

# Recurrent Pregnancy Loss is Associated with Increased Red Cell Distribution Width and Platelet Distribution Width

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## Abstract

**Background:** The aim was to compare platelet distribution width and red cell distribution width between pregnant women with a history of recurrent pregnancy loss and pregnant women without a history of pregnancy loss. **Methods:** This was a prospective study to the evaluation of 70 pregnant women with a history of recurrent pregnancy loss and 70 pregnant women without a history of pregnancy loss in the first trimester. **Results:** It was observed that the mean RDW-SD of cases is higher i.e.  $48.94 \pm 5.78$  than controls i.e.  $42.87 \pm 4.49$ . The mean RDW-CV values of cases and controls. It was observed that the mean RDW-CV of cases is higher i.e.  $16.90 \pm 1.86$  than controls i.e.  $14.93 \pm 1.02$ . It was observed that the mean PDW of cases is higher i.e.  $16.07 \pm 1.45$  than controls i.e.  $12.89 \pm 1.00$ . **Conclusions:** An increased platelet distribution width and red cell distribution width with recurrent pregnancy loss.

**Keywords:** Platelet distribution width, Red cell distribution width, Recurrent pregnancy loss.

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## INTRODUCTION

Recurrent pregnancy loss is defined as three or more consecutive pregnancy losses at or less than 20 weeks of gestation or with a fetal weight less than 500 grams [1].

Pregnancy causes many alterations in hemostatic balance and thus leads to a tendency towards thrombophilia. Such a tendency is considered as a mechanism that compensates for the hemostatic challenge of delivery. The natural inclination towards thrombophilia in pregnancy is due to the increase in several clotting factors, including factor I, factor VII, factor VIII and von Willebrand. Moreover other markers reflecting hypercoagulability (such as D-dimer and/or prothrombin fragment) are increased during pregnancy. Different polymorphisms of thrombophilic disorders are diagnosed in up to 40% of women who have experienced recurrent miscarriages. However, this association depends on the type of thrombophilic disorder and the gestational age at which fetal loss occurs. Thrombophilia is related to several biological markers that reflect either coagulation activation (such as prothrombin fragment and thrombin-antithrombin complex) or platelet activation (such as  $\beta$

thrombomodulin or soluble platelet Pselection). Thrombophilia refers to the qualitative failure of the physiological coagulation inhibitors. Either the qualitative or the quantitative impairment of physiological coagulation inhibitors results in a procoagulatory imbalance which eventually leads to a condition of compensated coagulopathy. This chronic state of coagulation is associated with an enhancement in platelet activation. The enhancement in platelet activation causes the discoid platelets to become more spherical and to acquire pseudopodia. Such an alteration in platelet shape helps the platelets to obtain a larger surface. Platelet distribution width (PDW) due to platelet activation, resulting from platelet swelling and pseudopodia formation [2].

## MATERIALS AND METHODS

### Study area

The study will be conducted in the antenatal outpatient clinic at the Department of Obstetrics and Gynaecology, Apollo BGS Hospitals, Mysore during the study period.

## STUDY POPULATION

The study will be conducted on pregnant women attending the antenatal clinic at the Department of Obstetrics and Gynaecology, Apollo BGS Hospitals and those women meeting inclusion criteria of the study and willing to participate in the study.

### Study design

Hospital based comparative study.

### Study duration

May 2017 to May 2018

## INCLUSION CRITERIA

Pregnant women with h/o recurrent pregnancy loss (case) and without h/o pregnancy loss (control).

## EXCLUSION CRITERIA

- Uterine anomalies
- Diabetes mellitus
- Thyroid disease
- Immunological factors
- Infectious causes
- Cardiac diseases
- Other Haemoglobinopathies

### Sample size with justification

The sample size is calculated at 80% study power and an alpha error of 0.05 assuming SD of 3.8fl in PDW as found in reference article (Recurrent pregnancy loss by Ozgur Dundar, Mine kanat Pektas, Serkan Bodur, Lale Vuslat Bakir and Ahmet Cetin). For a minimum detectable difference of 2fl in PDW, 58 participants in each group are required as sample size. It was further enhanced and rounded off to 70 cases in each group as final sample size assuming 20% drop outs/ attrition.

## METHODOLOGY

Ethical clearance was taken from the Ethical Clearance Committee. All pregnant women attending the antenatal clinic at the Department of Obstetrics and Gynaecology, Apollo BGS Hospital will be included in the study. Pregnant women with h/o recurrent pregnancy loss and meeting the inclusion criteria will be in the study group (cases) and pregnant women with no h/o recurrent pregnancy loss will be in the control group (controls). Convenience sampling method is used.

- After taking their informed written consent, detailed history, general and systemic examination will be done.
- Patient's samples will be collected for routine laboratory examination along with sample for

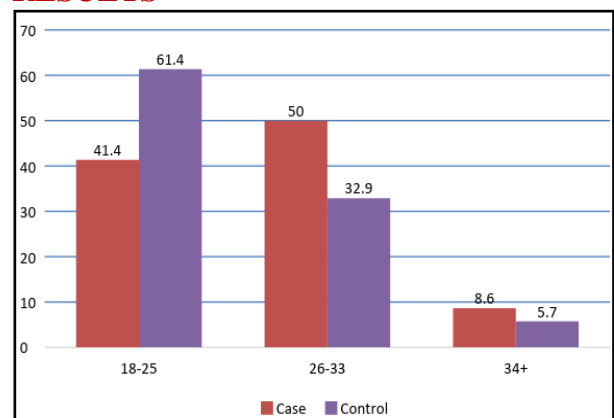
RDW and PDW in an EDTA vial from antecubital vein puncture.

- Red cell distribution width and platelet distribution width will be measured using full automated 5/6 parts hematology analyser –ADVIA 2120.
- RDW and PDW are measured by the technique of hydrodynamic focusing method, flow cytometry method using semiconductor laser.
- Collected samples will be sent to a designated laboratory of our hospital and reports will be procured personally.
- All information and reports will be recorded on a predesigned performa and will be entered in Microsoft excel sheet to prepare master chart.

## STATISTICAL METHODS

- Continuous variables will be summarized as mean and SD while Nominal/ Categorical variables as percentages. Unpaired T test will be used for analysis of continuous variables whereas Chi square test will be used for Nominal/Categorical variables. P value <0.05 will be taken as significant. SPSS Statistics 20 will be used for all statistical calculation.

## RESULTS



In case group out of 70 study subjects, maximum i.e. 35 (50%) subjects were lying in the age group 26-33 years followed by 29 (41.4%) were lying in the age group 18- 25 years and 6 (8.6%) in the age group  $\geq 34$  yrs. The mean age of this group subjects was  $27.37 \pm 4.54$  years. In control group out of 70 study subjects, maximum i.e. 43 (61.4%) subjects were lying in the age group 18- 25 years followed by 23 (32.9%) were lying in the age group 26-33 years and 4 (5.7%) were lying in  $\geq 34$  years respectively. The mean age of this group subjects was  $24.92 \pm 4.99$  years.

**Table-1: Mean  $\pm$  SD of RDW-SD of case and Control group subjects**

Parameter	Mean $\pm$ SD		P-value	Significance
	Case (n=70)	Control (n=70)		
RDW-SD	$48.94 \pm 5.78$	$42.87 \pm 4.49$	<.001	HS

The above table shows the mean RDW-SD values of cases and controls. It was observed that the mean RDW-SD of cases is higher i.e.  $48.94 \pm 5.78$  than controls i.e.  $42.87 \pm 4.49$ .

We reject the null hypothesis and mean difference of cases and controls group statistically differ highly significantly i.e.  $p < 0.001$ .

**Table-2: Mean  $\pm$  SD of RDW-CV of case and Control group subjects**

Parameter	Mean $\pm$ SD		P-value	Significance
	Case (n=70)	Control (n=70)		
RDW-CV	$16.90 \pm 1.86$	$14.93 \pm 1.02$	<.001	Sig

The above table shows the mean RDW-CV values of cases and controls. It was observed that the mean RDW-CV of cases is higher i.e.  $16.90 \pm 1.86$  than controls i.e.  $14.93 \pm 1.02$ .

We reject the null hypothesis and mean difference of cases and controls group statistically differ highly significantly i.e.  $p < 0.001$ .

**Table-3: Mean  $\pm$  SD of PDW of case and Control group subjects**

Parameter	Mean $\pm$ SD		P-value	Significance
	Case (n=70)	Control (n=70)		
PDW	$16.07 \pm 1.45$	$12.89 \pm 1.00$	<.001	HS

The above table shows the mean PDW values of cases and controls. It was observed that the mean PDW of cases is higher i.e.  $16.07 \pm 1.45$  than controls i.e.  $12.89 \pm 1.00$ .

We reject the null hypothesis and mean difference of cases and controls group statistically differ highly significantly i.e.  $p < 0.001$ .

## DISCUSSION

Our study was a hospital based comparative analysis study done between pregnant women with h/o recurrent pregnancy loss (case) and without h/o of pregnancy loss (control) attending department of Obstetrics and Gynaecology, Apollo BGS Hospitals, Mysore. The sample size is calculated at 80% study power and an alpha error of 0.05 assuming SD of 3.8fl in PDW. For a minimum detectable difference of 2fl in PDW, 58 participants in each group are required as sample size. It was further enhanced and rounded off to 70 cases in each group as final sample size assuming 20% drop outs/attrition. Seventy pregnant women having h/o recurrent pregnancy loss as cases and 70 pregnant women without h/o of recurrent pregnancy loss as controls would be included on first cum first basis after beginning the study assuming 20% drop outs. Complete blood count including RDW and PDW were done in these patients and the data collected and analyzed.

In present study both groups were compared on the basis of age, religion, literacy, rural/urban, socioeconomic status, height, body weight and BMI ( $P > 0.05$  for each). There is no significant difference in the mean value of haemoglobin, total leukocyte count, hematocrit cases group when compared to control groups. Ahmet Uysal *et al.* conducted a study showed that no statistically significant differences in

haemoglobin, haematocrit and white blood cells count (WBC) between 2 groups ( $p > 0.05$ , respectively)[3].

It was observed that the mean RDW-SD of cases is higher i.e.  $48.94 \pm 5.78$  than controls i.e.  $42.87 \pm 4.49$ . The mean RDW-CV values of cases and controls. It was observed that the mean RDW-CV of cases is higher i.e.  $16.90 \pm 1.86$  than controls i.e.  $14.93 \pm 1.02$ . It was observed that the mean PDW of cases is higher i.e.  $16.07 \pm 1.45$  than controls i.e.  $12.89 \pm 1.00$ . We observed that increased RDW and PDW were associated with recurrent pregnancy loss.

## CONCLUSION

Increased RDW and PDW are associated with recurrent pregnancy loss which is helpful in the early management of these high-risk patients. Complete blood count is a simple test and can be performed easily at primary health centre level and early identification of high risk cases is possible so that patient can be timely referred to higher centres and early pregnancy loss can be prevented.

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