



## PREDICTIVE VALUE OF PLATELET INDICES IN DEVELOPMENT OF PREECLAMPSIA

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**ABSTRACT**

**Introduction:** Preeclampsia (PE) is a multisystem hypertensive disorder that is a major contributor to maternal, neonatal morbidity and mortality. In modern obstetrics, identification of pregnant women with an increased PE risk is an objective of paramount importance. In preeclampsia, increased platelet indices may occur earlier than development of other recognized manifestations like hypertension and proteinuria. On the other hand, lowered platelet count and increased platelet indices in pregnant women during antenatal check may be considered as a risk factor for development of preeclampsia and eclampsia. This group of pregnant women may be considered for special attention to prevent the development of preeclampsia. So, the present study was conducted with an aim to assess the association between changes in platelet indices and development of pre-eclampsia. **Objectives:** To estimate the prevalence of preeclampsia among pregnant women and assess the changes occurring in platelet indices in pregnant women with duration of gestation. **Material And Methods:** A Prospective Observational study was carried out over a period of 6 months i.e., from March to August 2022 in pregnant women with history of normal blood pressure before 24 weeks of gestational age. Institutional ethical committee clearance was obtained for the study. Data collected was entered into MS-Excel 2013 spreadsheet. The collected data was analysed using IBM statistical package for social sciences. Chi-square test and Unpaired t-test was used to find the significant difference between two groups. ROC analysis was done to find out the cut-off values of platelet indices in diagnosing preeclampsia. **Results:** The prevalence of preeclampsia in the present study was 6.5%. The mean age of the study population was  $23.47 \pm 2.68$  Years. There was a statistical significant association between platelet indices and preeclampsia ( $p < 0.05$ ) at various weeks of gestational period with high mean value in the preeclamptic women. At 24–28 Weeks of gestational age the cut-off  $> 9.5$ fL for MPV the sensitivity of detecting preeclampsia was 92.3% and specificity was 80.7%. At cut-off  $> 15.5\%$  for PDW the sensitivity of detecting preeclampsia was 84.6% and specificity was 69.5%. At cut-off  $< 0.22\%$  for PCT the sensitivity of detecting preeclampsia was 53.8% and specificity was 59.4%. **Conclusion:** Patients with preeclampsia are more likely to have rapid and significant decrease in platelet count and plateletcrit, increase in PDW and MPV in comparison to the normotensive counterparts. These significant changes can be observed at an earlier gestational age than significant rise in BP can be observed and changes are more significant in patients who are destined to develop progressive preeclampsia. Thus estimation of platelet indices seems to be a reliable, rapid, easy and economical method for early detection of preeclampsia.

**KEYWORDS :** Preeclampsia, platelet, hypertension**INTRODUCTION**

Pregnancy is a unique period during a woman's life which is characterized by complex physiological and hormonal changes. An estimated 6 to 8% of pregnancies are complicated by hypertension. Preeclampsia (PE) is a pregnancy specific multisystem hypertensive disorder that is a major contributor to maternal, neonatal morbidity and mortality. It complicates about 2 to 7% of pregnancies and is responsible for an estimated 50,000–60,000 pregnancy related deaths per year worldwide. Preeclampsia is associated with new-onset hypertension in the second half of pregnancy and is often associated with proteinuria. Complications such as eclampsia, haemorrhagic stroke, haemolysis, elevated liver enzymes and low platelets (HELLP syndrome), renal failure and pulmonary edema may be associated with PE.

Preeclampsia is currently classified as a pregnancy-specific syndrome characterized by the presence of new-onset hypertension in a previously normotensive woman after 20 weeks gestation with proteinuria. Blood pressure (BP) criteria include a systolic BP  $> 140$  mm Hg or a diastolic BP  $> 90$  mm Hg. Proteinuria is defined as urinary excretion of  $\geq 0.3$  grams of protein in a 24-hour specimen, which correlates with a random  $\geq 1+$  urine dipstick in the absence of a urinary tract infection. Furthermore, eclampsia is classified as the presence of seizures, non-attributable to other causes, in a woman diagnosed with preeclampsia. Preeclampsia (PE) is a pregnancy-specific multisystem disorder characterized by abnormal vascular response to placentation which is associated with increased systemic vascular resistance, enhanced platelet aggregation, activation of the coagulation system, and endothelial cell dysfunction with resultant reduced organ perfusion.

In modern obstetrics, identification of pregnant women with an increased PE risk is an objective of paramount importance. Recognition of sensitive, specific, cost-effective, and easy to perform biomarkers would allow not only detection of women at risk of PE, but it would also allow a close surveillance, a precise PE diagnosis and a timely intervention. Because PE can progress rapidly, it requires prompt intervention that may include observation in a tertiary care

setting and termination of pregnancy, either by inducing labour or by Caesarean section, which is the only known cure for this condition. As it affects multiple organs, no single, specific and cost-effective marker to predict PE has yet been proposed. The goal of researchers for many decades was safe, reliable, and cost-effective screening tests for prediction of preeclampsia, aiming to improve maternal and foetal outcome, despite the fact that the only effective treatment is delivery because pathologic changes caused by preeclampsia are reversible once pregnancy has ended.

Platelet activation begins in the first month of pregnancy in women with risk for preeclampsia. Several studies suggested that when platelets are activated they become larger in size which causes increased platelet indices such as mean platelet volume (MPV), platelet distribution width (PDW) and platelet large cell ratio (PLCR). So, platelet indices can give an idea of platelet activation. In preeclampsia, increased platelet indices may occur earlier than development of other recognized manifestations like hypertension and proteinuria. On the other hand, lowered platelet count and increased platelet indices in pregnant women during antenatal check up may be considered as a risk factor for development of preeclampsia and eclampsia. This group of pregnant women may be considered for special attention to prevent the development of preeclampsia.

**AIM AND OBJECTIVES****AIM:**

To evaluate the association between changes in platelet indices (PCT, PDW, MPV) and development of preeclampsia.

**OBJECTIVES:**

1. To estimate the prevalence of preeclampsia among pregnant women.
2. To assess the changes occurring in platelet indices in pregnant women with duration of gestation.

**MATERIALS AND METHODS**

**Study Design:** Prospective Observational study

**Study Period:** The study was carried out over a period of 6 months from March 2022 to August 2022.

**Study Place:** The present study was conducted at Department of Obstetrics and Gynaecology, Sri Venkateshwara medical college, Tirupati.

**Study Population:** Pregnant women with history of normal blood pressure before 24 weeks of gestational age.

**Inclusion Criteria:**

1. Pregnant women at 24 weeks of gestation
2. Healthy normotensive pregnant women at  $\geq 24$  weeks gestation with a live singleton fetus.

**Exclusion Criteria:**

1. Coagulation disorder like idiopathic thrombocytopenia
2. Epilepsy
3. Drug intake affecting platelet count
4. Diabetes mellitus
5. Renal disease
6. Sickle cell disease
7. Viral hepatitis
8. Chronic hypertension
9. Dengue

**Sample Size:** 200

**METHOD OF COLLECTION OF DATA:**

A written and informed consent was taken from patients who had participated in the present study. Blood pressure was taken by auscultatory methods in sitting position after making the patient comfortable. Pregnant women above 24 weeks gestational period were considered preeclamptic if Systolic  $\geq 140$  mm Hg or diastolic  $\geq 90$  mm Hg, 2 occasions, 6 hr apart in previously normotensive woman and proteinuria  $\geq 300$  mg /24 hrs or greater or equal to 1+ by dipstick response measured on two occasions 6 hrs apart. Preeclamptic women were classified into mild and severe if, Mild preeclampsia - SBP 140-160 mm of Hg or DBP 90-110 mm of Hg, with proteinuria  $\geq 1+$  by urine dipstick Severe preeclampsia – Systolic BP  $>160$  mm of Hg or Diastolic BP  $>110$  mm of Hg, with proteinuria  $\geq 2+$  by urine dipstick Clinical examination of the patient- Detailed obstetric, menstrual and medical histories of each patient was taken. General physical examination, systemic examination, per-abdominal examination to be done.

**METHOD OF COLLECTION OF SPECIMEN**

**PROCEDURE:** Blood sample was be collected by venepuncture in tubes containing EDTA anticoagulant and processed within 2 hrs. The platelet indices were analyzed in whole blood using a blood cell counter. Modern haematology analysers in routine diagnostic use would measure platelet indices.

At each visit blood pressure was recorded, it is done monthly from 24-40 wks Random urine samples were collected and spot urine dipstick test for proteinuria was done in the patients who were diagnosed with hypertension and categorised into mild and severe pre eclampsia.

Patients who have developed hypertension were called more frequently i.e twice a week and are investigated and treated at the earliest Data regarding changes in platelet indices with increase in gestational age was collected and analysed.

**Data Analysis:**

Data collected was entered into MS-Excel 2013 spreadsheet. The collected data was analysed using IBM statistical package for social sciences (IBM SPSS) version 23 software (trial version)

**Statistical Tests:**

1. Continuous variables was reported as mean  $\pm$  standard deviation (SD) while categorical variables was expressed as absolute values and percentages.
2. Microsoft Excel 2013 was used for generating charts and diagrams.
3. Chi-square test and unpaired t-test was applied to find the significant difference between preeclampsia and normotensive pregnancy.
4. Receiver operator curve (ROC) was used to find the cut-off value for platelet indices in diagnosing preeclampsia.
5. Statistical significance was taken at 95% confidence interval i.e.,  $p < 0.05$ .

**RESULTS**

The mean age of the study population was  $23.47 \pm 2.68$  Years with an

age range of 19 – 31 yrs. Majority (44%) of the pregnant women were in age group 22 – 25 Years. Only 2 (1%) of the study group was  $\geq 30$  Years. Out of 200 pregnant women studied, 58% belongs to multigravida and 42% belongs to primigravida.

Based on the Modified BG Prasad socioeconomic status 2019 classification, 37.5% of study population belongs to middle class, 32% belongs to lower middle class and 30.5% belongs to upper middle class.

**Table 1: Distribution Of Pregnant Women According Level Of Preeclampsia**

		NUMBER	PERCENTAGE
NORMAL		187	93.5%
PRE ECLAMPSIA	MILD	11	5.5%
	SEVERE	2	1%
Total		200	100.0

Based on the blood pressure measured and urine dipstick test for hypertensive during gestation, 6.5% had preeclampsia. 11 (5.5%) had mild preeclampsia and 2 (1%) had severe eclampsia. The mean age in the preeclampsia women  $24.4 \pm 3.5$  yrs was high than the normal pregnant women  $23.4 \pm 2.6$  yrs, however there was no statistical significant association between age and preeclampsia. ( $p > 0.05$ ).

In primigravida women 10.7% had preeclampsia, while in multigravida women 3.5% had preeclampsia. There was a statistical significant association found between gravida and preeclampsia ( $p < 0.05$ ).

The prevalence of preeclampsia was high in lower middle class pregnant women 9.4%. In the upper middle class 6.6% had preeclampsia and in middle class 4% had preeclampsia. There was no statistical significant association between socioeconomic status and preeclampsia ( $p > 0.05$ ).

**Table 2: Platelet Count At Various Weeks Of Gestational Period**

Gestational period	Mean Platelet count ( $10^3$ /cu. mm)		
	Pre-eclampsia	Normotensive pregnancy	P - value
24 – 28 Weeks	$210.2 \pm 19.1$	$278.7 \pm 31.4$	0.000
28 – 32 Weeks	$200.8 \pm 18.6$	$270.6 \pm 31.7$	0.000
32 – 36 Weeks	$191.2 \pm 28.1$	$267.9 \pm 31.9$	0.000
36 – 40 Weeks	$185.8 \pm 27.9$	$264.6 \pm 31.8$	0.000

The mean platelet count ( $10^3$ /cu. mm) in preeclampsia women at 24 – 28 Weeks gestational age was  $210.2 \pm 19.1$  and it was decreased to  $185.8 \pm 27.9$  at 36 – 40 Weeks. There was a statistical significant association between platelet count and preeclampsia ( $p < 0.05$ ) at various weeks of gestational period with high mean value in the normotensive pregnancy.

**Table 3: MPV At Various Weeks Of Gestational Period**

Gestational period	Mean platelet volume (MPV) fL		
	Pre-eclampsia	Normotensive pregnancy	P - value
24 – 28 Weeks	$10.81 \pm 1.05$	$8.36 \pm 1.02$	0.000
28 – 32 Weeks	$11.47 \pm 1.03$	$8.88 \pm 1.03$	0.000
32 – 36 Weeks	$11.91 \pm 1.34$	$8.96 \pm 1.02$	0.000
36 – 40 Weeks	$12.31 \pm 1.37$	$9.27 \pm 1.03$	0.000

The mean platelet volume (fL) in preeclampsia women at 24 – 28 Weeks gestational age was  $10.81 \pm 1.05$  and it was increased to  $12.31 \pm 1.37$  at 36 – 40 Weeks. There was a statistical significant association between platelet volume and preeclampsia ( $p < 0.05$ ) at various weeks of gestational period with high mean value in the preeclamptic women.

**Table 4: Plateletcrit (PCT %) At Various Weeks Of Gestational Period**

Gestational period	Plateletcrit (PCT) %		
	Pre-eclampsia	Normotensive pregnancy	P - value
24 – 28 Weeks	$0.21 \pm 0.02$	$0.22 \pm 0.01$	0.001
28 – 32 Weeks	$0.20 \pm 0.01$	$0.22 \pm 0.01$	0.000
32 – 36 Weeks	$0.19 \pm 0.01$	$0.21 \pm 0.01$	0.000
36 – 40 Weeks	$0.19 \pm 0.02$	$0.21 \pm 0.01$	0.000

The mean plateletcrit (%) in preeclamptic women at 24 – 28 Weeks gestational age was  $0.21 \pm 0.02$  and it was decreased to  $0.19 \pm 0.02$  at 36 – 40 Weeks. There was a statistical significant association between plateletcrit and preeclampsia ( $p < 0.05$ ) at various weeks of gestational period with low mean value in the preeclamptic women.

**Table 5: Change In Platelet Indices Over Pregnancy**

PLATELET INDICES	PREECLAMPSIA	NORMOTENSIVE PREGNANCY	
PC	12%	5%	↓
MPV	14%	11%	↑
PDW	12%	3%	↑
PCT	9.5%	9%	↓

During the follow-up, PC and PCT decreased during pregnancy in both the groups but the mean decrease was high in preeclampsia group when compared to normotensive pregnancy. MPV and PDW increased with increase in gestational age during pregnancy and it was high in preeclampsia group when compared to normotensive pregnancy.

## DISCUSSION

Preeclampsia (PE) is one of the significant causes of maternal and fetal mortality and morbidity in developing countries. Widely available and cost-effective CBC parameters such as platelet count and platelet indices (MPV, PDW and Plateletcrit) are suggested to be useful to predict the prognosis of preeclampsia. Based on the blood pressure measured during gestation, 6.5% had preeclampsia in which 11 (5.5%) had mild preeclampsia and 2 (1%) had severe eclampsia. Similar rate of prevalence 5.4% was reported by Sajith M et al.<sup>3</sup>

The mean age of the study population was  $23.47 \pm 2.68$  years with an age range of 19 – 31 yrs. The mean age in the preeclampsia women  $24.4 \pm 3.5$  yrs was high than the normal pregnant women  $23.4 \pm 2.6$  yrs, however there was no statistical significant association between age and preeclampsia. ( $p > 0.05$ ). Dadhinch et al<sup>1</sup> and Dhakre et al<sup>6</sup> had reported similar mean age in their study which was  $23.45 \pm 3.23$  yrs and  $24.45 \pm 4.23$  years respectively. But the mean age in the Elgarhey et al.,<sup>4</sup> study was  $28.92 \pm 5.67$  yrs which was high when compared to the present study.

Out of 200 pregnant women studied, 58% belongs to multigravida and 42% belongs to primigravida. In primigravida women 10.7% had preeclampsia, while in multigravida women 3.5% had preeclampsia and a statistical significant association found between gravida and preeclampsia ( $p < 0.05$ ). Nooh AM et al.,<sup>86</sup> had also reported a significant association between gravida and preeclampsia and with high prevalence among primigravida.

Based on the Modified BG Prasad socioeconomic status 2019 classification, 37.5% of study population belongs to middle class, 32% belongs to lower middle class and 30.5% belongs to upper middle class. The prevalence of preeclampsia was high in lower middle class pregnant women 9.4%. In the upper middle class 6.6% had preeclampsia and in middle class 4% had preeclampsia. There was no statistical significant association between socioeconomic status and preeclampsia ( $p > 0.05$ ). Nooh AM et al.,<sup>2</sup> had also reported no significant association between socioeconomic status and preeclampsia which was similar to the present study.

In the present study, PC showed a significant decrease in Preeclampsia group compared to normotensive pregnant women. This appears to be in consistent with the pathophysiology of PE, which states that an endothelial activation induced increase in platelet aggregation and consumption resulting in decrease PC.

The mean platelet count ( $10^3/\text{cu. mm}$ ) in preeclampsia women at 24 – 28 weeks gestational age was  $210.2 \pm 19.1$  and it was decreased to  $185.8 \pm 27.9$  at 36 – 40 weeks and a statistical significant association between platelet count and preeclampsia ( $p < 0.05$ ) at various weeks of gestational period with high mean value in the normotensive pregnancy.

Similar findings were found in Dadhinch et al<sup>1</sup> when counts at monthly intervals from 20 weeks to 40 weeks were compared, the mean reduction in platelet count was 7.4% in normotensive pregnancy and 19.4% in preeclampsia.

In the present study the mean platelet volume (fL) in preeclampsia women at 24 – 28 Weeks gestational age was  $10.81 \pm 1.05$  and it was increased to  $12.31 \pm 1.37$  at 32 – 36 Weeks. This may be due to the fact that increased consumption and destruction of platelets, bone marrow produces and release large platelets leading to increase MPV in PE. There was a statistical significant association between platelet volume and preeclampsia ( $p < 0.05$ ) at various weeks of gestational period with high mean value in the preeclamptic women. Similar findings were found in Dadhinch et al<sup>1</sup> when counts at monthly intervals from 20 weeks to 40 weeks were compared, the mean reduction in mean platelet volume was 9.2% in normotensive pregnancy and 44.5% in preeclampsia.

The mean platelet distribution width (%) in preeclamptic women at 24 – 28 Weeks gestational age was  $16.47 \pm 0.79$  and it was increased to  $18.39 \pm 0.72$  at 36 – 40 Weeks. There was a statistical significant association between platelet distribution width and preeclampsia ( $p < 0.05$ ) at various weeks of gestational period with high mean value in the preeclamptic women.

The increased PDW could be explained by an increase in platelet turnover following decrease in platelets survival time as a result of increase in platelets destruction. Increase in bone marrow activity of unknown stimulus could also contribute to the observed high PDW.<sup>105</sup> Hence, an increase in PDW during PE could be considered as one of the important indicators to predict disease severity. Similar findings were found in Dadhinch et al<sup>1</sup> when counts at monthly intervals from 20 weeks to 40 weeks were compared, the mean reduction in platelet distribution width was 29.45% in normotensive pregnancy and 47.19% in preeclampsia.

The mean plateletcrit (%) in preeclamptic women at 24 – 28 Weeks gestational age was  $0.21 \pm 0.02$  and it was decreased to  $0.19 \pm 0.02$  at 36 – 40 Weeks. There was a statistical significant association between plateletcrit and preeclampsia ( $p < 0.05$ ) at various weeks of gestational period with low mean value in the preeclamptic women.

During the follow-up, PC and PCT decreased during pregnancy in both the groups but the mean decrease was high in preeclampsia group when compared to normotensive pregnancy. MPV and PDW increased with increase in gestational age during pregnancy and it was high in preeclampsia group when compared to normotensive pregnancy. Kurtoglu E et al.<sup>5</sup> had also found that PC, MPV and PCT were significantly different in the pregnant women over 32 weeks gestation.

## CONCLUSION

From the above findings patients with preeclampsia are more likely to have rapid and significant decrease in platelet count and plateletcrit, increase in PDW and MPV in comparison to the normotensive counterparts. These significant changes can be observed at an earlier gestational age than significant rise in BP can be observed and changes are more significant in patients who are destined to develop progressive preeclampsia. Thus estimation of platelet indices seems to be a reliable, rapid, easy and economical method for early detection of preeclampsia.

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