

RELATIONSHIP OF RED CELL DISTRIBUTION WIDTH WITH PREECLAMPSIA AND CORRELATION WITH ITS SEVERITY

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Abstract

Background: Preeclampsia is a complex medical disorder associated with over 500,000 fetal and neonatal deaths and over 70,000 maternal deaths globally each year. It is the cause for 7% of maternal deaths in India. Redcell Distribution Width (RDW) is a measure of anisocytosis and used as an inflammation marker in systemic hypertension and coronary artery disease. But there is inadequate data on relationship between RDW and preeclampsia. The aim is to study the variation of RDW in preeclampsia and correlation of RDW with severity of preeclampsia. **Materials and Methods:** This study was conducted in Department of obstetrics and Gynecology, Government Medical College, Kottayam from January 2021 for 9 months. It is a cross sectional study done in 94 pregnant women with preeclampsia who satisfied the inclusion criteria and 94 matched controls. RDW was measured by an automated hematological analyser in entire study population. **Result:** Among 94 cases and control population the age of the subjects varied from 18 to 42 years. 41 were primigravidae. 22 cases were at gestational age 28-32 weeks, 52 cases >32-36 weeks and 20 were >36weeks. Analysis showed that difference in mean RDW values between cases and controls was statistically significant (14.095 ± 1.0884 , 12.949 ± 0.6694 , $P < 0.001$). In subgroup analysis it was confirmed that RDW levels were significantly higher in preeclampsia with severe features than preeclampsia with out severe features (14.389 ± 1.1349 , 13.525 ± 0.71 , $P < 0.001$). Also there was significantly high RDW in cases with Mean Arterial Pressure $MAP > 110$ mmHg than cases with $MAP \leq 110$ WITH t value -2.866 and P value 0.005 . **Conclusion:** RDW levels are associated with preeclampsia and severity of preeclampsia.

INTRODUCTION

Preeclampsia is best described as a pregnancy specific syndrome that can affect virtually every organ system. Preeclampsia is the occurrence of hypertension and proteinuria after 20 weeks of gestation in a women who had no previous hypertension or proteinuria. In the absence of proteinuria hypertension with evidence of acute kidney injury, liver dysfunction, neurological manifestations, hemolysis, thrombocytopenia and or fetal growth restriction is diagnostic of preeclampsia.^[1] It is a leading cause of maternal and perinatal mortality and morbidity. In United States from 2011-2013, 7.4% of maternal deaths are attributed to preeclampsia and eclampsia. It is theorized that poor or abnormal placentation in early pregnancy leads to placental ischemia and release of inflammatory mediators and vasoactive substances

which leads to endothelial activation and dysfunction.^[2-4]

Red Cell Distribution Width (RDW) is a measure of variation in size of circulating RBC and it's a readily available hematological index.^[5] It is a marker of anisocytosis.^[6] High RDW values are believed to reflect increased inflammation.^[7] but recent studies show that RDW is associated with hypertension and many other cardiovascular risk factors and shown to have prognostic value in cases of acute- chronic cardiac events in healthy normal population.^[8] This study is aimed to study the relationship between RDW and preeclampsia so that an increased RDW can be used as a marker of preeclampsia. If the association between RDW and preeclampsia is proven it can be considered as a candidate marker for predicting the occurrence of severe preeclampsia.

Objectives

1. To assess the variation of RDW in preeclampsia in patients admitted in dept. of Obstetrics and Gynecology Govt. medical college, Kottayam.

2. To assess the variation of RDW with severity of preeclampsia, in patients admitted in department of Obstetrics and Gynecology, Govt. Medical College Kottayam.

MATERIALS AND METHODS

The study was conducted in department of Obstetrics and Gynecology Government medical college Kottayam for a period of 9 months from January 2021 after getting approval from institutional review board (IRB No:115/2020). It was a cross sectional study. Sample size was calculated based on study by Zehra Vural Yilmaz et al,^[9] According to this study.

Cases: 118

Control: 120

RDW values are significantly higher in preeclampsia group compared with control group (15.23±1.96 vs 14.48±1.70), P<0.05) Also RDW values were significantly higher in severe preeclampsia group than mild preeclampsia in subgroup analysis (15.08±2.07 v/s 15.92±1.99, P<0.05).

Sample Size Calculation

No. of cases (n) = $r+1/r \times SD2 (Z1-\alpha/2 + Z1-\beta) 2 / d2$
r is the ratio of case and control. Here r=1

$SD2 = SD1^2 + SD2^2 / 2 = 1.96^2 + 1.70^2 / 2 = 3.36$

$Z(1-\alpha/2) = 1.96$ (For α as 5%)

$Z(1-\beta) = 0.842$ (for $\beta = 80\%$)

$d = M1 - M2$ hence $d^2 = (15.23 - 14.48)^2 = 0.56$

Hence $n = 1+1/1 \times 3.36(1.96+0.842)^2 / 0.56 = 2 \times 3.36 \times 7.84 / 0.56 = 94.08$

Hence no. of cases = 94, No. of controls = 94, Total 188 participants

A detailed history was taken from the cases and they are subjected to general physical examination, systemic and obstetric examination at admission.

Inclusion Criteria

Systolic BP more than or equal to 140 detected after 20 weeks gestation

Diastolic BP more than or equal to 90 detected after 20 weeks gestation

Urinary protein >1+(dipstick) or >0.3g/ 24 hours or urine Protein: creatinine ratio ≥ 0.3 or features of multisystem involvement

Singleton live fetus

Exclusion Criteria

Other medical complications (like diabetes, chronic hypertension, heart disease)

Infectious disease diagnosed during pregnancy

Premature rupture of membranes

Active labour

Polyhydramnios

Kidney disease

Anemia (Hb<11)

Haematological disorders

History blood transfusion in past 4 months

Maternal age, gestational age and parity matched control groups also selected. A complete hemogram of cases and controls were done at admission from which RDW- CV values were obtained using a BC 3000 PLUS haematological analyser.

Data was entered into M.S. Excel sheet and analysed using unpaired t test by statistical software SPSS 17. For subgroup analysis cases with systolic BP ≥ 160 , Diastolic BP ≥ 110 , Platelet count <1 lakh, liver enzymes elevated more than twice normal, persistent right upper quadrant/epigastric pain, progressive renal insufficiency (s. creatinine >1.1), pulmonary edema, new onset cerebral or visual disturbances were considered as severe features and tested using unpaired t test.

RESULTS

Total 94 cases and 94 controls were studied. Out of 94 cases with preeclampsia 62 cases had severe features.

Table 1: Mean age of cases

	N	Minimum	Maximum	Mean	SD
Age	94	18	42	28.21	6.363

61% of cases were less than 30 years.

Table 2: Gestational age of cases at admission

Gestational Age	Frequency	Percentage
28-32	22	24
>32-36	52	55
>36	20	21
Total	94	100

Among the participants in pre-eclampsia group 22 participants were of gestational age 28-32 weeks at the time of admission (24%), 52 participants were >32-36 weeks (55%) and 20 participants were of >36 weeks gestational age (21%).

Table 3: Comparison of mean Hb between the groups

Groups	N	Mean	Std. Deviation	Std. Error Mean	T	p value*
Preeclampsia	94	12.447	0.9130	0.0942	-0.071	0.943
Control	94	12.456	0.9352	0.0965		

*Significant when p value <0.05
Independent sample t-test

The difference in haemoglobin level between preeclampsia group and control group is not statistically significant.

Table 4: Comparison of mean TC between the groups

Groups	N	Mean	Std. Deviation	Std. Error Mean	T	p value*
Preeclampsia	94	11844.68	10246.691	1056.865	0.663	0.508
Control	94	10979	7401	763.411		

*Significant when p value <0.05
Independent sample t-test

The difference in total WBC count between preeclampsia group and control group is not statistically significant.

Table 5: Comparison of mean PLC between the groups

Groups	N	Mean	Std. Deviation	Std. Error Mean	T	p value*
Preeclampsia	94	2.2034	0.63376	0.06537	-0.173	0.863
Control	94	2.2194	0.63321	0.06531		

*Significant when p value <0.05
Independent sample t-test

The difference in plateletcount between preeclampsia group and control group is not statistically significant

Table 6: Comparison of mean RDW between the groups

Groups	N	Mean	Std. Deviation	Std. Error Mean	T	p value*
Preeclampsia	94	14.095	1.0884	0.1123	8.694	<0.001
Control	94	12.949	0.6694	0.0690		

*Significant when p value <0.05
Independent sample t-test

Table 7: Comparison of mean RDW between the subgroups

Subgroups	N	Mean	Std. Deviation	Std. Error Mean	T	p value*
Mild	32	13.525	0.7153	0.1264	-4.505	<0.001
Severe	62	14.389	1.1349	0.1441		

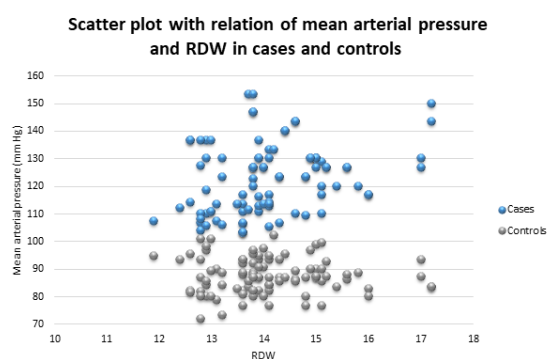
*Significant when p value <0.05
Independent sample t-test

Table 8: Comparison of mean RDW between high and medium MAP

Mean arterial pressure (mm Hg)	N	Mean	Std. Deviation	Std. Error Mean	T	p value*
95- 110	19	13.479	0.8162	0.1873	-2.866	0.005
> 110	75	14.251	1.0976	0.1267		

*Significant when p value <0.05
Independent sample t-test

Statistical significance of difference in mean RDW between cases with MAP ≤110 and cases with MAP>110 was tested by independent sample t test. t value was -2.866 and P value was 0.005. Hence difference in mean RDW between these two subgroups is statistically significant.



[Table 6] shows the comparison of RDW between preeclampsia group and control group. The mean RDW in preeclampsia group is 14.095±1.0884. The mean RDW in control group is 12.949±0.6694. Statistical significance was tested by independent sample t-test. t value was 8.694 and P value was <0.001 which shows that difference in mean RDW between preeclampsia and control group is statistically significant.

[Table 7] shows comparison of mean RDW between severe preeclampsia and mild preeclampsia. The

mean RDW in mild disease is 13.525±0.71. Mean RDW in severe preeclampsia group is 14.389±1.1349. Statistical significance was tested by independent sample t test. t value was -4.505 and P value was <0.001. Hence the difference in mean RDW between severe preeclampsia group and mild disease is statistically significant.

DISCUSSION

The present study on relationship of RDW with preeclampsia and correlation with its severity was done at department of OBG Government Medical College Kottayam, which is a tertiary care centre from January 2021 to September 2021.

In the present study the relationship of RDW with preeclampsia and RDW correlation with severity of preeclampsia were the main domains. 94 pregnant women with preeclampsia were the study population. For subgroup analysis cases were reclassified as mild preeclampsia and preeclampsia with severe features. Out of 94 cases 62 had severe disease and 32 had mild disease. This may be because the study is being done in a tertiary care centre which receives referral cases from peripheries. Control groups were 94 healthy

pregnant women matched for age, parity and gestational age.

Among 94 cases age distribution was from 18 to 42 years out of which 57 patients were less than 30 years and 37 were more than 30 years. Mean age was 28 years. Among the cases 41 patients were primi gravidae. All others constitute 53 in number.

Among the cases 22 belong to gestational age 28-32 weeks, 52 belong to 32-36 weeks and 20 participants belong to >36 weeks.

The findings of statistical analysis of this study are comparable with the results of previous studies regarding RDW correlation in preeclampsia patients. Comparison of mean RDW in cases and controls showed that the difference in mean RDW between preeclampsia and control group is statistically significant with a P value <0.001. The mean RDW preeclampsia group was 14.095 ± 1.0884 and in control group was 12.949 ± 0.6694 . While the difference in mean haemoglobin, total count and platelet count between preeclampsia group and control group were not statistically significant with P value >0.05. these findings are similar to the study by SG Reddy et al.^[10] Similar findings are seen in study by Zehra Vural Yilmaz et al in 2016.^[9]

As per the secondary objective subgroup analysis was done among the cases viz mild preeclampsia and preeclampsia with severe features. RDW values were significantly higher in severe preeclampsia group compared to mild disease. The mean RDW in severe disease group was 14.389 ± 1.1349 . The mean RDW in mild disease group was 13.525 ± 0.71 . P value was <0.001. Similar results are seen in study by RK Kurt et al in 2015.^[11] There was no statistical significance in difference in mean haemoglobin, total count and platelet count between severe preeclampsia group and mild disease group. These results are also in concordance with the findings of study by Ishag Adam et al and Rojjas et al.^[12,13]

In addition certain subgroup analysis were done among cases. It was found that RDW values are significantly high in preeclampsia patients with systolic BP>160 when compared to those cases with systolic BP≤160.

Difference in mean RDW between cases with fetal growth restriction and without fetal growth restriction was also found to be statistically significant.

Mean arterial pressure was calculated among cases. Cases were classified into two subgroups. One group with MAP 95-110 and second group with MAP>110. RDW was significantly elevated in case with map>110 when compared to cases with MAP≤110. P value was 0.005. This finding was also seen in study by Reddy SG et al. The scatter diagram shows that RDW is positively correlated with MAP which is the best-known marker of severity of preeclampsia.

Anisocytosis measured by RDW, is due to the disease itself or a reflection of an underlying cause or both elements is still unclear. In the present study, we have demonstrated that RDW is associated with the presence and severity of preeclampsia and can be

used to identify the severe preeclampsia. Study by Rojas et al,^[14] Kashyap et al,^[15] studied the use of RDW as a predictor of severe preeclampsia. Further studies involving larger population are required to evaluate the usefulness of RDW as a candidate marker for predicting the occurrence of severe preeclampsia.

CONCLUSION

1. RDW values are significantly high in preeclampsia compared to healthy pregnant women.
2. RDW values are still higher in preeclampsia with severe feature compared to mild preeclampsia.
3. No significant correlation is seen between hemoglobin level, total count or platelet count with occurrence of preeclampsia or with severity of preeclampsia.
4. RDW values are significantly high in preeclampsia patients with high MAP (MAP>110).
5. The reason for RDW elevation in preeclampsia, whether due to the disease itself or a reflection of an underlying cause or both elements is still unclear. Further studies involving larger population are required to evaluate the usefulness of RDW as a candidate marker for predicting the occurrence of severe preeclampsia.

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