 minutes then harvested the plasma.

Nycocard D-dimer single test: Nycocard D-dimer was used for rapid determination of fibrin degradation product in plasma. According to manufacture protocol 50 µL of washing solution was applied to test device avoid touching the membrane with pipette and allowed to soak in to the membrane , 50 µL of undiluted platelet citrated plasma was added to the test device the sample should be absorbed in to the membrane in less than 50 seconds .50 µL of conjugate applied to the test device the conjugate should be absorbed in to the membrane in less than 50 seconds then apply 50 µL of washing solution was added to the test device .test response should preferably be measured as soon as the washing solution has soaked completely in to the device. Siemens multifibrin analyzer: Was used to estimate Plasma fibrinogen by Clauss method.
multifibrin analyzer to 37°C before using, pipette into a test tube warmed to 37°C 100µL from sample and incubate for 60 seconds at 37°C, then add 200 µL from multifibrin analyzer reagent and determine coagulation time.

**Data analysis:** The collected data was analyzed to obtain the mean, standard deviation and the probability (p.value) of parameter studied of patients and control using spss computer programme. Significant level set as <0.05.

**Ethical consideration:** A consent was taken regarding acceptance to participate in this study and reassurance of confidentiality. Before the specimen was collected, the donor knew that this specimen was collected for research purposes.

**Results**
The study included fifty pregnant women in their third trimester with preeclampsia and fifty pregnant women in their third trimester with normal pregnancy were managed as control group. The mean values of fibrinogen and D-dimer for the preeclamptic pregnant women (358.30±138.6) (0.364±0.38) as compared to normal pregnant women (280.00±72.8) (0.148±0.06) respectively. The normal range for fibrinogen (180-350 mg/dL) and D-dimer (<0.3 mg/L).

The p.value of fibrinogen and D-dimer were significantly different between preeclamptic women and normal pregnant women. p.value for fibrinogen less than 0.001 (p.value < 0.001). While p.value for D-dimer less than 0.000 (p.value < 0.000). Table (1).

The level of fibrinogen in preeclamptic women was found within normal value in 26 (52%) of the patients, and high in 24 (48%), while in normal pregnant women fibrinogen was found within normal value in 41 (82%) and high in 9 (18%). (Table 2).

The level of D-dimer in preeclamptic women was found within normal value in 26 (52%) of the patients, and high in 24 (48%), while in normal pregnant women D-dimer was found within normal value in 47 (94%) and high in 3 (6%). (Table 3).

Table (1): Comparison between (Mean ± SD and P.value) in preeclamptic and normal pregnant women:

<table>
<thead>
<tr>
<th>Group</th>
<th>Pre-eclamptic pregnant women</th>
<th>Normal pregnant women</th>
<th>P.value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group statistics</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>P.value</td>
</tr>
<tr>
<td>Fibrinogen mg/dL</td>
<td>358.30±138.6</td>
<td>280.00±72.8</td>
<td>0.001</td>
</tr>
<tr>
<td>D-dimer mg/L</td>
<td>0.364±0.38</td>
<td>0.148±0.06</td>
<td>0.000</td>
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</tbody>
</table>
Table (2): Comparison between Frequency of fibrinogen in preeclamptic and normal pregnant women:

<table>
<thead>
<tr>
<th>Group</th>
<th>Pre-eclamptic pregnant women</th>
<th>Normal pregnant women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statistics</td>
<td>Frequency</td>
<td>Percent</td>
</tr>
<tr>
<td>Fibrinogen mg/dL</td>
<td>Normal</td>
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</tr>
<tr>
<td></td>
<td>Abnormal</td>
<td>24</td>
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</tbody>
</table>

Table (3): Comparison between Frequency of D-dimer in preeclamptic and normal pregnant women:

<table>
<thead>
<tr>
<th>Group</th>
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<th>Normal pregnant women</th>
</tr>
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<tbody>
<tr>
<td>Statistics</td>
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<tr>
<td>D-dimer mg/L</td>
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</tr>
<tr>
<td></td>
<td>Abnormal</td>
<td>24</td>
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</table>

**Discussion**

In this study, the plasma fibrinogen and D-dimer levels were significantly higher in preeclamptic women when compared to normal pregnant women. The results of our study showed that in Sudanese preeclamptic women the level of plasma fibrinogen was higher as compared to normal pregnant women, these results supports the findings of previous study done by Williams VK et al (2007) [19] in South Australia in the evaluation of fibrinogen concentration in preeclampsia and normal pregnant women they found fibrinogen level higher in women with preeclampsia compared with normal pregnancies (P <0.05).

Another study done by Sonal Sogani and Sarakar [20] was in concordance with the finding of our study, which showed that Preeclampsia is associated with high fibrinogen level as compared to normal pregnancy.

This increase in plasma fibrinogen in preeclampsia explains acute phase reaction indicating the inflammatory responses and the endothelial activation which are believed to the pathophysiological mechanism in preeclampsia.
This study also demonstrated high level of plasma D-dimer among preeclamptic pregnant women, our findings are compatible with those of Pinheiro Mde B et al. 2012 [21] in Brazil, this study indicated that increased plasma D-dimer is associated with preeclampsia in the third trimester of gestation in comparison to normotensive pregnant subjects.

Another study done by Zhou H. et al (1997)[22] in China, which estimated plasma D-dimer in preeclampsia, and showed great significance of plasma D-dimer level that appear in second and third trimester in pregnant women with hypertension, and this result agreed with our result our result. This elevation in D-dimer explains the increased fibrinolytic activity and intravascular coagulation in preeclampsia.

**Conclusion**

From this study, it is concluded that the level of fibrinogen and D-dimer is significantly increased in preeclamptic pregnant women when compared with normal pregnant women.

**References**


[10] Ustun Y, Engin-Ustun E, Kamaci M. Association of fibrinogen and CRP with