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A Cross-Sectional Study to Evaluate the Association of Platelet Indices in Preeclampsia and Healthy Pregnancy

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Abstract: ***Preeclampsia is a major hypertensive disorder of pregnancy associated with significant maternal and fetal morbidity and mortality. Platelet activation and increased platelet consumption are recognized features of its pathophysiology, making platelet indices potential biomarkers for its diagnosis and assessment of disease severity. This cross-sectional study evaluated the association of platelet indices with preeclampsia and healthy pregnancy among 90 pregnant women beyond 20 weeks of gestation, including 50 women with preeclampsia and 40 normotensive controls. Clinical details, blood pressure, and urine protein levels were recorded, and platelet indices were measured using an automated Sysmex hematology analyzer. Statistical analysis was performed with a p-value <0.05 considered statistically significant. Mean platelet volume (MPV) and platelet distribution width (PDW) were significantly higher in women with preeclampsia compared to normotensive controls (MPV: 9.8 vs. 8.7 fL; PDW: 13.5 vs. 12.1 fL; p<0.001). Plateletcrit (PCT) also showed a significant difference between the groups (p<0.001), whereas platelet count was lower in the preeclampsia group but did not reach statistical significance. MPV demonstrated the highest diagnostic performance with a sensitivity of 81% and specificity of 85%, followed by PCT (78% sensitivity) and PDW (72% sensitivity). Platelet count showed the highest specificity (95%) but comparatively lower sensitivity (73%). The findings suggest that MPV, PDW, and PCT are more reliable indicators of platelet activation in preeclampsia than platelet count alone and may serve as useful adjunctive biomarkers for the early diagnosis and evaluation of preeclampsia. Incorporating these inexpensive and routinely available platelet indices into antenatal assessment may facilitate earlier identification of women at risk and improve maternal and fetal outcomes. Larger multicenter prospective studies are recommended to validate these findings and establish their role in routine clinical practice.***

Keywords: Preeclampsia, Platelet indices, Maternal health, Diagnostic Biomarkers, Pregnancy

1. Introduction

Preeclampsia is a serious complication of pregnancy affecting 2-8%. It is said to be the second largest cause of maternal death globally after hemorrhagic diseases.[1] This hypertensive disorder typically manifests after 20 weeks of gestation and is characterized by high blood pressure and the presence of proteinuria or signs of organ dysfunction.[2,3] The pathophysiology of preeclampsia is complex and multifactorial, often involving endothelial dysfunction, inflammation, and abnormal placentation, which collectively contribute to systemic vasoconstriction and increased vascular permeability.[4-7]

One of the hematological changes associated with preeclampsia is thrombocytopenia, which is indicative of increased platelet consumption and activation.[8] This observation has led to an interest in platelet indices as potential biomarkers for the early detection and monitoring of preeclampsia. Platelet indices such as Platelet count (PC), Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), and Plateletcrit (PCT) are readily available through routine blood tests and provide insights into platelet activation and turnover.

Given the significant health implications of preeclampsia, early detection and timely intervention are crucial. The current study investigates the utility of platelet indices, particularly MPV, PDW and PCT in predicting the occurrence and severity of preeclampsia. The study also aims to assess the diagnostic accuracy of these indices, thereby exploring their potential role in enhancing prenatal care and improving maternal and fetal outcomes.

2. Materials and Methods

Study Design: A cross-sectional study was conducted in the Department of Pathology, Bangalore Medical College and Research Institute (BMCRI) after obtaining clearance from the institutional ethical committee. The study included 90 pregnant women (50 cases and 40 controls) attending the antenatal clinic in the Obstetrics and Gynaecology department who gave consent for the study.

Sample size: Based on the study of Bawore SG. et al, platelet count in normotensive and preeclamptic pregnant women were 251±76.5 x10^3 /µL and 170±63.8 x10^3 /µL respectively.[9] Assuming the minimum expected difference between two groups to be 30 x10^3 /µL, the sample size is calculated to be 86 which is rounded off to 90.

Inclusion Criteria:
- Women with singleton pregnancies beyond 20 weeks gestation
- For cases, women with pregnancies diagnosed as preeclampsia according to NICE guidelines, 2010
- For controls, healthy women with singleton pregnancies with blood pressure within normal limits and no proteinuria
- Pregnant women admitted to the hospital who gave consent to participate in the study.

Exclusion Criteria:
- Gestational or insulin-dependent diabetes and known previous hypertension
- Multiple gestation
- History of preeclampsia, renal or hepatic dysfunction, disseminated intravascular coagulation
- Patients taking drugs which alter platelet count such as heparin, corticosteroid

Methodology

Informed consent was obtained from all individual participants included in the study. Pregnant women beyond 20 weeks were enrolled and divided into healthy controls and preeclampsia cases per NICE guidelines (blood pressure is ≥140/90 mmHg after 20 weeks of pregnancy with the presence of proteinuria). Demographic data, blood pressure, and urine albumin levels were recorded. Blood samples were analyzed for platelet indices using a Sysmex analyzer. Statistical analysis compared the groups with significance set at P<0.05 using SPSS software version 21.0.

Outcome measures:
- Primary: Differences in platelet indices between cases and controls.
- Secondary: Correlation of platelet indices with the severity of preeclampsia.

Statistical analysis:
- Data was analysed by descriptive statistics such as mean, median, standard deviation, inter-quartile range, percentages, tables and graphs wherever necessary.
- Independent T test was used to determine significant difference in platelet indices between preeclampsia and normotensive pregnant women.
- ANOVA test was used to determine significant differences in platelet indices among normotensive, non-severe preeclampsia and severe preeclampsia.
- The strength of the association between each of the platelet indices and MAP was estimated using the Pearson correlation coefficient (r). To estimate the sensitivity value as a severity marker of PE, receiver operating characteristic (ROC) analysis was performed.
- The diagnostic indices like sensitivity, specificity, positive predictive value and negative predictive value were used to know the diagnostic potential of the test.
- SPSS version 21.0 was used for data analysis. The differences were considered to be statistically significant when the p value obtained was *P<0.05*.

3. Results

In our study of 90 pregnant women (50 with preeclampsia and 40 controls), age, gravidity, and parity were similar across groups with no statistical significance (Table 1).

Table 1: Clinical characteristics of study participants

Characteristics	Normotensive (n=40)	Non severe Preeclampsia (n=29)	Severe preeclampsia (n=21)
Age	25.1 (21-31)	27.3 (22-35)	26.2 (20-37)
Gravidity	1 (1-4)	2 (1-5)	2 (1-4)
Parity	1(0-3)	1 (0-3)	1 (0-3)
SBP	116.7 (110-120)	145.2 (130-180)	158.7 (130-190)
DBP	78.4 (74-82)	93.3 (80-120)	101.7 (90-120)
MAP	87.8 (83.1-93.3)	108.6 (96-133.3)	120.89 (108-173.3)
Proteinuria	0	2+(1-3)	3+(1-3)

Blood pressure increased with preeclampsia severity: systolic (116.7 mmHg in controls vs. 158.7 mmHg in severe cases) and diastolic pressures showed similar trends (Tables 2 and 3).

Table 2: Comparisons of blood pressure between normotensive and PE

BP	Normotensive	Preeclampsia	P value
SBP	116.7 (110-120)	150.9 (130-190)	<0.001
DBP	78.4 (74-82)	96.8 (80-120)	<0.001
MAP	87.8 (83.1-93.3)	114.5 (96.6-143.3)	<0.001

Table 3: Comparisons of blood pressure between non severe and severe PE

BP	Non severe preeclampsia	Severe preeclampsia	p value
SBP	145.2 (130-180)	158.7 (130-190)	<0.001
DBP	93.3 (80-120)	101.7 (90-120)	<0.001
MAP	108.6 (96-133.3)	120.89 (108-143.3)	<0.001

Platelet indices, particularly MPV and PDW were significantly higher in preeclamptic women compared to controls (MPV: 9.8 vs. 8.7 fl; PDW: 13.5 vs. 12.1 fl; both *P<0.001*). Sensitivities for MPV and PDW were 81% and 72%, respectively. MPV was significantly higher in the preeclampsia group (mean = 9.8 fl) compared to the control group (mean = 8.7 fl) (*P<0.001*). PDW was also significantly elevated in the preeclampsia group (mean = 13.5fL) compared to controls (mean = 12.1%fL) (*P<0.001*). PCT was also significantly elevated in the preeclampsia group (mean = 0.16%) compared to controls (mean = 0.22%) (*P<0.001*). The mean platelet count was slightly lower in the preeclampsia group (mean = 202 x 10^9/L) compared to controls (mean = 217 x 10^9/L), but this difference was not statistically significant (*P>0.05*) (Tables 4 and 5).

Table 4: Comparisons of platelet indices between normotensive and pre-eclamptic pregnant women

Platelet indices	Normotensive	Preeclampsia	p value
PC(x10^3/µm)	217 (130-380)	202 (60-441)	>0.05
MPV (fL)	8.7 (6.7-11.4)	9.8 (7.3-11.5)	<0.001
PDW (fL)	12.1 (7.4-13.4)	13.5 (8.4-17.8)	<0.001
PCT (%)	0.17 (0.15-0.34)	0.18 (0.05-0.24)	<0.001

Table 5: Comparisons of platelet indices among normotensive, non-severe, and severe pre-eclamptic pregnant mothers (PC: Platelet count, MPV: Mean Platelet Volume, PDW: Platelet distribution Width, PCT: Plateletcrit)

Platelet indices	Normotensive pregnant women (n=40)	Non-severe pre-eclampsia group (n=29)	Severe pre-eclampsia group (n=21)	p value
Platelet count (x10^3/µm)	217 (130-380)	236 (78-432)	214 (60-441)	>0.05
MPV (fL)	8.7 (6.7-11.4)	9.2 (7.7-11.4)	9.3 (7.3-11.5)	<0.001
PDW (fL)	12.1 (7.4-13.4)	12.7 (8.9-17.8)	12.6 (8.4-15.4)	<0.001
PCT (%)	0.17 (0.15-0.34)	0.17 (0.06-0.24)	0.15 (0.05-0.24)	<0.001

Diagnostic accuracy of platelet indices (Table 6):
Platelet Count: The sensitivity of platelet count at a cutoff value of <170 x 10³/µL was 73%, with a specificity of 95%, a positive predictive value (PPV) of 95.6%, and a negative predictive value (NPV) of 75.3%.

MPV: The sensitivity of MPV at a cutoff value of >8.2 fL was 81%, with a specificity of 85%, a PPV of 76.4%, and a NPV of 88.3%.

PDW: Using a cutoff value of >12 fL, PDW had a sensitivity of 72%, specificity of 83%, PPV of 83.7%, and NPV of 70.2%.

PCT: With a cutoff value of <0.19%, PCT showed a sensitivity of 78%, specificity of 70%, PPV of 76.5%, and NPV of 71.2%.

Table 6: Diagnostic Accuracy of platelet indices (PPV: Positive predictive value, NPV: Negative predictive value)

Parameters (cutoff value)	PC (<170x10^3/µm)	MPV (>8.2fL)	PDW (>12fL)	PCT (<0.19%)
Sensitivity	73%	81%	72%	78%
Specificity	95%	85%	83%	70.00%
PPV	95.60%	76.40%	83.70%	76.50%
NPV	75.30%	88.30%	70.20%	71.20%

4. Discussion

Chung & Lee found that MPV, PDW, and PCT were effective markers for the prediction of preeclampsia in Asian populations, reinforcing the idea that platelet indices can offer valuable diagnostic insights in diverse populations.[10]

Muzaffer Temur et al. observed that MPV was significantly higher in preeclamptic patients (9.66 ± 1.62 fl) compared to normotensive controls (8.92 ± 1.33 fl, $p < 0.001$).[11] This is in line with our results, where preeclamptic patients had an MPV of 9.8 fl versus 8.7 fl in the normotensive group. These elevated MPV values in preeclampsia highlight a disturbance in platelet production and function associated with the condition. The significance of MPV in predicting preeclampsia is further supported by a meta-analysis conducted by Kocabay & Erdogan, whose results aligned with our study.[12]

Nitesh Thalor et al. also noted that MPV was significantly higher in preeclamptic patients, further validating our findings.[13] The study by Shaifali Dadhich et al. reported a 44.5% increase in MPV among preeclamptic patients compared to a 9.22% increase in normotensive controls.[4] This corroborates our observation that MPV is a reliable marker for preeclampsia and suggests its potential as an early diagnostic tool.

Bawore et al. found that PDW and MPV significantly increased with the severity of preeclampsia.[9] The study reported an area under the curve (AUC) of 0.986 for PDW in predicting preeclampsia, emphasizing its high diagnostic value. Our study supports this, with significant differences in MPV and platelet count across varying severities of preeclampsia. Furthermore, Tunc & Dogan emphasized that platelet indices not only aid in the early detection of preeclampsia but also correlate with its severity, which is further supported by our findings on the diagnostic performance of MPV and PDW.[14]

The significant increase in MPV among women with preeclampsia suggests that larger, more active platelets may play a crucial role in the disease's progression. This supports existing literature associating MPV with platelet activation and thrombotic disorders. Elevated PDW in preeclampsia indicates increased platelet production due to heightened consumption from endothelial damage, contributing to the disease's prothrombotic state.

5. Conclusion

Overall, MPV, PDW, and PCT emerged as more effective markers for detecting preeclampsia compared to platelet count, aligning with the increased platelet activation and turnover observed in preeclamptic patients. These findings support the utility of these platelet indices in the diagnostic and prognostic evaluation of preeclampsia.

The consistency across these studies, including our own, emphasizes the importance of MPV and PDW as biomarkers for preeclampsia. Elevated MPV, in particular, appears to be a promising indicator for early detection and management of preeclampsia, complementing traditional methods such as blood pressure monitoring. Future research should continue to refine these indices and explore their integration into routine prenatal care to improve outcomes for affected pregnancies.

Strengths

The study focuses on a well-defined population of pregnant women, making the findings directly relevant to this group. The use of automated hematology analyzers ensures standardized and precise measurements, reducing the likelihood of measurement bias. The study addresses a significant clinical issue by exploring the potential of platelet indices as early markers for preeclampsia, which could lead to improved prenatal care. The inclusion of both a control group and a case group allows for direct comparison, enhancing the validity of the findings. Lastly, the comprehensive data collection enables a thorough analysis of the potential associations between platelet indices and preeclampsia.

Limitations

One limitation is its cross-sectional design, which restricts the ability to establish a causal relationship between platelet indices and preeclampsia. Additionally, being conducted at a single medical center may limit the generalizability of the results to a broader population. The sample size, while statistically significant, is relatively small, potentially affecting the robustness of the conclusions. Furthermore, the study may not fully account for confounding factors such as diet, stress, and underlying health conditions that could influence platelet indices. The temporal variation in platelet indices, with only a single measurement taken, may not accurately reflect changes over the course of pregnancy.

Declarations

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Author Contribution: P.C. conceptualized the study, collected the data, performed the statistical analysis, interpreted the results, and wrote the first draft of the manuscript. A.M. contributed to the study design, data collection and data interpretation. L.B. supervised the study, contributed to the methodology, and critically reviewed and edited the manuscript. S.M.A. contributed to the study design, interpretation of results, and critical revision of the manuscript. All authors read and approved the final manuscript.

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