

# Red Cell Distribution Width and Platelet Indices in Women with Pre-eclampsia: A Cross-sectional Study

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## ABSTRACT

**Introduction:** To determine the prognosis and fetomaternal outcome in eclampsia and pre-eclampsia, a simple and cost-effective approach is to assess the Red cell Distribution Width (RDW) and platelet count. RDW, Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), and platelet markers such as Mean Platelet Volume (MPV) have been the subject of research.

**Aim:** To compare the variation of RDW, NLR, PLR, and platelet indices between women with pre-eclampsia and gestational age-matched healthy controls.

**Materials and Methods:** A cross-sectional study was conducted among 208 pregnant women (104 with pre-eclampsia and 104 controls) at the Department of Obstetrics and Gynaecology, Bangalore Medical College and Research Institute, Bengaluru, Karnataka, India, from January 2020 to June 2021. RDW, NLR, PLR, and platelet indices were analysed after obtaining detailed history, conducting clinical examinations, and relevant investigations. An

Independent t-test was used as a test of significance to identify the mean difference between the two quantitative variables.

**Results:** The RDW among cases was  $17.05 \pm 4.01$ , whereas among controls, it was  $15.09 \pm 1.86$ . The mean age of subjects among case group was  $25.72 \pm 4.741$  years, while in the control group it was  $23.25 \pm 3.803$  years. There was a significant difference in mean Red cell Distribution Width- Coefficient of Variation (RDW-CV) between the two groups. The MPV among cases was  $9.86 \pm 1.14$ , while among controls, it was  $8.92 \pm 1.40$  ( $p$ -value=0.001). The PDW among cases was  $11.30 \pm 2.20$ , and among controls, it was  $12.72 \pm 3.50$ . The mean NLR among cases was  $5.92 \pm 4.94$ , whereas among controls, it was  $4.59 \pm 2.22$ . There was a significant difference in mean platelet count, MPV, PDW, and NLR between the two groups.

**Conclusion:** According to the findings of the current study, RDW, NLR, and MPV were all shown to be higher in women with pre-eclampsia. Additionally, pre-eclamptic women consistently exhibited decreased PDW and platelet counts.

**Keywords:** Mean platelet volume, Neutrophil-to-lymphocyte ratio, Platelet-to-lymphocyte ratio

## INTRODUCTION

Hypertensive Disorders of Pregnancy (HDP) are one of the leading causes of maternal and neonatal morbidity and mortality worldwide. The reported incidence of Pregnancy Induced Hypertension (PIH) in India ranges from 5% to 15% [1]. These disorders form a deadly triad in conjunction with haemorrhage and infection, significantly contributing to maternal morbidity and mortality [2]. To be defined as HDP, one of the following criteria has to be fulfilled American College of Obstetricians and Gynaecologists (ACOG) classification [3]:

- Gestational hypertension: Two or more Blood Pressure (BP) readings of 140/90 mmHg or higher measured at least six hours apart after the 20<sup>th</sup> week of pregnancy in a woman who was previously normotensive without proteinuria.
- Pre-eclampsia (PE): Hypertension during pregnancy with proteinuria (2+ by dipstick, or >300 mg in 24-hour urine).
- Severe PE: Serum creatinine  $\geq 1.1$  mg/dL, platelet count  $< 1$  lac/L, liver enzymes  $> 80$  IU/L, BP  $\geq 160/110$  mmHg, blurred vision, headache, shortness of breath, epigastric pain.

Haematological parameters that may get deranged in some women with HDP include numerical and functional platelet anomalies such as platelet dysfunction and thrombocytopenia, as well as alterations in Haemoglobin (Hb) and erythrocytic parameters such as increased Haematocrit (HCT) and Microangiopathic Haemolytic Anaemia (MAHA). A limited number of studies have examined platelet indicators such as MPV, PLR, NLR, and RDW in pre-eclampsia [4-9]. Some investigations, particularly in patients with severe cases of pre-eclampsia [4], have revealed a statistically significant rise in NLR and MPV in this condition. Contrarily, a study by Toptas M et al., found no statistically significant differences in MPV or PLR

between patients with severe pre-eclampsia and healthy pregnant or non pregnant controls [8].

Alterations in RDW and a decrease in platelet count are proportional to the severity of the disease. Assessing RDW and platelet count is a simple, cost-effective, and sensitive method to determine the prognosis and fetomaternal outcome in eclampsia and pre-eclampsia. Hence, the present study was conducted to compare variations in RDW, NLR, PLR, and platelet Indices between women with pre-eclampsia and gestational age-matched healthy controls.

## MATERIALS AND METHODS

This cross-sectional study was conducted from January 2020 to June 2021 in the Department of Obstetrics and Gynaecology at Bangalore Medical College and Research Institute, Begaluru, Karnataka, India. Ethical clearance was obtained from the Institutional Ethical Committee (BMCRI/PG/352/2019-20), and patients fulfilling the inclusion criteria were enrolled after obtaining informed consent. Based on a previous study by Gogoi P et al., the mean RDW in pre-eclampsia patients was reported as  $17.14 \pm 2.7$ , while in the control group, it was  $16.19 \pm 2.0$  [4]. The intended sample size was 192, but authors included 208 patients.

**Inclusion criteria:** Preeclamptic pregnant women aged 18 to 40 years, between 28 and 42 weeks of pregnancy were included in the study.

**Exclusion criteria:** Patients who were unwilling to provide informed consent, those with a history of ruptured membranes, anaemia, infections, fever, complete Haemolysis, Elevated liver enzymes, and Low Platelets (HELLP) syndrome, multiple pregnancies, eclampsia, and women with additional co-existing morbidities like diabetes, hypothyroidism, chronic hypertension, collagen vascular disease, renal disease, and ischaemia heart disease were excluded from the study.

## Study Procedure

The diagnosis of pre-eclampsia was based on ACOG guidelines (2017) [3], which required a blood pressure of  $\geq 140/90$  mmHg on two occasions measured four hours apart after 20 weeks of pregnancy, along with any of the following features: thrombocytopenia, renal insufficiency, impaired Liver Function Test (LFT), pulmonary oedema, cerebral or visual disturbances. The control group included healthy pregnant women at similar gestational ages.

A total of 104 pregnant women diagnosed with pre-eclampsia according to ACOG guidelines were included as cases, while another group of 104 normotensive pregnant women were included as controls. Data was collected using a prestructured questionnaire that included patient personal data, medical history (noting the severity of pre-eclampsia symptoms such as blurred vision, upper abdominal pain, vomiting), obstetric examination, blood pressure measurement, urine albumin estimation using a dipstick test, and a 24-hour urine sample. Venous blood samples were collected from all subjects using 2 mL Ethylenediamine Tetra-Acetic Acid (EDTA) tubes. Complete Blood Count (CBC) was analysed using a Sysmex XN analyser. RDW, NLR, PLR, and platelet indices were analysed and compared.

## STATISTICAL ANALYSIS

The data were analysed using Statistical Packages for Social Sciences (SPSS) version 22 software. Categorical data were presented as frequencies and proportions, while continuous data were presented as means and standard deviations. An independent t-test was used as a test of significance to identify the mean difference between two quantitative variables. A p-value  $< 0.05$  was considered statistically significant.

## RESULTS

The study group enrolled 208 women, with 104 women in the pre-eclampsia group and 104 gestational-age-matched healthy pregnant women in the control group. The mean age of women with pre-eclampsia was  $25.7 \pm 4.7$  years, while in the control group, it was  $23.25 \pm 3.8$  years ( $p = 0.002$ ). The mean haemoglobin levels in the study and control groups were  $12.1 \pm 1.27$  g/dL and  $11.49 \pm 1.37$  g/dL, respectively ( $p = 0.005$ ) [Table/Fig-1]. Among the participants, 55 women had non severe pre-eclampsia, whereas 49 had severe pre-eclampsia. The mean NLR was higher in women with pre-eclampsia compared to women in the control group ( $5.92 \pm 4.94$  versus  $4.59 \pm 2.22$ ;  $p = 0.016$ ).

Parameters	Study group (n=104)	Control group (n=104)	p-value (n=208)
Age (years)	$25.72 \pm 4.741$	$23.25 \pm 3.803$	0.002
Parity (median)	2 (1-4)	3 (1-5)	0.943
Mean pregnancy duration (weeks)	$37.1 \pm 2.1$	$38.4 \pm 2.2$	0.005
Haemoglobin (g/dL)	$12.01 \pm 1.27$	$11.49 \pm 1.37$	0.005
Systolic blood pressure (mmHg)	$151.83 \pm 12.16$	$115.67 \pm 7.01$	$< 0.001$
Diastolic blood pressure (mmHg)	$100.06 \pm 8.75$	$75.38 \pm 5.69$	$< 0.001$

**[Table/Fig-1]:** Baseline variables.

\*Values were given as mean $\pm$ SD or median (range), unless indicated otherwise.  
\*p-value obtained by independent t-test.

The RDW in women with pre-eclampsia was  $17.05 \pm 4.01$ , while in the control group, it was  $15.09 \pm 1.86$  ( $p = 0.001$ ) [Table/Fig-2]. The NLR in non severe pre-eclampsia was  $5.65 \pm 4.99$ , which was lower than the NLR in severe pre-eclampsia ( $6.22 \pm 4.93$ ); however, the differences were not statistically significant [Table/Fig-3].

Variables	Study group	Control group	*p-value
Neutrophils (%)	$76.69 \pm 7.93$	$75.30 \pm 7.74$	0.201
Lymphocytes (%)	$16.99 \pm 6.54$	$17.73 \pm 6.60$	0.417

Neutrophil-to-Lymphocyte Ratio (NLR)	$5.92 \pm 4.94$	$4.59 \pm 2.22$	0.016
Platelet-to-Lymphocyte Ratio (PLR)	$139.70 \pm 57.28$	$132.74 \pm 43.32$	0.337
Platelets $\times 10^9/L$	$267 \pm 75.9$	$288 \pm 76.3$	0.044
Mean Platelet Volume (MPV) (fL)	$9.86 \pm 1.14$	$8.92 \pm 1.40$	$< 0.001$
Red cell Distribution Width (RDW) (%)	$17.05 \pm 4.01$	$15.09 \pm 1.86$	0.001
Platelet Distribution Width (PDW) (fL)	$11.30 \pm 2.20$	$12.72 \pm 3.5$	0.001
Plateletcrit (%)	$0.26 \pm 0.069$	$0.26 \pm 0.065$	0.337

**[Table/Fig-2]:** Comparison of outcome of parameters between women with pre-eclampsia and those with normotensive pregnancy.

\*p-value obtained by independent t-test; \*Values were given as mean $\pm$ SD unless indicated otherwise

Variables	Non severe pre-eclampsia (n=55)	Severe pre-eclampsia (n=49)	*p-value
Neutrophils (%)	$75.69 \pm 7.72$	$77.82 \pm 8.09$	0.174
Lymphocytes (%)	$17.45 \pm 6.45$	$16.47 \pm 6.66$	0.446
Neutrophil-to-Lymphocyte Ratio (NLR)	$5.65 \pm 4.99$	$6.22 \pm 4.93$	0.560
Platelet-to-Lymphocyte Ratio (PLR)	$151.75 \pm 60.74$	$126.18 \pm 50.36$	0.022
Platelets ( $10^9/L$ )	$276 \pm 76.3$	$257 \pm 74.86$	0.188
Mean Platelet Volume (MPV) (fL)	$9.93 \pm 1.18$	$9.78 \pm 1.09$	0.499
Red cell Distribution Width (RDW) (%)	$15.71 \pm 2.17$	$18.09 \pm 4.79$	0.065
Platelet Distribution Width (PDW) (fL)	$11.44 \pm 2.22$	$11.14 \pm 2.20$	0.500
Plateletcrit (%)	$0.27 \pm 0.075$	$0.25 \pm 0.062$	0.157

**[Table/Fig-3]:** Outcome of parameters stratified by severity of pre-eclampsia.

\*p-value obtained by independent t-test; \*Values were given as mean $\pm$ SD unless indicated otherwise

## DISCUSSION

As presented in the present study, similar age, distributions were observed in studies by Bawore SG et al., and Kashyap D et al., where they reported 25 (20-36) years and mean age  $26.22 \pm 3.64$  years as the age of normotensive women, and 28 (18-37) years and mean age  $25.35 \pm 3.59$  years in pre-eclamptic women, respectively [10, 11]. In the present study, the mean gestational age at admission was 37.1 weeks among cases and 38.4 weeks among controls. In the study by Kashyap D et al., the mean gestational age was  $35.7 \pm 3.24$  weeks among cases and  $36.82 \pm 2.27$  weeks among controls [11]. Regarding parity, there was no significant difference between the two groups in the present study. In the study by Sachan R et al., most of the women were primigravida, with 39.2% in the control group, 61.8% in non severe pre-eclampsia, and 68.8% in severe pre-eclampsia [12]. In terms of RDW, the mean RDW among cases in the present study was  $15.64 \pm 2.08$ , compared to  $14.91 \pm 1.64$  among controls [11]. These findings were similar to the present study. Sachan R et al., reported a mean RDW of  $15.05 \pm 0.46$  among NSPE,  $15.05 \pm 0.46$  among SPE, and  $12.96 \pm 0.51\%$  among controls, showing a significant increase in RDW among pre-eclampsia cases compared to controls [12]. This finding aligns with the present study. It is speculated that inflammation may contribute to the elevated RDW levels in pre-eclampsia, as interleukin-6 levels rise due to inflammation, hindering erythrocyte maturation [4]. Regarding platelet count, the mean platelet count among cases in the present study was  $267 \pm 75.9$  ( $10^9/L$ ), while among controls it was  $288 \pm 76.3$  ( $10^9/L$ ). There was a significant difference in mean platelet count between the two groups. Agrawal N et al., observed that the mean platelet count among cases was  $280.4 \pm 80.4$  ( $10^3/mm^3$ ) and among controls was  $253.8 \pm 65.6$  ( $10^3/mm^3$ ) [13].

In terms of MPV, the present study reported a mean MPV of  $9.86 \pm 1.14$  among cases and  $8.92 \pm 1.40$  among controls, showing a significant difference between the two groups. Kashyap D et al., observed that the mean MPV among cases was  $12.19 \pm 1.38$  and among controls it was  $12 \pm 1.68$  [11]. In a person with a low platelet count, a high percentage of big platelets (high MPV) indicate that the bone marrow is actively manufacturing platelets and swiftly releasing them into the bloodstream. In contrast, the MPV may

be low in persons with low platelet counts as a result of a bone marrow-related illness. The present study shows MPV is increased MPV in pre-eclampsia observed in the present study aligns with Giles et al., [14]. However, a contrasting study suggested that platelet count and MPV cannot predict the risk of pre-eclampsia [4]. Regarding PDW, the mean PDW among cases in the present study was  $11.30 \pm 2.20$ , while among controls it was  $12.72 \pm 3.50$ , showing a significant difference between the two groups. Kashyap D et al., also reported a similar finding in their study, with a mean PDW of  $18.31 \pm 4.57$  among cases and  $18.66 \pm 4.38$  among controls [11].

### Limitation(s)

It was a single centre study. Multicentre studies are needed to confirm these findings. The cross-sectional study design does not allow for the determination of predictors of pre-eclampsia and the prognostic value of RDW and platelet indices in patients with pre-eclampsia.

### CONCLUSION(S)

The parameters RDW, NLR, and MPV were all found to be higher in pre-eclamptic women, according to the findings of the current study. Measuring RDW, NLR, MPV, platelet count, and PDW during prenatal follow-up may be helpful in predicting pre-eclampsia in high-risk women. Among the platelet indices, PLR was the only one that could distinguish between mild and severe pre-eclampsia.

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