

THE ROLE OF PLATELET PARAMETERS AS A BIOMARKER IN THE DIAGNOSIS AND IN PREDICTING THE SEVERITY OF PREECLAMPSIA

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ABSTRACT:

Aim: To compare platelet count, mean platelet volume and platelet distribution width in preeclampsia and normal pregnant females in diagnosis and assessing the severity preeclampsia.

Materials and Methods: Case control study comprising of 50 preeclamptic females between 20 to 24 weeks of gestation as cases and 50 normotensive pregnant females matched for age and gestation as controls. Preeclamptic patients were separated into three groups as mild (25), moderate (13) and severe preeclampsia (12). Platelet count, mean platelet volume and platelet distribution width measured by automated hematology analyzer sysmex KX 21 was recorded in all the groups and analyzed.

Results: Platelet count decreased significantly in patients with preeclampsia as compared to normotensive healthy females. (Mean platelet count in lakhs/cumm \pm SD - 1.6688 \pm .71890 vs 2.5888 \pm .66881, $p < 0.0001$) Among preeclamptic patients there was significant decrease in platelet count with the increasing severity (mild, moderate and severe preeclampsia - 2.2044 + 0.594, 1.176 + 0.267, 1.0917 + 0.385, $p < 0.0001$).

There was significant increase in PDW in preeclampsia when compared to normotensive pregnant females. (PDW in fl - 15.488 \pm 2.4685, 11.755 \pm 1.4206, $p < 0.0001$)

There were no significant differences in MPV in normal and preeclampsia and between severities of preeclampsia.

Conclusion: Platelet count emerges as a reliable indicator for diagnosing preeclampsia and predicting the severity of disease. Though, PDW is also another reliable marker for diagnosis of preeclampsia, its role in assessing the severity of preeclampsia need to be explored. Also increased MPV is not a significant predictor of preeclampsia in pregnancy.

Key Words: Preeclampsia, Mean platelet volume, Platelet distribution width, Platelet count

INTRODUCTION

Preeclampsia is a part of clinical syndrome characterized by increase in blood pressure and proteinuria occurring after 20 weeks of gestation. It is a major cause of morbidity and mortality among mother and fetus. If untreated it may progress to eclampsia and eventually prove fatal. [1] Preeclampsia is usually asymptomatic and treatment being not standardized prevention by early diagnosis holds implications, which requires an easy and cost effective test.

In the past decade, much research has been done to develop a reliable test to predict preeclampsia. Recently several biochemical markers have been described such as angiogenic/anti-angiogenic factors, placental proteins, etc. for predicting preeclampsia. However their role in resource poor hospitals is doubtful.

Alteration in endothelial function, platelets, coagulation and fibrinolytic system is implicated in pathogenesis of preeclampsia [1]. Platelets get activated and attach to the endothelium at the site of injury. As a result bone marrow releases young Platelets which are large increased Mean platelet volume (MPV). [2]

MPV and platelet distribution width (PDW) are simple platelet indices, which increase during

platelet activation. PDW is a more specific marker of platelet activation, since it does not increase during simple platelet swelling. [3]

The present study compared three platelet parameters i.e., platelet count, MPV and PDW in preeclamptic and normotensive pregnant women, to evaluate their role in diagnosing and assessing the severity of preeclampsia.

MATERIAL AND METHODS

This was a case control study conducted by the department of Pathology and obstetrics and gynecology. The study population included 50 cases of pregnant women diagnosed with preeclampsia in 20 to 24 weeks of gestation and 50 normotensive pregnant women matched for age and gestation were taken as control and reviewed.

Cases of gestational diabetes, gestational or chronic hypertension, renal disease in pregnancy and pregnancy with thrombocytopenia due to other causes like infections (viral) or autoimmune disease were excluded from the study.

DEFINITION FOR PREECLAMPSIA:

1. Systolic blood pressure greater than 140 mmHg, diastolic blood pressure (BP) greater than 90 mmHg

on two measurements taken 6 hours apart or on one measurement >150/110 mmHg plus

2. Proteinuria more than 300 mg in 24 hours urine were included in the preeclampsia group

This PE group was further divided into three categories as:

Mild Preeclampsia- If diastolic BP is between 90 and 100 mmHg

Moderate Preeclampsia- If diastolic BP is between 100 and 110 mmHg

Severe Preeclampsia- If BP > 160/110 mmHg, oliguria (<400 ml in 24 hours urine), headache, blurred vision, right epigastric- right upper quadrant pain, pulmonary edema and cyanosis, >5 gr proteinuria in 24 hours urine or > +++ proteinuria in spot urine sample, thrombocytopenia (<100.000/mm³), abnormal liver function tests.

Platelet parameters: Platelet count, MPV and PDW were obtained from the fully automated quantitative hematology analyzer Sysmex k X-21is analyzed in the two groups.

Statistical analysis: Data was being expressed as mean values, standard deviation. Quantitative variables between two groups (preeclamptic and normotensive pregnant women) was analysed by independent t test. Various platelet parameters among three groups based on severity of preeclampsia (mild, moderate and severe) were analysed by anova test. P value <0.005 was considered as statistically significant

RESULTS

Demography: The mean age (\pm SD) of preeclampsia group was 24.56 (\pm 4.756) years and that of control group was 25.33 (\pm 3.819) years. The mean gestational age (\pm SD) of preeclampsia and control group was 32.912 (\pm 5.0510) and 32.663 (\pm 6.1009) respectively. Out of 50 cases in preeclampsia group 28 (56%) were primigravida.

Platelet parameters in preeclampsia and control group: (Table 1)

Comparison of the three platelet parameters i.e., Platelet count, MPV and PDW among the preeclampsia and normotensive pregnant control group was done by using independent t test.

Platelet count was lower in the preeclampsia group as compared to control group and this was statistically significant ($p < 0.0001$)

Though MPV was higher in preeclampsia group as compared to control group, the finding was not statistically significant ($p < 0.180$)

However PDW was significantly higher in preeclampsia group as compared to the control group ($p < 0.0001$).

Severity of preeclampsia (Table 2)

Based on the criteria described in the methodology section, out of 50 cases in PE group; 25 (50%) were mildly preeclamptic, 13 (26%) were moderately preeclamptic and 12 (24%) were severely preeclamptic.

ANOVA test was applied to analyze the platelet parameters in three PE group based on severity. P value of < 0.005 was considered as statistically significant. Platelet count was low in patients with mild preeclampsia when compared to moderate preeclampsia and least in severe preeclampsia patients. These finding was statistically significant ($p < .0001$). [Table 2]

PDW was significantly higher in PE group as compared to normotensive pregnant group ($p < 0.0001$). [Table 1] There was increase in the PDW values with increasing severity of hypertension from mild to severe but was non-significant ($p < .495$). [Table 2] The MPV values in case of mild preeclampsia patients were high when compared to moderate preeclampsia and highest in severe preeclampsia patients. However, these findings were not statistically significant ($p < .624$).

Table 1: Shows the comparison of platelet count, mean platelet volume and platelet distribution width in preeclampsia and control group.

| Parameters | Preeclampsia (n=50) | Control (n=50) | P value |
|--|---------------------|---------------------|---------|
| Platelet count \pm SD (Lakhs/ Cumm) | 1.6688 \pm .71890 | 2.5888 \pm .66881 | <.0001 |
| Mean Platelet value \pm SD (fl) | 9.308 \pm 1.2090 | 8.894 \pm .9690 | <.180 |
| Platelet distribution width \pm SD | 15.488 \pm 2.4685 | 11.755 \pm 1.4206 | <.0001 |

Table 2: Comparison of platelet count, mean platelet volume and platelet distribution width between mild, moderate and severe preeclampsia patients.

| Parameters | Mild pe (n =25) | Moderately pe (n=13) | Severely pe (n=12) | P value |
|-------------------------------|--------------------|----------------------|--------------------|---------|
| Platelet count [Lakhs / cumm] | 2.2044 \pm 0.594 | 1.176 \pm 0.267 | 1.0917 \pm 0.385 | <.0001 |
| MPV [fl] | 9.216 \pm 1.231 | 9.308 \pm 1.223 | 9.608 \pm 1.203 | <.624 |
| PDW | 15.324 \pm 2.442 | 16.17 \pm 2.341 | 15.083 \pm 2.711 | <.495 |

Table 3: Comparison of platelet counts [in Lakhs/cumm] reported by various authors and present study.

| Parameters | Vamseedhar et. al., | Vrunda et. al., | Giles et. al., | Present study |
|--------------|---------------------|-----------------|----------------|---------------|
| Normal | 2,18,440 | 2,20,000 | 2,38,000 | 2,58,880 |
| Preeclamptic | 1,55,500 | 1,40,000 | 1,90,000 | 1,66,880 |

DISCUSSION

Preeclampsia is a clinical syndrome characterized by increase in blood pressure and proteinuria occurring after 20 weeks of gestation.^[1] Preeclampsia is a leading cause of maternal mortality. The WHO estimates that over 100,000 women die from preeclampsia each year. Preeclampsia may lead to convulsions [eclampsia], kidney failure, liver failure, and death of mother. It is also leading cause of both pre mature delivery and IUGR.^[1]

A glance at the literature reveals conflicting results over the role of platelets in diagnosing preeclampsia.

Santos et al, found no difference in platelet count in normotensive and preeclampsia women. However, all other platelet indices were significantly higher in the preeclampsia.^[4]

Ceyhan et al observed no prognostic significance of complete blood count, platelet count and MPV on presence and/or severity of preeclampsia condition.^[5] However there are studies which establish significant difference in platelet count and platelet parameters in preeclampsia and normotensive pregnant women, thus suggesting these tests for diagnosis and predicting the severity of preeclampsia.^[1]

As seen in the literature, platelet parameters in normal pregnancy show varying trends. Since platelet parameters are easily obtained in the cell counter report, they can be readily used by the clinicians in diagnosis and management of preeclampsia. Of all the hematological changes that occur in preeclampsia, change in platelet parameters are the most common hematological abnormality noted.^[6] Other investigations are costly, unreliable and unsuitable for a routine hospital.

An attempt was made in the present study to determine the usefulness of platelet count, MPV and PDW in diagnosis of preeclampsia. A further attempt was made to assess whether these parameters can be used to predict the severity of preeclampsia.

28 (56%) of the total 50 cases in the preeclampsia group were primigravida. The findings were similar to that reported by Shefali et al who observed the incidence of preeclampsia in primigravida of 53.84%.^[1] Similarly various studies have demonstrated bad obstetric history and previous history of hypertension as risk factors for preeclampsia.^[7, 8]

Platelet count was significantly decreased in preeclampsia patients as compared to normal

pregnant controls. (Table 1) Similar findings were demonstrated by various other studies (Table 3).^[9,10,11] 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 present study, the platelet count decreased significantly with the severity of preeclampsia. Similar findings were demonstrated by Shefali et al who observed declining platelet count with severity of preeclampsia. They also noted that the decrease in platelet count was antedating significant increase in blood pressure by 4 to 6 weeks. As a result, the authors concluded that this Platelet parameter can be used to predict development of progressive hypertension in at risk patients.^[1] Accordingly similar inverse relation between platelet count and severity of preeclampsia was also documented by Vaseemdhara et al., and Mohapatra et al.^[9,12]

Due to increased consumption of platelets, bone marrow produces and release large platelets leading to increase MPV in preeclampsia. However literature reveals conflicting results regarding the relation between MPV and preeclampsia. There are studies which demonstrate increase in MPV even in healthy individuals.^[13] Shefali et al., in their study described MPV as a good marker of platelet dysfunction in preeclampsia.^[1] Similar findings were observed by Yin set. al.^[14] In the present study MPV was proportionally higher in preeclampsia as compared to normal pregnant females but the difference was not statistically significant. Cyehan et al did not find any significant difference in the MPV between preeclampsia and normal pregnant group.^[5] In a recent study by Kashanian et al, the authors observed that MPV changes did not predict preeclampsia or preterm labour.^[15]

This confusing behavior of MPV in various studies may be explained by the differences in equipment and method of automated cell counter.^[5]

In the present study there was no significant increase in MPV with increasing severity of preeclampsia. Though several studies demonstrate a direct relationship between MPV and preeclampsia severity our findings did not correlate with these studies.^[1,14] However a recent study by Altibas also observed that MPV is not a significant predictor of preeclampsia severity.^[16]

In the present study PDW was significantly higher in preeclampsia group than in normal control group. (Table 1) Similar findings was reported by

Shefali et al, who demonstrated a month wise increase in PDW in preeclampsia group as compared to those in normal pregnant group.^[1]

The reason for 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.^[1] However this result was different than the findings in present study which again may be explained by the differences in the equipment's used.

Limitations of the study: This being a retrospective study, has limitations and that further longitudinal studies are required which could evaluate the serial platelet count and other platelet parameters at various gestational ages of pregnancy to highlight the role of these parameters in diagnosing and predicting severity of preeclampsia.

CONCLUSION

Platelet count emerges as a reliable indicator for diagnosing preeclampsia and predicting the severity of disease. Though, PDW is also another reliable marker for diagnosis of preeclampsia, its role in assessing the severity of preeclampsia need to be explored. Also increased MPV is not a significant predictor of preeclampsia in pregnancy.

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