



## Can Red Cell Distribution Width (RDW) and Platelet Indices Predict the Severity of Pre-eclampsia?

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### Authors' contributions

This work was carried out in collaboration among all authors. All authors designed the study. Author DK collected the data and analysed it. All authors revised the manuscript and approved the final version of the manuscript.

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### ABSTRACT

**Objective:** The aim was to study the relationship between platelet indices and red cell distribution width (RDW) with pre-eclampsia and its severity.

**Methods:** A matched case-control hospital-based observational study was performed with 80 pre-eclamptic women and a control group of 80 normotensive women in the gestational age of 28+0 weeks - 40+6 weeks. Blood samples for routine blood count and RDW levels were analyzed.

**Results:** The RDW levels were significantly higher in pre-eclampsia group compared to the control group. We also confirmed that the RDW levels were significantly higher in women with severe pre-eclampsia as compared to women with non severe pre-eclampsia on subgroup analysis.

**Conclusion:** There is a statistically significant association between the RDW and risk of pre-eclampsia and also its severity. It is a marker which is easy to use, inexpensive and can be calculated as a part of routine blood count. It has significant prognostic value in patients with pre-eclampsia.

**Keywords:** Pregnancy; pre-eclampsia; platelet indices; red cell distribution width.

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## 1. INTRODUCTION

Pre-eclampsia is among the commonest medical disorders during pregnancy. It complicates about 5 to 10% of the pregnancies and continues to be a major cause of maternal and perinatal morbidity and mortality [1]. Pre-eclampsia is defined as “new onset hypertension and proteinuria that occurs during pregnancy, diagnosed for the first time after 20 weeks of gestation and resolves after delivery” [2]. It is a multi-system disease of unknown etiology and there is a constant search for better prognostic markers to predict the progression and severity of the disease in order to predict and if possible prevent complications like placental abruption, hemolysis, elevated liver enzymes low platelet (HELLP) syndrome, eclampsia, etc [3].

Although the exact pathophysiology of pre-eclampsia is still not completely understood, certain factors can be related to it, which include: profound changes in the coagulation and fibrinolytic system, endothelial dysfunction and deficient trophoblastic invasion of maternal vessels that can lead to a subsequent reduction of placental blood flow [4,5,6]. Changes in the coagulation system occur such that it is activated by the contact of platelets with the injured epithelium, leading to platelet consumption and subsequently, it's increased production in the bone marrow [7]. We studied various platelet indices like platelet count, platelet distribution width (PDW), mean platelet volume (MPV) and plateletcrit to measure platelet functions. Tanindi et al, in their study had shown that RDW, a marker of anisocytosis, is increased in hypertension and cardiovascular disease [4]. It is a readily available hematological index which can be used as a marker of inflammation [4,8]. However, there is limited data available on the combined usefulness of platelet indices and RDW in pregnant women in hypertensive disorders of pregnancy. In a internet search using Pubmed and Google scholar, we could only find one study on the mentioned subject [9]. Therefore, the current study was undertaken to understand the relationship of these parameters with pre-eclampsia and its association with its severity.

## 2. MATERIALS AND METHODS

This matched case control study was conducted in the Department of Obstetrics and Gynaecology in collaboration with the Department of Biochemistry, Lady Hardinge

Medical College, and Smt. Sucheta Kriplani Hospital, New Delhi. An approval from the ethical committee was taken. A total of 160 patients were enrolled in this study within period of 1 year, comprising a case group of 80 pre-eclamptic women and a control group of 80 normotensive women. The control group was matched for age, gestational age and parity. Pre-eclampsia was diagnosed as per the criteria recommended by the American College of Obstetrics and Gynaecology (ACOG) [10]. The cases were further classified as being mild or severe as per ACOG recommendations [10]. A case was defined as being mild if a systolic blood pressure of  $\geq 140$  mmHg or a diastolic blood pressure of  $\geq 90$  mmHg with proteinuria was recorded after 20 weeks of gestation in a previously normotensive woman. Severe pre-eclampsia was defined if the pregnant woman had any one of the following [10].

- ❖ A systolic blood pressure of 160 mmHg or more, or a diastolic blood pressure of 110 mmHg or more on two occasions, atleast 4 hours apart.
- ❖ Renal insufficiency (serum creatinine concentration  $>1.1$  mg/dl or a doubling of the serum creatinine concentration in the absence of any other renal disease).
- ❖ Pulmonary edema.
- ❖ Impairment of liver function tests as indicated by abnormally elevated blood concentration of liver enzymes ( to twice the upper limit of normal concentration) and severe persistent right upper quadrant or epigastric pain unresponsive to medication.
- ❖ Visual disturbances.
- ❖ New-onset headache unresponsive to medication.
- ❖ Thrombocytopenia (platelet count  $< 100,000 \times 10^9$ ).

Exclusion criteria was strictly adhered to and pregnant women with a history of any medical disorder, symptomatic infectious disease, anemia, or smoking were excluded from the study.

After obtaining an informed written consent from all the test subjects, 3 mL of venous blood was obtained from each patient at the time of admission, but before the onset of labor. The blood samples were collected in vacutainers containing Ethylene-diamine-tetra-acetic Acid (EDTA). Complete blood count was done within 2- 6 hours of sample collection by an automated hematology analyzer (SYSMEX XP-100, SYSMEX XP Series hematology analyzer, Kobe,

Japan). The age, gestational age, body mass index, blood pressure measurement, and pregnancy outcome were recorded for each test subject.

Categorical variables were presented in number and percentage and continuous variables were presented as mean  $\pm$  SD and median. The normality of data was tested by the Kolmogorov-Smirnov test. If the normality was rejected then a non-parametric test was used. Statistical tests were applied as follows-1. Quantitative variables were compared using the Independent t-test/Mann-Whitney Test (when the data sets were not normally distributed) between the two groups.2. Qualitative variables were correlated using the Chi-Square test/Fisher's exact test. A p-value of  $<0.05$  was considered statistically significant. The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

### 3. RESULTS

A total of 160 women were included in the study. The demographic profile and clinical characteristics of the participants are shown in Table 1 and Table 2. The age and parity of the pregnant women in the two groups was compared and there was no statistically significant difference between them, thus minimizing any potential confounding effect of these two variables.

A comparison of the blood count parameters has been depicted in tabular form (Table 3). In our study the platelet count, platelet distribution width and plateletcrit were found to be lower in the cases as compared to control group, while the mean platelet volume was found to be higher though the difference was not statistically significant. On the other hand, when RDW was compared between the two groups, the difference was statistically significant with the women in case group having higher values of RDW( $p<0.01$ ). We also did an intra-group analysis by segregating the case group into pregnant women with mild pre-eclampsia and pregnant women with severe pre-eclampsia and observed that the difference in RDW between the 2 groups was statistically significant, but the difference of other platelet indices was statistically not significant (Table 4). On doing ROC analysis we found the value of RDW to distinguish between normotensive and pre-

eclamptic women to be 13.0 with 95% specificity and 95% sensitivity.

### 4. DISCUSSION

In the present study, we found statistically significant different values of RDW between the cases and the control group and this difference was highly significant in patients with severe pre-eclampsia when compared to normal healthy pregnant women. We also found a positive association between RDW and blood pressure in our study.

RDW, for a long time has been used to differentiate between various types of anemia but after many researches it is found to have a role in inflammation and oxidative stress, and can be used as a predictor of morbidity and mortality in many diseases, especially in cardiovascular diseases [3,10,11]. Although, there have been studies on the role of RDW in hypertensive disorders in non-pregnant females, but literature on the role of RDW in hypertensive disorders of pregnancy is still lacking. Kurt et al. and Yilmaz et al., in their study suggested that RDW was significantly higher in pregnant woman with pre-eclampsia and was also associated with the severity of the disease, similar to results obtained in our study [12,13]. Thus, it can be argued that as the severity of pre-eclampsia increases, the systemic inflammation sets in, leading to changes in the value of red cell distribution width.

In our study, when platelet indices were compared, we found that platelet count and plateletcrit were decreased in the case group whereas mean platelet volume and platelet distribution width were increased. The decrease in platelet count and plateletcrit signifies the ongoing peripheral consumption of platelets, which in turn leads to their active turnover causing immature platelets to enter into the circulation. This further leads to increase in the mean platelet volume(MPV) and platelet distribution width (PDW), but these changes were not found to be significant. This may be due to the fact that majority of our cases were mild pre-eclamptic. When we looked into the literature, a study done by Freitas et al. showed a decrease in platelet count and plateletcrit and an increase in PDW and MPV in women with severe PE when compared to normotensive women [14]. The difference between the two groups was statistically significant in their study in contrast to our study, which showed.

**Table 1. Demographic and clinical characteristics of the study groups**

Parameters	Cases	Controls
Age (years)	25.35 ± 3.59	26.22 ± 3.64
BMI (kg/m <sup>2</sup> )	23.65 ± 3.26	22.31 ± 2.81
Gestational age at admission	35.7 ± 3.24	36.82 ± 2.27

Women in the case group had elevated blood pressure as compared to woman in the control group (Table 2)

**Table 2. Mean blood pressure in the case and control group**

Mean BP	Cases	Controls	p-value
Systolic	152.72 ± 11.18	118.92 ± 8.09	<0.0001
Diastolic	104.82 ± 7.66	76.8 ± 6.22	<0.0001

Note: BP- Blood Pressure p-value<0.05 was considered to be statistically significant

**Table 3. Comparison of platelet indices and red cell distribution width between cases and controls**

Parameters	Cases	Controls	P-value
PC (Iacs)	2.25 ± 0.68	2.26 ± 0.82	>0.5
PDW (fl)	18.66 ± 4.38	18.31 ± 4.57	>0.5
Plateletcrit (%)	39.85 ± 8.71	39.56 ± 11.12	>0.5
MPV (fl)	12.19 ± 1.38	12 ± 1.68	>0.1
RDW (%)	15.64 ± 2.08	14.91 ± 1.64	<b>0.004</b>

Note: PC- Platelet count, PDW- platelet distribution width, MPV- Mean platelet volume RDW- red cell distribution width

**Table 4. Comparison of platelet indices and red cell distribution width between control group and severe pre-eclampsia**

Parameters	Severe PE	Controls	p-value
PC (Iacs)	2 ± 0.74	2.26 ± 0.82	>0.1
PDW(fl)	18.44 ± 4.93	18.1 ± 4.57	>0.1
Plateletcrit (%)	39.66 ± 11.12	40.87 ± 8.78	>0.1
MPV (fl)	12.54 ± 1.46	12 ± 1.68	>0.1
RDW (%)	16.64 ± 2.1	14.91 ± 1.64	<b>&lt;0.01</b>

Note: PC- Platelet count, PDW- platelet distribution width, MPV- Mean platelet volume, RDW- red cell distribution width

In an another study from Saudi Arabia done by Alsheeha et al, 60 pre-eclamptic women and 60 healthy pregnant women were compared [15]. The results in their study were similar to that of our study with no significant difference in PDW and MPV between the pre-eclamptic and healthy pregnant women. Both PC and PC/MPV ratios were significantly lower in the women with pre-eclampsia compared with the controls in their study [15].

## 5. CONCLUSION

In conclusion, our study showed that the value of RDW was found to be significantly higher in women with pre-eclampsia when compared to normotensive women. RDW is an inexpensive

marker which is routinely calculated as a part of blood cell count and can be used as a significant diagnostic as well as prognostic marker in patient with pre-eclampsia akin to other cardiovascular diseases. However the platelet indices, like platelet count and plateletcrit were lower in women with pre-eclampsia, and indices like mean platelet volume and platelet distribution width were higher in pre-eclamptic women but the difference was insignificant for all the indices suggesting that although they are important parameters but can not be used for the definitive diagnosis of pre-eclampsia. More studies with larger sample size are required to better understand the causative role of RDW in patients with pre-eclampsia.

## CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

This matched case control study was conducted in the Department of Obstetrics and Gynaecology in collaboration with the Department of Biochemistry, Lady Hardinge Medical College, and Smt. Sucheta Kriplani Hospital, New Delhi. An approval from the ethical committee was taken.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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