

Clinical correlation of platelet indices in preeclamptic patients without HELLP syndrome

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ABSTRACT

Objectives: To understand the relationship between the indices of platelet with preeclampsia and to determine if these parameters may be used for early diagnosis. **Methods:** A prospective case-control study was done on 50 women and they were divided into two groups - the non-severe preeclampsia group (n=36) and the severe preeclampsia group (n=14). Platelet indices - platelet count, mean platelet volume, platelet distribution width, platelet crit and platelet large cell ratio were analyzed and correlated with the observed clinical severity status, organ system affected and fetomaternal outcomes. **Results:** Findings showed that there was a statistically significant decrease in platelet count ($p<0.001$) and an increase in mean platelet volume ($p<0.001$) and platelet distribution width ($p<0.05$) in mothers of severe preeclampsia group as compared to non-severe preeclampsia group. In the severe preeclampsia group, two out of 14 mothers had abnormal maternal outcomes and all 14 babies were abnormal. Furthermore, platelet count was significantly decreased and plateletcrit was non-significantly decreased in the abnormal maternal prognosis group of mothers. Also, mean platelet volume and platelet distribution width were significantly ($p<0.001$) increased in the abnormal maternal prognosis group of mothers. **Conclusion:** As pregnancy advances, the platelet counts decrease while mean platelet volume and platelet distribution width increase, and these kinds of changes are more evident in severe preeclampsia mothers than in non-severe preeclamptic mothers. Thus, platelet indices could be used as biomarkers for early diagnosis of the severity of preeclampsia.

Keywords: Preeclampsia, platelet indices, platelet count, MPV, PDW.

Preeclampsia is a pregnancy-specific multisystem disorder characterized by the abnormal vascular response to placentation, associated with increased systemic vascular resistance, enhanced platelet aggregation, activation of the coagulation system, and endothelial cell dysfunction with resultant reduced organ perfusion. The cause of preeclampsia remains unclear despite extensive research^{1,2}. Preeclampsia is one of the significant health concerns complicating around 3–8% of pregnancies causing maternal morbidity and mortality³. Present criteria for preeclampsia diagnosis require the presence of de-novo hypertension (blood pressure of $\geq 140/90$ mm Hg), with proteinuria or any of the other multisystem abnormalities, with onset after the 20th week of

gestation^{4,5}.

Platelet indices viz. platelet count, mean platelet volume (MPV) and platelet distribution width (PDW), plateletcrit (PCT), and platelet large cell ratio (P-LCR) constitute part of the data measurable by the complete blood count (CBC) test. These indices' applicability has been studied for the clinical and pathophysiological understanding of vascular diseases, including preeclampsia, but their importance has not been thoroughly substantiated yet⁶. During preeclampsia advancement, a declining platelet count is observed and is proposed to be a symptom of worsening preeclampsia⁷. This drop-in platelet count restores quickly to its normal range upon delivery. It was also observed that during pregnancy,

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MPV rises and is higher in preeclampsia women. Before the onset of preeclampsia symptoms, there will be an increase in MPV. Therefore, it may be considered a valuable marker for the occurrence of preeclampsia⁶. Also, these indicators are cost-effective and easily obtainable as they are developed from routine blood tests. Platelet indices may be utilized as an early marker for the diagnosis of thromboembolic diseases⁸.

Several research studies demonstrated that D-dimer, soluble vascular endothelial growth factor receptor and platelet distribution width might be used as diagnostic markers for preeclampsia; however, various effects vary coagulation-fibrinolytic system in preeclampsia in late pregnancy, and no conclusive evidence was drawn¹⁵. With this scenario, in our study, we aimed to understand the relationship between the platelet indices viz. platelet count, MPV PDW, PCT, and P-LCR with preeclampsia, and tried to assess in early diagnosis of preeclampsia, these parameters could be used as markers or not.

Materials and methods

A prospective case-control study was done on 50 women at the department of obstetrics and gynaecology, Dr D. Y. Patil Medical College, Hospital and Research Centre, Pune, Maharashtra. The study cohort was subdivided into two groups viz. non-severe preeclampsia group (n=36) and the severe preeclampsia group (n=14). Institutional ethics committee approval and written informed consent were obtained from each patient before starting the study. The following inclusion and exclusion criteria were followed while enrolment of study subjects.

Inclusion criteria:

- 1) All patients presenting with preeclampsia, non-severe preeclampsia (as per ACOG guidelines; BP $\geq 140/90$ mm Hg at two intervals 4 hours apart with or without significant proteinuria).
- 2) Severe preeclampsia (As per ACOG guidelines, BP $\geq 160/110$ mmHg, and proteinuria >5 gm/24 hours) were included.

Exclusion criteria:

- 1) Women with Hb level <10 g/dL.
- 2) Women with pre-existing medical disorders like hepatitis, nephropathy, and diabetes mellitus.
- 3) Women on steroids, anticoagulant medications, or antiplatelet medication.
- 4) Patients with known platelet/haematological pathologies like immune thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP) and aplastic anaemia.

- 5) Women with hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome, acute fatty liver of pregnancy (AFLP), obstetric cholestasis (OC).

Socio-demographic details of all the study subjects were recorded. Blood pressure and proteinuria were estimated in all the subjects. Data on the presence of nausea, vomiting, headache, urine output less than 400ml/24hrs, haemogram, hypoproteinaemia, raised liver enzymes, deranged KFT, and presence of hemolysis were also recorded. Platelet indices viz. platelet count, MPV, PDW, PCT, and P-LCR are the primary outcome of study parameters analyzed and correlated with the observed clinical severity status and organ system affected preeclamptic patients. Platelet indices were also correlated with fetal affection and well-being.

The data were entered in a Microsoft excel sheet and were analyzed using SPSS (Statistical Package for Social Sciences) version 20 software. The categorical data was represented in the form of frequency and percentage. Continuous data were represented as mean and standard deviation. Quantitative data were analyzed using the student t-test, while categorical data were analyzed using the chi-square test. $p < 0.05$ was considered statistically significant.

Results

A total of 50 pregnant women were included in the study. The age distribution of the pregnant mothers is described in table 1. Of 50 women, 36 had non-severe pre-eclampsia and 14 had severe pre-eclampsia. The mean (SD) age of women in non-severe pre-eclampsia and severe pre-eclampsia was 25.4 (3) and 31.2 (4.4) years respectively; women with severe pre-eclampsia were older than those with the non-severe condition and was statistically significant ($p < 0.05$).

Primigravidas were predominance (64% and 78.6%) in non-severe preeclampsia and severe preeclampsia

Table 1: Age profile of patients enrolled in the study

Age (years)	Non severe preeclampsia (N=36)	Severe preeclampsia (N=14)	Total
Mean	25.4	31.2	28.5
SD	3	4.4	3.7
Median	25	26	27
Minimum	21	20	20
Maximum	34	36	35

respectively. Primigravida had more risk of developing preeclampsia than multigravida. But p-value was not statistically significant in our study. In the non-severe preeclampsia group majority of the mothers, 20/36 (55.6%), were in the gestational age of 36 weeks, whereas in the severe preeclampsia group majority of the study subjects, i.e., 8/14 (57.1%) were in gestational age of 34 weeks. There

was no significant difference in the mean gestation age of both study groups.

Table 2: Parity and gestational age distribution of patients enrolled in the study

Characteristic	Non-severe pre-eclampsia		Severe pre-eclampsia	
	N	%	N	%
Parity				
Primigravida	23	63.9	11	78.6
Multigravida	13	36.1	3	21.4
Total	36	100.0	14	100.0
Gestational age in weeks				
30	0	0.0	1	7.1
32	0	0.0	3	21.4
33	0	0.0	1	7.1
34	4	11.1	8	57.1
35	6	16.7	1	7.1
36	20	55.6	0	0.0
37	6	16.7	0	0.0
Total	36	100.0	14	100.0

The comparison of platelet indices between mothers with non-severe preeclampsia and severe preeclampsia was represented in table 3. Study findings revealed that there was a statistically significant decrease in platelet count ($p < 0.001$) and an increase in MPV ($p < 0.001$), and PDW ($p < 0.05$) was observed in mothers of severe preeclampsia group as compared to mothers of non-severe preeclampsia group. However, P-LCR (%) and PCT (%) were non-significantly increased and decreased, respectively.

Table 3: Comparison of platelet indices between study groups.

Platelet indices	Non-severe preeclampsia (N=36)	Severe preeclampsia (N=14)
Platelet count (lacs/cu. mm)	1.80 ± 0.50	***0.70 ± 0.20
MPV (fl)	10.70 ± 1.10	***13.50 ± 0.50
PDW (fl)	17.90 ± 2.98	*19.60 ± 2.13
P-LCR (%)	38.20 ± 1.90	49.90 ± 6.20
PCT (%)	0.20 ± 0.00	0.10 ± 0.00

MPV - Mean platelet volume, PWD - Platelet distribution width, PCT - Plateletcrit, P-LCR - Platelet large cell ratio (P-LCR).

Values are expressed as Mean ± Standard deviation

*** $p < 0.001$ and * $p < 0.05$ as compared to the non-severe preeclampsia group based on unpaired t-test

In the non-severe preeclampsia group, none of the mothers had an abnormal maternal outcome. Whereas in the severe preeclampsia group, two mothers (14.3%) had abnormal outcomes, i.e., one mother had abruptio and the other developed eclampsia. With regards to fetal outcome findings in non-severe preeclampsia group, eight babies (22.2%) had abnormal outcomes (RDS-16.7%; RDS+HIE-5.6%) compared to 14 babies (100%) in severe preeclampsia

Table 4: Comparison of maternal and fetal outcomes between the study groups.

Outcomes	Non-severe preeclampsia		Severe preeclampsia	
	N	%	N	%
Maternal outcomes				
Normal	36	100.0	12	85.7
Abnormal	0	0.0	2	14.3
Total	36	100.0	14	100.0
Chi-square = 5.35; $p = 0.62$				

Fetal outcomes				
Normal	28	77.8	0	0.0
Abnormal	8	22.2	14	100.0
Total	36	100.0	14	100.0
Chi-square = 24.75; $p < 0.001$				

group (IUGR-21.4%; RDS-14.3%; IUFD-7.1%; RDS+HIE-21.4%; IUGR+Septicaemia-7.1%; IUGR+RDS-21.4%; RDS+HIE+Septicaemia -7.1%). The difference was statistically significant ($p < 0.001$). The comparison of maternal and fetal outcomes between study groups was represented in table 4.

Table 5: Comparison of platelet indices and maternal prognosis.

Platelet indices	Maternal prognosis (Normal)	Maternal prognosis (Abnormal)
Platelet count (lacs/cu. mm)	1.50 ± 0.60	***0.50 ± 0.00
MPV (fl)	11.40 ± 1.50	***14.10 ± 0.10
PDW (fl)	19.30 ± 2.90	***24.30 ± 0.20
P-LCR (%)	41.00 ± 5.90	54.00 ± 2.80
PCT (%)	0.20 ± 0.00	0.10 ± 0.00

MPV - Mean platelet volume, PWD - Platelet distribution width, PCT - Plateletcrit, P-LCR - Platelet large cell ratio (P-LCR).

Values are expressed as Mean ± SD.

*** $p < 0.001$ as compared to maternal prognosis (normal) based on unpaired t-test.

The platelet indices viz. MPV (fl), and PDW (fl), were significantly ($p < 0.001$), and P-LCR (%) was non-significantly increased in the abnormal maternal prognosis group of mothers as compared to normal maternal prognosis mothers. Whereas, platelet count (lacs/cu. mm) and PCT (%) was significantly ($p < 0.001$) and non-significantly decreased in the abnormal maternal prognosis group of mothers as compared to the normal maternal prognosis group (table 5).

Discussion

Preeclampsia continues to be a significant cause of maternal and fetal morbidity and mortality since it is linked to increased risk of preterm delivery, IUGR, and placental abruption¹⁰. Also, there is a significant concern about preeclampsia's long-term consequences, as women who experience this disorder represent a high-risk group later in

life for subsequent premature cardiovascular, cerebrovascular, peripheral arterial diseases, and other chronic illnesses^{11, 12}. Furthermore, in developing countries like India, pregnancy-induced hypertension has been a significant cause of maternal and perinatal morbidity and mortality¹³. Hence in the present study, an attempt was made to understand the relationship between the platelet indices viz. platelet count, MPV, PDW, PCT, and P-LCR with preeclampsia and tried to evaluate whether these parameters could be used as markers in early diagnosis of preeclampsia.

In our study, the mean age of study subjects was 25.4 ± 3.0 years and 31.2 ± 4.4 years in the non-severe preeclampsia and severe preeclampsia group. These findings were comparable to previous reports published by various researchers in the literature. Prakash et al reported mean age of 28.7 ± 3.4 years; however, a study done by Onisai et al observed a higher mean age compared to the present study^{14,15}. In the present study, most mothers, i.e., 55.6% and 57.1% were in the gestational age of 36 and 34 weeks in non-severe and severe preeclampsia groups respectively.

In preeclampsia, thrombocytopenia has been observed and reported to be an early marker in various studies^{3,16,17}. Furthermore, a study reported by Siddiqui et al have stated that approximately 50% of preeclampsia cases will develop thrombocytopenia¹⁸. Similar to literature findings in our study, 27.8% of mothers in the non-severe preeclampsia group were diagnosed with thrombocytopenia. Whereas, in the severe preeclampsia group, all the 14 mothers (100%) were diagnosed as thrombocytopenia.

In predicting and recognizing the pathogenesis of preeclampsia, studies have investigated platelet indices. In assessing the severity of pregnancy-induced hypertension cases, Vijaya et al reported that platelet indices are considered an early, economical and rapid method¹⁹. In our study, the comparison of platelet indices between mothers with non-severe preeclampsia and severe preeclampsia revealed that there was a statistically significant decrease in platelet count ($p < 0.001$) and an increase in MPV ($p < 0.001$), and PDW ($p < 0.05$) was observed in mothers in severe preeclampsia group as compared to non-severe preeclampsia group. Dadhich et al reported substantial increases in PDW (pre-eclamptic subjects - 47.19% versus 29.4% of control subjects) and MPV (44.5% vs. 9.22%). The platelet count decreased to 9.22% compared to the control, i.e. 44.5%²⁰.

In contrast, Alisi et al reported just a mild rise in PDW values²¹. The rise in PDW level is likely to reflect increased platelet turnover which would support the theory that platelet survival time is reduced, leading to increased platelet

destruction²². The platelet distribution width variation would also suggest that preeclampsia, due to endothelial dysfunction, results in younger and larger platelet production of different sizes to compensate for the platelet count reduction as the disease advances²³. Kirbas et al reported utilizing PDW levels in the early diagnosis of preeclampsia and eclampsia²⁴. Kurtoglu et al findings were in accordance with our present study that platelet indices are a favourable indicator in predicting preeclampsia and eclampsia²⁵.

In the present study in the severe preeclampsia group, two out of 14 mothers (14.3%) had abnormal maternal outcomes, i.e. one mother had abruptio and the other developed eclampsia. Regarding fetal outcome findings, eight babies (22.2%) in the non-severe preeclampsia group had abnormal outcomes compared to 14 babies (100%) in the severe preeclampsia group. Furthermore, platelet count (lacs/cu. mm) and PCT (%) was significantly ($p < 0.001$) and non-significantly decreased in mothers in the abnormal maternal prognosis group as compared to mothers in the normal maternal prognosis group. Studies conducted by Wasiluk et al and Kannar et al reported that compared to term neonates, platelet counts and PCT in preterm neonates are low^{28,29}. MPV measures the platelet's average size in blood, and PDW reflects the platelet size variation. In our study, MPV (fl), and PDW (fl), were significantly ($p < 0.001$), and P-LCR (%) was non-significantly increased in the abnormal maternal prognosis group of mothers as compared to normal maternal prognosis group mothers. These findings were in accordance with findings published by various researchers in the literature^{28,29}. In preterm neonates, lower platelet counts were found probable due to the limitations in the developmental capability to enhance megakaryocyte size, and placental dysfunction may also be the reason for the change of platelet count in newborns at birth^{30,31}. Platelet count reduction and their function regarding gestational age may lead to a greater risk of bleeding tendency in preterm neonates³¹. Elevated PDW levels without much MPV changes may indicate that PDW is a more sensitive index for estimating platelet size changes^{32,33}. The increase in PDW may be due to a negative correlation between gestational age and birth weight³². PDW may help detect conditions like sepsis and platelet consumption at an early stage³⁴. In conditions like disseminated intravascular coagulation associated with platelet activation and consumption, an increase in MPV is observed. Thus, platelet indices determined by automated haematological analyzers may help diagnose hemostatic disorders and infections seen more commonly in preterm newborns.

Conclusion

The present study demonstrated that platelet count decreases while MPV and PDW increase as pregnancy progresses, and these changes are more prominent in severe preeclampsia mothers than in non-severe preeclamptic mothers. We also found an association between platelet indices viz. platelet count, MPV & PDW, and severity of preeclampsia, and hence platelet indices viz. platelet count, MPV and PDW could be used as an early diagnostic marker for preeclampsia.

Conflict of interest: None. **Disclaimer:** Nil.

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