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Evaluation of platelet indices and their significance in Preeclampsia

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Abstract: Objective: to evaluate the platelet indices and their significance in assessment of severity of preeclampsia and their correlation with pregnancy outcome. **Patient and methods**: The present study was a prospective study that was done from January 2012 to March 2013 in EL-Galaa Teaching Hospital and comprised 200 pregnant women who were: 100 normotensive and 100 preeclampsia (68 cases were mild preeclampsia and 32 cases were sever preeclampsia), blood samples were analyzed for platelet indices and the pregnant women were followed up for both maternal and fetal outcome. **Results**: The present study found that the platelet count decreased, while MPV, PDW and PLcr increased with severity of preeclampsia, poor maternal prognosis and poor fetal prognosis. And from ROC curves we found that in differentiating mild from sever preeclampsia a PLT count cut-off value of 168,000 / mm^3 showed a sensitivity of 87.5 % and specificity of 72.1 %, a MPV cut-off value of 10.3 fl showed a sensitivity of 87.5 % and specificity of 85.3 %, a PDW cut-off value of 16.2 fl showed a sensitivity of 87.5 % and specificity of 85.3 % and a PLcr cut-off value of 29.7 % showed a sensitivity of 87.5 % and specificity of 83.8 %. We also found in predicting poor maternal prognosis a PLT count cut-off value of 116,000 / mm^3 showed sensitivity of 83.7 % and specificity of 88.5 %, a MPV cut-off value of 12.1 fl showed sensitivity of 83.7 % and specificity of 88.5 %, a PDW cut-off value of 18.7 fl showed sensitivity of 83.7 % and specificity of 88.5 % and a PLcr cut-off value of 34.7 % showed sensitivity of 83.7 % and specificity of 88.5 %. We also found that in predicting poor neonatal prognosis a PLT count cut-off value of 128,500 / mm^3 showed sensitivity of 92.3 % and specificity of 94.7 %, a MPV cut-off value of 11.3 fl showed sensitivity of 92.3 % and specificity of 94.7 %, a PDW cut-off value of 17.8 fl showed sensitivity of 92.3 % and specificity of 94.7 % and a PLcr cut-off value of 32.9 % showed sensitivity of 92.3 % and specificity of 94.7 %. **Conclusion**: We found a relationship between platelet indices and severity of preeclampsia and pregnancy outcome.

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Keywords: platelet indices, significance, Preeclampsia

1- Introduction

Pre-eclampsia is a multisystem disorder of unknown cause that is unique to human pregnancy. It is characterized 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. The clinical findings of pre-eclampsia can manifest as either a maternal syndrome (hypertension and proteinuria with or without other multisystem abnormalities) or fetal syndrome (fetal growth restriction, reduced amniotic fluid and abnormal oxygenation).[(1)]

Activation of coagulation system in small vessels and increased platelet aggregation is present in preeclampsia. It is clear that preeclampsia is one of the causes of maternal thrombocytopenia and the platelet count increased rapidly after the delivery. There are studies suggesting the storage of platelet in the areas with endothelial damage which is the cause of thrombocytopenia. [(2)]

The aim of this study is evaluation of platelet indices and their significance in assessment of severity of preeclampsia and their correlation with pregnancy outcome.

2- Patient and methods

The present study was a prospective study that was done from January 2012 to March 2013 in El-Galaa Teaching Hospital and comprised (200) pregnant women who were divided into two groups: 100 normotensive and 100 with preeclampsia (68 cases were mild preeclampsia

and 32 cases were sever preeclampsia). Preeclampsia was diagnosed when Bp ≥ 140/90 mmHg after 20 weeks gestation and proteinuria ≥ 300 mg/ 24 hours urine. Sever preeclampsia was diagnosed when Bp ≥ 160/ 110 plus one or more of the following criteria: protineinuria ≥3 gm /24 hours, headache, visual disturbances, upper abdominal pain, oliguria (< 400 ml/24 hours), serum creatinine elevaled >1.2 mg/dl, thrombocytopenia (platelet <100,000/mm^3), marked elevation of serum transaminase AST or ALT, fetal growth restriction and pulmonary edema. Blood samples were analyzed for platelet indices (platelet count, mean platelet volume (MPV), platelet distribution width (PDW) and platelet large cell ratio (PLcr) by automated hematology analyzer. And the pregnant women were followed up for pregnancy outcome as regard: maternal morbidity and mortality, fetal Apgar score, weight and if needed incubator or not and neonatal mortality. Data were statistically described in terms of mean ± standard deviation (±SD), median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using one way analysis of variance (ANOVA) test with multiple 2-group comparisons. For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5. Accuracy was represented using the terms sensitivity, and specificity. Receiver operator characteristic (ROC) analysis was used to determine the optimum cut off value for the studied diagnostic markers. *p* values less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

3- Results

This study included 2 groups of pregnant women: first group included 100 pregnant women with normal blood pressure and second group included 100 pregnant women with preeclampsia, 68 cases of second group were mild preeclampsia and 32 cases of second group were sever preeclampsia.

There was a significant difference between the three studied groups as regards BMI which increased with severity of preeclampsia (P<0.05).While there was no significant difference between the three studied groups as regards age, gravidity and parity (P >0.05).

We found that platelet count decreased with severity of preeclampsia, while MPV, PDW and PLcr increased with severity of preeclampsia (P <0.05).(as shown in table 1).

Table (1): Comparison of platelet indices among 3 groups (normotensive pregnant women, mild preeclampsia and sever preeclampsia cases):

Group / Platelet indices	Normotensive pregnant women (n=100)	Mild preeclampsia cases (n=68)	Sever preeclampsia cases (n=32)	*P* value
PLT count (/mm^3) Mean ± SD	252,600 ± 45,715	183,850 ± 38,002	134,880 ± 34,005	<0.05
MPV (fl) Mean ± SD	8.522 ± 0.8555	9.843 ± 0.7008	11.294 ± 1.1714	<0.05
PDW (fl) Mean ± SD	11.091 ± 2.0476	14.296 ± 1.8800	17.394 ± 2.1378	<0.05
PLcr (%) Mean ± SD	17.15 ± 4.453	25.02 ± 4.689	31.93 ± 4.645	<0.05

The present study found that sever preeclamptic women with poor maternal prognosis had significantly low platelet count, while the MPV, PDW and PLcr were significantly higher than those with good maternal prognosis (P < 0.05). (as shown in table 2).

In this study we found that sever preeclamptic women whose neonates needed admission to NICU had a significantly low platelet count, while the MPV, PDW and PLcr were significantly higher than those whose neonates did not need admission to NICU (P<0.05).(as shown in table 3).

Table (2): Relation between platelet indices and maternal prognosis within sever preeclampsia

Maternal prognosis / Platelet indices	Good maternal prognosis (n=26 cases)	Poor maternal prognosis (n=6 cases)	*P* value
PLT count (/mm^3) Mean ± SD	144,000 ± 30,317	95,330 ± 16,269	<0.05
MPV (fl) Mean ± SD	10.919 ± 0.9174	12.917 ± 0.6401	<0.05
PDW (fl) Mean ± SD	16.846 ± 1.9718	19.767 ± 0.7607	<0.05
Plcr (%) Mean ± SD	30.85 ± 4.476	36.60 ± 1.175	<0.05

Table (3): Relation between platelet indices and neonatal admission to intensive care unit in cases with sever preeclampsia:

Neonatal admission to NICU / Platelet indices	No neonatal admission to NICU (n=19)	Neonatal admission to NICU (n=13)	*P* value
PLT count (/ mm^3) Mean ± SD	153,890 ± 29,685	107,080 ± 15,987	<0.05
MPV (fl) Mean ± SD	10.547 ± 0.7727	12.385 ± 0.6914	<0.05
PDW (fl) Mean ± SD	16.216 ± 1.9469	19.115 ± 0.8444	<0.05
PLcr (%) Mean ± SD	29.56 ± 4.595	35.39 ± 1.477	<0.05

The present study found that in sever preeclamptic women the platelet count was significantly lower in cases with neonatal mortality, while MPV, PDW and PLcr were significantly high (P<0.05). (as shown in table 4).

Table (4): Relation between platelet indices and neonatal mortality in cases with sever preeclampsia:

Neonatal mortality / Platelet indices	No neonatal mortality (n=29)	Neonatal mortality (n=3)	*P* value
PLT count (/mm^3) Mean ± SD	140,100 ± 31,041	84,330 ± 14,364	<0.05
MPV (fl) Mean ± SD	11.079 ± 0.9940	13.367 ± 0.5686	<0.05
PDW (fl) Mean ± SD	17.093 ± 2.0084	20.300 ± 0.6245	<0.05
PLcr (%) Mean ± SD	31.36 ± 4.500	37.47 ± 0.503	<0.05

In the present study we found that sever preeclamptic women whose neonates had Apgar score 5 < 7 had a significantly low platelet count, while the MPV, PDW and PLcr were significantly higher than those whose neonates had Apgar score 5 ≥ 7 (P<0.05).(as shown in table 5).

Table (5): Relation between platelet indices and Apgar-5 in cases with sever preeclampsia

Apgar score / Platelet indices	Apgar-5 less than 7 (n=13)	Apgar-5 ≥ 7 (n=19)	*P* value
PLT count (/mm^3) Mean ± SD	107,080 ± 15,987	153,890 ± 29,685	<0.05
MPV (fl) Mean ± SD	12.385 ± 0.6914	10.547 ± 0.7727	<0.05
PDW (fl) Mean ± SD	19.115 ± 0.8444	16.216 ± 1.9469	<0.05
PLcr (%) Mean ± SD	35.39 ± 1.477	29.56 ± 4.595	<0.05

From ROC curve (1) for platelet indices in differentiating mild from sever preeclampsia we found the following cut off values for platelet indices as shown in table (6)

Table (6): ROC curve (1) for platelet indices in differentiating mild from sever preeclampsia

Item / Platelet indices	Cut off	Sensitivity	Specificity
PLT count (/ mm^3)	168,000	87.5%	72.1%
MPV (fl)	10.3	87.5%	85.3%
PDW (fl)	16.2	87.5%	85.3%
PLcr (%)	29.7	87.5%	83.8%

From ROC curve (2) for platelet indices in predicting poor maternal prognosis within sever preeclampsia we found the following cut off values for platelet indices as shown in table (7)

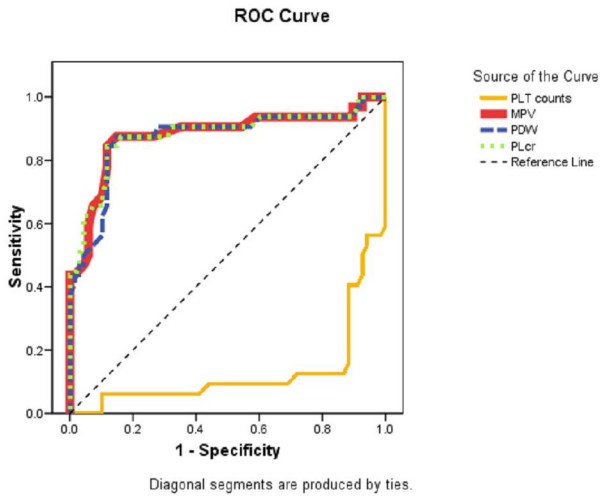
Table (7): ROC curve (2) for platelet indices in predicting poor maternal prognosis within sever preeclampsia

Item / Platelet indices	Cut off	Sensitivity	Specificity
PLT count (/ mm^3)	116,000	83.7%	88.5%
MPV (fl)	12.1	83.7%	88.5%
PDW (fl)	18.7	83.7%	88.5%
PLcr (%)	34.7	83.7%	88.5%

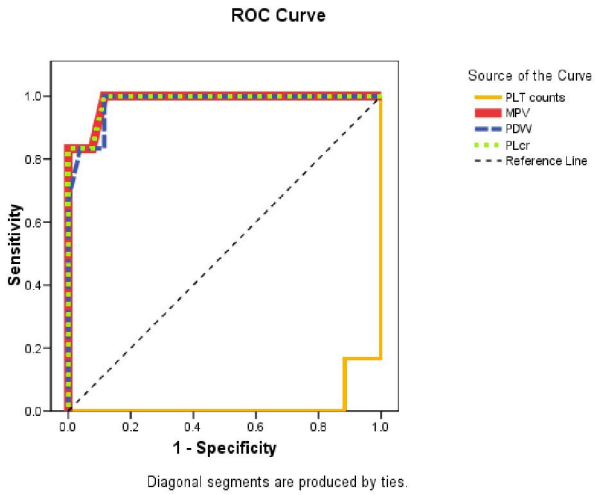
From ROC curve (3) for platelet indices in predicting poor neonatal prognosis within sever preeclampsia we found the following cut off values for platelet indices as shown in table (8).

Table (8): ROC curve (3) for platelet indices in predicting poor neonatal prognosis within sever preeclampsia

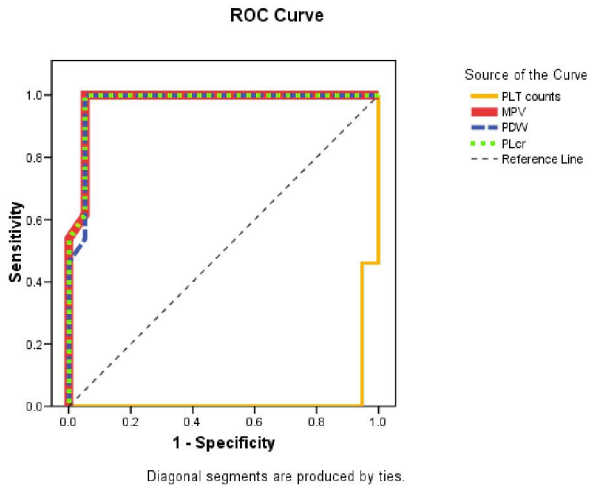
Item / Platelet indices	Cut off	Sensitivity	Specificity
PLT count (/ mm^3)	128,500	92.3%	94.7%
MPV (fl)	11.3	92.3%	94.7%
PDW (fl)	17.8	92.3%	94.7%
PLcr (%)	32.9	92.3%	94.7%



Curve (1): ROC curve for platelet indices in differentiating mild from sever preeclampsia



Curve (2): ROC curve for platelet indices in predicting poor maternal prognosis within sever preeclampsia



Curve (3): ROC curve for platelet indices in predicting poor neonatal prognosis within sever preeclampsia

4- Discussion

The present study was a prospective study that was done from January 2012 to March 2013 in El-Galaa Teaching Hospital and comprised (200) pregnant women who were divided into two groups: 100 normotensive and 100 with preeclampsia (68 cases were mild preeclampsia and 32 cases were sever preeclampsia).

There was a significant difference between the 3 studied groups as regards the BMI which increased with severity of preeclampsia ($P < 0.05$). While there was no significant difference between groups as regards age, gravidity and parity ($P > 0.05$).

In this study an attempt has been made to assess the role of platelet indices in assessment of severity of preeclampsia and their correlation with pregnancy outcome.

In the present study severity of preeclampsia and thrombocytopenia observed are closely correlated which indicates that thrombocytopenia is directly proportional to the severity of preeclampsia. The platelet count values in the present study were: normotensive pregnant women (252,600 ± 45,715 / mm^3), mild preeclampsia (183,850 ± 38,002 / mm^3), and sever preeclampsia (134,880 ± 34,005 / mm^3). So PLT count decreased with severity of preeclampsia. The P values here were less than 0.05 so it was considered statistically significant. From ROC curve (1) we found that a PLT count cut off value of 168,000 / mm^3 showed sensitivity = 87.5 % and specificity = 72.1 % in differentiating mild from sever preeclampsia. So in cases with preeclampsia when PLT count was ≤ 168,000 / mm^3, it suggested severity of preeclampsia.

This agreed with the results reported by Dube *et al.*[3], Mohapatra *et al.*[4], Annam *et al.*[2], Dadhich *et al.*[5], Freitas *et al.*[6] and Mohamed *et al.*[7].

In the present study there is a gradual increase in MPV from normotensive pregnant women (8.5 ± 0.8 fl) to mild preeclampsia (9.8 ± 0.7 fl) and sever preeclampsia (11.2 ± 1.1 fl). So MPV increased with severity of preeclampsia. The *P* values here were less than 0.05 so it was considered statistically significant. From ROC curve (1) we found that a MPV cut off value of 10.3 fl showed sensitivity = 87.5 % and specificity = 85.3 % in differentiating mild from sever preeclampsia. So in cases with preeclampsia when MPV was ≥ 10.3 fl, it suggested severity of preeclampsia. This increase in MPV in sever preeclampsia probably indicate hyperdestruction of platelets due to shorter platelet half life[2].

The results of this study were in agreement with that reported by Ahmed *et al.*[8], Santos and Filho[9], Annam *et al.*[2], Dadhich *et al.*[5], Freitas *et al.*[6] and Mohamed *et al.*[7].

In the present study there is a gradual increase in PDW from normotensive pregnant women (11.09 ± 2.04 fl) to mild preeclampsia (14.29 ± 1.8 fl) and sever preeclampsia (17.39 ± 2.1 fl). So PDW increased with severity of preeclampsia. The *P* values here were less than 0.05 so it was considered statistically significant. From ROC curve (1) we found that a PDW cut off value of 16.2 fl showed sensitivity = 87.5 % and specificity = 85.3 % in differentiating mild from sever preeclampsia. So in cases with preeclampsia when PDW was ≥ 16.2 fl, it suggested severity of preeclampsia. This increase in PDW in sever preeclampsia probably reflects increased platelet turnover which would support the idea that platelet survival time is decreased resulting in increased destruction of platelets[2].

These results were in agreement with that reported by Santos and Filho[9], Annam *et al.*[2], Dadhich *et al.*[5], Freitas *et al.*[6] and Mohamed *et al.*[7].

In the present study there is a gradual increase in PLcr from normotensive pregnant women (17.15 ± 4.45 %), to mild preeclampsia (25.02 ± 4.68 %) and sever preeclampsia (31.93 ± 4.64 %). So PLcr increased with severity of preeclampsia. The *P* values here were less than 0.05 so it was considered statistically significant. From ROC curve (1) we found that

a PLcr cut off value of 29.7 % showed sensitivity = 87.5 % and specificity = 83.8 % in differentiating mild from sever preeclampsia. So in cases with preeclampsia when PLcr was ≥ 29.7 %, it suggested severity of preeclampsia. This increase in PLcr in sever preeclampsia suggests increased bone marrow activity[2].

The results of this study agreed with that reported by Santos and Filho[9] and Annam *et al* [2].

Thus increase in MPV, PDW, PLcr may form basis for prediction of severity of preeclampsia in pregnancy.

In the present study we found that there was relationship between platelet indices in sever preeclampsia and pregnancy outcome, where in sever preeclampsia when (platelet count was low, MPV was high, PDW was high and PLcr was high) these associated with bad pregnancy outcome (on mother and fetus). In this study sever preeclampsia cases with poor maternal prognosis were complicated by eclampsia, death from brain insult, pulmonary oedema, reversible acute tubular necrosis and HELLP syndrome. While Poor neonatal prognosis in sever preeclampsia cases was in neonates needed NICU, Apgar-5 < 7 and neonatal mortality.

The present study found that maternal prognosis was good when (PLT count = 144,000 ± 30,317 / mm^3, MPV = 10.9 ± 0.9 fl, PDW = 16.8 ± 1.9 fl and PLcr = 30.8 ± 4.4 %) and maternal prognosis was poor when (PLT count = 95,330 ± 16,269 / mm^3, MPV = 12.9 ± 0.6 fl, PDW = 19.7 ± 0.7 fl and PLcr = 36.6 ± 1.1 %). So when platelet indices were (low PLT count, high MPV, high PDW and high PLcr) the maternal prognosis was poor. The P values here were less than 0.05 so it was considered statistically significant. From ROC curve (2) we found that in predicting poor maternal prognosis within sever preeclampsia the cut off values were: (a PLT count cut off value of 116,000 / mm^3 showed a sensitivity = 83.7 % and specificity = 88.5 %), (a MPV cut off value of 12.1 fl showed a sensitivity = 83.7 % and specificity = 88.5 %), (a PDW cut off value of 18.7 fl showed a sensitivity = 83.7 % and specificity = 88.5 %) and (a PLcr cut off value of 34.7 % showed a sensitivity = 83.7 % and specificity = 88.5 %).

So in cases with sever preeclampsia when platelet indices were (PLT ≤ 116,000 / mm^3, MPV ≥ 12.1 fl, PDW ≥ 18.7 fl and PLcr ≥ 34.7 %) the maternal prognosis was poor.

The present study also found that neonates did not need incubator when (PLT count = 153,890 ± 29,685 / mm^3, MPV = 10.5 ± 0.7 fl, PDW = 16.2 ±1.9 fl and PLcr = 29.5 ±4.5 %) and neonates needed incubator when (PLT count = 107,080 ± 15,987 / mm^3, MPV = 12.3 ±0.6 fl, PDW = 19.1 ± 0.8 fl and PLcr = 35.3 ± 1.4 %).

The present study also found that there was no neonatal mortality when (PLT count = 140,100 ± 31,041 / mm^3, MPV = 11 ± 0.9 fl, PDW = 17 ± 2 fl and PLcr = 31.3 ±4.5 %) and there was neonatal mortality when (PLT count = 84,330 ± 14,364 / mm^3, MPV = 13.3 ±0.5 fl, PDW = 20.3 ± 0.6 fl and PLcr = 37.4 ± 0.5 %).

The present study also found that Apgar-5 was ≥ 7 when (PLT count = 153,890 ± 29,685 / mm^3, MPV = 10.5 ± 0.7 fl, PDW = 16.2 ±1.9 fl and PLcr = 29.5 ± 4.5 %) and the Apgar-5 was < 7 when (PLT count = 107,080 ± 15,987 / mm^3, MPV = 12.3 ± 0.6 fl, PDW = 19.1 ± 0.8 fl and PLcr = 35.3 ± 1.4 %).

From ROC curve (3) in sever preeclamptic cases the cut off values of platelet indices in predicting poor neonatal prognosis as (neonates needed incubators, low Apgar score and neonatal mortality) were: (a PLT count cut off value of 128,500 / mm^3 showed a sensitivity = 92.3 % and specificity = 94.7 %), (a MPV cut off value of 11.3 fl showed a sensitivity = 92.3 % and specificity = 94.7 %), (a PDW cut off value of 17.8 fl showed a sensitivity = 92.3 % and specificity = 94.7 %) and (a PLcr cut off value of 32.9 % showed a sensitivity = 92.3 % and specificity = 94.7 %). So in cases with sever preeclampsia when platelet indices were (PLT count ≤ 128,500 / mm^3, MPV ≥ 11.3 fl, PDW ≥ 17.8 fl and PLcr ≥ 32.9 %) the neonatal prognosis was poor.

Study of Demir *et al.* [10] agreed with the present study which found that in preeclampsia there was a statistically significant relation between maternal complications and low platelet levels.

Study of Parnas *et al.*[11] also agreed with the present study which found that moderate to severe maternal thrombocytopenia points to a higher degree of severity of the primary disease, which increases perinatal complications (as preterm deliveries, Apgar score < 7 in 5 min, IUGR, stillbirth and placental abruption). However, the adverse outcome is specifically attributed to preeclampsia, HELLP syndrome, and rare causes.

Study of Gioia *et al.*[12] agreed with the present study which found that in pregnant

women with preeclampsia when MPV ≥ 10 fl this was significantly related to compromised fetuses (as neonates need oxygen support more than 2 days or intubation and / or pH < 7.2 at umbilical blood gas analysis).

Study of Laskin *et al.*[13] agreed with the present study which found that the decrease in platelet count (below 100,000 / mm^3) is associated with an increased risk of abnormal coagulation and maternal adverse outcomes in women with preeclampsia.

Onisâi *et al.*[14] also agreed with us who reported that thrombocytopenic preeclampsia was significantly associated with low birth weight newborn and thrombocytopenia in pregnancy was associated with perinatal morbidity, with the strongest association for preeclampsia and HELLP syndrome - for both prematurity and low-birth-weight: the lower the platelet count, the higher the risks for the fetus/newborn.

Thus the PLT count decreased and the (MPV, PDW, PLcr) increased with the severity of preeclampsia, poor maternal prognosis and poor fetal prognosis. So the estimation of platelet indices can be considered as an early, economical and rapid procedure of assessment of severity of preeclampsia. Also platelet indices can assess the prognosis of the preeclampsia in pregnant women.

Conclusion

Finally to conclude, that the estimation of platelet indices method can be considered as an early, economical and rapid procedure of assessment of severity of preeclampsia. Also platelet indices can assess the prognosis of preeclampsia in pregnant women and can have significant impact on maternal and perinatal outcome.

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