THE SIGNIFICANCE OF PLATELET COUNT, MEAN PLATELET VOLUME AND PLATELET WIDTH DISTRIBUTION IN PREECLAMPSIA

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ABSTRACT

Background: Preeclampsia (PE) characterized by de novo hypertension and proteinuria after the 20th week gestation. It is usually associated with maternal and neonatal adverse outcome. The aim of this study: was to evaluate the relationship between platelet count and platelet indices; mean platelet volume (MPV) and platelet distribution width (PDW) and severity of preeclampsia and to evaluate their role in prediction of preeclampsia.

Methods: This cross sectional study was carried out at Al-Zahraa University Hospital between January 2012 and December 2012. One hundred and fifty pregnant women with singleton pregnancy between 32-40 weeks gestation were recruited and divided into three groups; normal pregnant women (n = 50) as a control group, women with mild preeclampsia (n = 50) and women with severe preeclampsia (n = 50). Blood samples were recruited upon and analyzed for platelet indices; platelet count, mean platelet volume (MPV) and platelet width diameter (PWD) by automated hematology analyzer. Statistical analysis was performed by analysis of variance and t-test. The receiver-operating characteristic (ROC) curves of these indices were generated and the predictive values of the selected potential parameters were examined in binary regression analysis. P- Value ≤ 0.05 was considered significant.

Results: platelet count was significantly lower in women with severe PE compared to women with mild PE and normal pregnant women groups (139.340 ± 32.610,183.940 ± 37.380 and 249.120 ± 38.350 with P < 0.001) respectively. Mean platelet volume and platelet width distribution were significantly higher in women with severe PE compared to women with mild PE and normal pregnant women groups (11.07 ± 1.08 vs. 9.82 ± 0.68 and 8.50 ± 0.75 with p < 0.001 for MPV and 17.09 ± 2.12 vs. 14.26 ± 1.84 and 11.01 ± 1.77 with p < 0.001 for PDW)
respectively. **Conclusion:** due to increased platelet destruction and platelet turnover in patient with preeclampsia, decreasing platelet count and increasing MPV and PWD may play a role in predicting preeclampsia. Platelet indices are simple, cheap and practical tools in predicting severity of PE. **Key words:** preeclampsia, platelet indices, platelet count, mean platelet volume, platelet width distribution.

**INTRODUCTION**

Preeclampsia is a complex, multisystem disorder of unknown etiology that is unique to human pregnancy. It is a disorder of widespread vascular endothelial malfunction and vasospasm that occurs after 20 weeks gestation and can present as late as 4-6 weeks postpartum (1). It complicates 5-10% of pregnancies and continues to be a major cause of maternal and perinatal morbidity and mortality (2).

According to the International Society for the Study of Hypertension in Pregnancy (ISSHP), PE can be defined as de novo hypertension occurring after 20 weeks of pregnancy together with proteinuria. Hypertension is defined as a systolic blood pressure 140 and/or a diastolic blood pressure 90 mmHg measured at two occasions with at least 4 hours in between. Proteinuria is defined as 300 mg per day (3).

Despite of decades of research, the exact pathophysiology of preeclampsia is not yet fully understood. Numerous pathophysiological mechanisms, alone or in combination, have been suggested to be responsible for the diverse subsets of PE. They include impaired vascular remodeling of the maternal–fetal interface, excessive immune response to paternal antigens, systemic inflammatory response, and dysfunctional placental or endothelial response, all of these processes being modulated by genetic and environmental parameters (4-7).

Abnormal vascular response associated with increased systemic vascular resistance, enhanced platelet aggregation, activation and alteration of the coagulation system, and endothelial cell dysfunction are believed to play an important role in the pathogenesis of preeclampsia (8). The fall in the platelet count is most frequent abnormality and is probably due to consumption during low grade intravascular coagulation (9).

Several studies suggested that platelet may play a major role in the etiopathogenesis of preeclampsia. Out of all haematological changes that occur in preeclampsia, thrombocytopenia is the most common. The degree of thrombocytopenia increases with the severity of the disease. The pathogenesis
of thrombocytopenia in preeclampsia is not clear; it may be due to activation of the coagulation system and accelerated platelet consumption (10).
Platelet volume indices (PVIs) are a group of parameters which are inexpensive to measure and are derived from routine blood counts. The mean platelet volume (MPV) and platelet distribution width (PDW) are the best validated and prominent of these and are attractive indices for research in clinical settings due to their widespread availability to clinicians (11).
Platelet indices are potentially useful markers for the early diagnosis of thromboembolic diseases. As an increase in both mean platelet volume (MPV) and platelet distribution width (PDW) due to platelet activation, resulting from platelet swelling and pseudopodia formation was hypothesized (12).
In the present study, an attempt was made to assess the relationship between platelet indices and preeclampsia and to assess whether these parameters can be used as prognostic markers or not.

METHODS
This cross sectional study was carried out at Al- Zahraa University Hospital between January and December 2012 to evaluate the relationship between the severity of preeclampsia and platelet indices including; platelet count, mean platelet volume (MPV) and platelet distribution width (PWD). The protocol of the study was approved by (The Review Board of Al-Zahraa University Hospital). 150 women with a singleton pregnancy between 32- 40 weeks of gestation who were attending Al-Zahraa University Hospital were recruited. The study participants were divided into three groups: Normal pregnant women (n = 50) as a control group, pregnant women with mild PE (n = 50) and pregnant women with severe PE (n = 50).
Preeclampsia was defined as elevated blood pressure of ≥ 140 / 90 mmHg after 20 weeks gestation with proteinuria ≥ 300 mg / 24 hours urine or > 1+ dipstick. Severe preeclampsia was diagnosed using the following: a blood pressure elevation ≥ 160/110 mmHg, Oliguria (≤ 400 ml in 24 hours urine), persistent headache, blurred vision, right epigastric/right upper quadrant pain, Pulmonary edema and cyanosis, >5 gm proteinuria in 24 hours urine or > +++ proteinuria in spot urine sample, Thrombocytopenia (<100,000/mm3) and Abnormal liver function tests.
Women with a history of diabetes, renal disease, hypertension, cardiovascular illness, symptomatic infectious diseases, chronic medical disorders, a history of smoking, or those with a fetal structural or genetic anomaly were excluded from
the study. Women with HELLP syndrome and low platelet were excluded from the study.

Blood samples were collected upon admission in tubes with potassium ethylene diamine tetra acetate (EDTA) as an anticoagulant. The platelet count and platelet indices were estimated using the Sysmex Xe-2100 automated quantitative hematology analyzer (Sysmex Corp., Kobe, Japan).

Statistical analysis:
Data was collected, verified, revised and tabulated then introduced into IBM P.C. with Excel windows 2010 and statistically analyzed using statistical package version 17 (SPSS Inc. Chicago, U.S.A). Continuous data were presented by minimum, maximum, arithmetic mean and standard deviation. Correlations between parameters were performed by using linear correlation coefficient (Person r) between groups and Analysis of variance (ANOVA) test to make comparison between the 3 groups. P value ≤ 0.05 was considered significant. When significant P-value was obtained at comparing the 3 groups, post-hock test (Tukey's test) was done and then considered significant only if p-value was < 0.016 (0.05/3). Receiver operating characteristics (ROC) curves were used to estimate the predictive values for all variables of the study using the cut off values, sensitivity, specificity, positive predictive value (PPV), negative predictive values (NPV) when correlating each two groups together.

RESULTS
Table 1 : Demographic and clinical data of normal pregnant women control group, women with mild PE and women with severe PE.

<table>
<thead>
<tr>
<th></th>
<th>Normal pregnant women group (n = 50)</th>
<th>Mild PE (n = 50)</th>
<th>Severe PE (n = 50)</th>
<th>P- Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (years)</td>
<td>27 ± 2.3</td>
<td>28 ± 1.9</td>
<td>30 ± 1.8</td>
<td>&lt; 0.09</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.4 ± 1.2</td>
<td>26.5 ± 0.9</td>
<td>27 ± 1.1</td>
<td>0.06</td>
</tr>
<tr>
<td>Nullipara (%)</td>
<td>12 (24%)</td>
<td>13 (26%)</td>
<td>15 (30%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Duration of pregnancy (weeks)</td>
<td>38 ± 0.5</td>
<td>36.7 ±0.5</td>
<td>35.1 ± 0.44</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>116 ± 7.8</td>
<td>150 ± 5.5</td>
<td>165±5.7</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>70 ± 4.9</td>
<td>95 ± 6.4</td>
<td>110 ± 5.2</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>24 h urine protein (g)</td>
<td>0.0 ± 0.0</td>
<td>1.3 ± 0.6</td>
<td>3.8 ± 1.8</td>
<td>&lt; 0.01*</td>
</tr>
</tbody>
</table>

*Significant p-value ≤ 0.05
Table 2: Platelet indices of normal pregnant women control group, women with mild PE and women with severe PE.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Normal pregnant women group (n = 50)</th>
<th>Mild PE (n = 50)</th>
<th>Severe PE (n = 50)</th>
<th>P- Value</th>
<th>Tukey’s post-hock test**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet count/mm³</td>
<td>249.120 ± 38.350</td>
<td>183.940 ± 37.380</td>
<td>139.340 ± 32.610</td>
<td>&lt; 0.001*</td>
<td>&lt; 0.016*</td>
</tr>
<tr>
<td>Mean platelet volume (fl)</td>
<td>8.50 ± 0.75</td>
<td>9.82 ± 0.68</td>
<td>11.07 ± 1.08</td>
<td>&lt; 0.001*</td>
<td>&lt; 0.016*</td>
</tr>
<tr>
<td>Platelet width distribution (fl)</td>
<td>11.01 ± 1.77</td>
<td>14.26 ± 1.84</td>
<td>17.09 ± 2.12</td>
<td>&lt; 0.001*</td>
<td>&lt; 0.016*</td>
</tr>
</tbody>
</table>

*Significant (produced by ANOVA test).
**Post hock test was significant if < 0.016 when comparing all groups as regard studied variables.

Table 3: ROC curve output for all groups including cut off value, sensitivity, specificity, PPV, NPV and accuracy for platelet indices.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Cut off value</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive PV (%)</th>
<th>Negative PV (%)</th>
<th>Accuracy of the test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet count</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control -mild PET</td>
<td>≤ 198,000</td>
<td>90.0</td>
<td>92</td>
<td>91.8</td>
<td>90.2</td>
<td>0.866</td>
</tr>
<tr>
<td>Mild- severe PET</td>
<td>≤ 149,000</td>
<td>84</td>
<td>92</td>
<td>91.5</td>
<td>86</td>
<td>0.681</td>
</tr>
<tr>
<td>Mean Platelet Volume (MPV)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control- mild PET</td>
<td>≥ 9.3</td>
<td>90.0</td>
<td>92</td>
<td>91.8</td>
<td>90.2</td>
<td>0.885</td>
</tr>
<tr>
<td>Mild- severe PET</td>
<td>≥ 10.4</td>
<td>82</td>
<td>92</td>
<td>91.1</td>
<td>83.6</td>
<td>0.865</td>
</tr>
<tr>
<td>Platelet Width Distribution (PWD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control- mild PET</td>
<td>≥ 12.6</td>
<td>90.0</td>
<td>92</td>
<td>91.8</td>
<td>90.2</td>
<td>0.886</td>
</tr>
<tr>
<td>Mild- severe PET</td>
<td>≥ 16.4</td>
<td>84</td>
<td>92</td>
<td>91.3</td>
<td>85.2</td>
<td>0.862</td>
</tr>
</tbody>
</table>

DISCUSSION

Preeclampsia is a multisystem disorder of unknown cause, it is characterised by abnormal vascular response to placentation that is associated with increased systemic vascular resistance, enhanced platelet aggregation, activation of the coagulation system and endothelial cell dysfunction (13).

In the present study, the three groups were comparable as regard maternal age, BMI and parity. Duration of pregnancy was significantly shorter in patients with severe PE than mild PE and normotensive pregnant women groups (P-value < 0.01) (Table 1).
As expected, patients with mild and severe PE had significantly higher systolic and diastolic blood pressure than normotensive pregnant women group (P-value < 0.01) (Table 1). Patients with mild and severe PE had significantly increased 24- h urine protein (1.3 ± 0.6 and 3.8 ± 1.8 respectively) compared to zero urine protein in the control group (P-value < 0.01) (Table 1). According to the pathophysiology of preeclampsia, endothelial activation leads to increased platelet aggregation which in turn is responsible for decrease in the platelet count. In the current study, there is a significant gradual decrease in platelet count from normotensive pregnant women (249,120 ± 38,350/ mm$^3$) to mild PE group (183,940 ± 37,380/ mm$^3$) and severe PE group (139,340 ± 32,610/ mm$^3$) (Table 2). By ROC curve analysis we found that platelet count at cut off value < 198,000 can differentiate normotensive pregnant women from mild PE patients with a sensitivity of 90% and specificity of 92% and at a cut off value of < 149,000 can differentiate mild PE from severe PE patients with sensitivity of 84% and specificity of 92 % (Table 3) (Figure 1, 2). Similar findings were reported by Dadhich et al. (14) who observed declining platelet count with severity of preeclampsia and noted that the decrease in platelet count was antedating significant increase in blood pressure by 4 to 6 weeks and concluded that this Platelet parameter can be used to predict development of progressive hypertension in at risk patients. Accordingly similar inverse relation between platelet count and severity of preeclampsia was also documented by Annam et al. (15), Mohapatra et al. (16), Freitas et al. (17) and Mohamed et al. (18).
Figure 1: ROC curve for correlation between normotensive pregnant women and mild PE groups as regard platelet count.

Figure 2: ROC curve for correlation between mild and severe PE groups as regard platelet count.

In the current study, there is a gradual increase in MPV from normotensive pregnant women (8.5 ± 0.75 fl) to mild preeclampsia (9.82 ± 0.68 fl) and severe preeclampsia patients (11.07 ± 1.08 fl) with P-value < 0.001. ROC curve analysis showed that MPV can differentiate normotensive pregnant women...
from mild PE at a cut off value $\geq 9.3\text{fl}$ with sensitivity of 90 % and specificity of 92 % and can differentiate mild from severe PE at a cut off value $\geq 10.4 \text{fl}$ with sensitivity of 82 % and specificity of 92 % (Table 2) (Figure 3, 4).

These results are in agreement with Dadhich et al. and Yin et al. (14, 19) as they described MPV as a good marker of platelet dysfunction in preeclampsia. On the other hand, Cyehan et al. (20) did not find a significant difference in the MPV between preeclampsia and normal pregnant group and Kashanian et al. (21) observed that MPV changes did not predict preeclampsia or preterm labour. Also, Altibas et al. (22) reported that MPV is not a significant predictor of severity of preeclampsia.

That increase in MPV in PE patients may be due to increased platelet consumption and destruction and so, bone marrow produces large platelets leading to increased MPV (23).

![ROC curve](image.png)

Figure 3: ROC curve for correlation between normotensive pregnant women and mild PE groups as regard MPV.
There was significant increase in PWD from normotensive pregnant women (11.01 ± 1.77 fl) to mild PE (14.26 ± 1.84 fl) and severe PE groups (17.09 ± 2.12 fl) with P-value < 0.001. ROC curve analysis showed that PWD can differentiate normotensive pregnant women from mild PE at a cut off value ≥ 12.6fl with sensitivity of 90 % and specificity of 92 % and can differentiate mild from severe PE at a cut off value ≥ 16.4fl with sensitivity of 84 % and specificity of 92 % (Table 2) (Figure 5, 6).
Figure (6): ROC curve for correlation between mild and severe PE groups as regard PWD.

These results are supported by Dadhich et al. (14) who demonstrated a month wise increase in PDW in preeclampsia group as compared to those in normal pregnant group. These results were in agreement with that reported by Santos and Filho (24), Annam et al. (15), Freitas et al. (17) and Mohamed et al. (18). The increased PDW is explained by increased platelet turnover which would support the idea that platelet survival time is decreased resulting in increased destruction of platelets. This may be also because of increased bone marrow activity of unknown stimulus. Similarly rise in PDW serves as an important indicator of disease severity.

CONCLUSION

The estimation of platelet indices may be considered as an easy, reliable, economic and rapid method for detection of preeclampsia and assessment of its severity.

ACKNOWLEDGEMENT

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الملخص العربي
قيمة قياس دلالات الصفائح الدموية في التنبؤ بحذوة ودرجة تسمم الحمل

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الغرض من الدراسة:
تقييم أهمية دلالات الصفائح الدموية في التنبؤ بحذوة ودرجة تسمم الحمل.

طريقة البحث:
دراسة وصفية تشمل 150 حالة من الحوامل بحول مفرد ما بين الأسبوع الثاني والثلاثين إلى الأسبوع الاربعين من الحمل ومن المتزوجات على مستشفى الزهراء الجامعة مقسمة إلى ثلاث مجموعات:

المجموعة الأولى: وتشتمل 50 حالة لا يعانين من ارتفاع في ضغط الدم وتسمى المجموعة الضابطة.
المجموعة الثانية: وتشتمل 50 حالة من اللاتي تعانين من تسمم حمل من الدرجة البسيطة.
المجموعة الثالثة: وتشتمل 50 حالة من اللاتي تعانين من تسمم حمل من الدرجة الشديدة.

تم عمل قياس لدلاليات الصفائح الدموية لكل المجموعات وتشمل عدد الصفائح، متوسط حجم الصفائح والقطير العرضي للصفائح وتم مقارنة ذلك إحصائيا.

أهم النتائج:
1- يوجد زيادة في عدد الصفائح الدموية في المجموعة الضابطة عنها في المجموعات التي أظهرت تسمم الحمل كما أن عدد الصفائح أيضا يقل كلما زادت درجة تسمم الحمل.
2- بالنسبة للدلاليات الأخرى التي تشمل متوسط حجم الصفائح الدموية والقطير العرضي للصفائح فقد تناوبت هذه الدلالات طرديا مع زيادة درجة تسمم الحمل وأظهرت معدلات أقل في المجموعة الضابطة.

وتستخلص من الدراسة أنه:
توجد علاقة بين قياس دلالات الصفائح الدموية ودرجة تسمم الحمل ولذلك يمكن استخدام هذه الدلالات كعوامل للتنبؤ بحذوة تسمم الحمل ودرجته.