RESEARCH PAPER

Temporal Dynamics of Red Cell Distribution Width (RDW) and C-Reactive Protein (CRP) Across the Menstrual Cycle in Young Healthy Females: A Comprehensive Research Study

Soumya Tewari[1], Dr. Naushi Mujeeb[2], Dr. Aparna A[3], Dr. Kirti Jaiswal[4]

[1]*PhD Scholar, Department of Physiology, National Institute of Medical Science & Research, Jaipur, Rajasthan, India*
[2]*Professor, Department of Physiology, National Institute of Medical Science & Research, Jaipur, Rajasthan, India (Corresponding Author)*
[3]*Professor, Department of Physiology, Balvir Singh Tomar Institute of Medical Sciences and Research Jaipur, Rajasthan, India*
[4]*Professor, Department of Physiology, Uttar Pradesh University of Medical Science, Saifai Etawah, UP, India*

ABSTRACT

Background: Menstruation is a normal process in fertile women, comprising three phases: Follicular, Ovulatory, Luteal phases. Red Cell Distribution Width (RDW) and C-Reactive Protein (CRP) are increasingly recognized biomarkers of hematological variability and low-grade inflammation. However, their physiological fluctuations across the menstrual cycle remain poorly understood, leading to potential misinterpretation of laboratory values in reproductive-age women. This study examines the impact of menstrual cycle phases on RDW and CRP dynamics in young females.

Aim: This study examined in detail about the Temporal Dynamics of RDW and CRP across Menstrual Cycle in young females.

Methodology: This study was conducted at Uttar Pradesh University of Medical Sciences involving 50 females aged 18 to 30 with regular menstrual cycles (28±3 days). Ethical approval and informed consent were obtained. Blood samples (3 ml) were taken during three cycle phases: days 3-5 (Follicular), around day 14 (Ovulatory), and days 20-24 (Luteal). Red cell distribution width (RDW) and C-reactive protein (CRP) levels were measured using automated analyzers.

Results: RDW demonstrated a significant rising trend from the follicular to the luteal phase. In contrast, CRP did not exhibit any consistent rising or falling pattern across phases, and differences were not statistically significant. No correlation was found between RDW and CRP in any phase.

Conclusion: RDW shows clear temporal variation across the menstrual cycle, whereas CRP remains physiologically stable in healthy women. These findings suggest that RDW is a more sensitive biomarker for cycle-related hematological changes, while CRP is less influenced by menstrual physiology. Understanding these dynamics may improve interpretation of laboratory results in reproductive-age females.

Keywords: Menstrual Cycle Phases, Red Cell Distribution Width (RDW), C-Reactive Protein Biomarkers (CRP)

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INTRODUCTION

The menstrual cycle is divided into three main phases: Follicular, Ovulatory, and Luteal. Each phase is characterized by distinct hormonal changes, particularly in estrogen and progesterone levels; these hormonal changes not only affect reproductive function but also influence systemic physiology, including immune activity and various physiological parameters. As we all know that Both C-reactive protein (CRP) and Red Blood Cell Distribution Width (RDW) levels fluctuate across the menstrual cycle in young females due to hormonal changes. CRP, a marker of inflammation, shows significant variation throughout the cycle. RDW, a measure of the variation in red blood cell size, is also affected by the menstrual cycle. Red cell distribution width (RDW) is inexpensive and routinely assessed as part of the complete blood count (CBC) to gather information on the heterogeneity in the size of circulating erythrocytes. It quantifies the differences between the smallest and largest red blood cells in a sample.[(1)] A sensitive marker for detecting early changes in iron metabolism, even before hemoglobin or other indices reflect the deficiency. Increased RDW values reflect greater variability in RBC size, which generally indicates dysfunctional Erythropoiesis, shortened RBC lifespan, or premature release of Reticulocytes. Elevated RDW levels are associated with a range of conditions, including anemia,[(3)] chronic inflammation,[(4)] cardiovascular diseases.[(2)] and HbA1c[(5)] Understanding its natural variation during the menstrual cycle can reduce the risk of misinterpreting results due to hormonal or physiological changes. A normal RDW ranges between 11–15%[(2)] C-reactive protein (CRP) is an acute-phase protein primarily synthesized in hepatocytes and plays a critical role in inflammation response.[(6)] It's a marker used to detect inflammation in the body, which can be a sign of various conditions, from infections to autoimmune diseases. CRP

**Author for Correspondence: Dr. Naushi Mujeeb*

levels rise when there's inflammation and a CRP test can help doctors assess the extent and progression of inflammation. RDW (Red Cell Distribution Width) and CRP (C-Reactive Protein) are both markers that can be elevated in inflammatory conditions.[7] While RDW is primarily associated with the variation in size of red blood cells, CRP is a well-established inflammatory marker. Studies have shown a positive correlation between RDW and CRP, suggesting that increased RDW may be linked to the inflammatory response.[3] This study was conducted to investigate the temporal trends of RDW and CRP across different menstrual phases in healthy young females and also to evaluate their potential as biomarkers of physiological inflammation and reproductive health status. It was also intended to assess the Impact of Menstrual Cycle Phases on varying dynamics of Red Cell Distribution Width (RDW) and C-Reactive protein in young female subjects.

Aims and Objectives

Aims and Objectives of this study were to investigate the temporal trends of RDW and CRP across different menstrual phases in healthy young females and evaluate their potential as biomarkers of physiological inflammation and reproductive health status.

Materials and Methods

This study was conducted at the Uttar Pradesh University of Medical Sciences in Saifai, Etawah, and included 50 females with regular menstrual cycles. The inclusion criteria required participants to be between 18 and 30 years of age, with menstrual cycles lasting 28±3 days. Ethical approval was obtained, and informed consent was collected from all participants. Oral and written informed consents were obtained from subjects. The purpose and methodology of the study was fully explained to all of them for their full cooperation. Simple random sampling procedure was utilized for precise sample selection process. Randomization was also employed so as to optimize the accuracy of data and related outcomes. Randomization is the process of assigning participants to different study groups by chance, ensuring each participant has an equal chance of getting selected, which prevents any possible bias The Anthropometric Measurements of the subjects and their brief medical history was taken. Blood samples of approximately 3 ml were taken during three phases of the menstrual cycle. The blood was collected by venipuncture of antecubital vein under aseptic conditions after the subjects are made comfortable. About 3 ml of the first sample was collected on days 3 to 5 of menstruation (Follicular phase), the second around day 14 of the menstrual cycle (Ovulatory phase), and the third on days 20 to 24 of the cycle (Luteal phase). Red cell distribution width (RDW) was measured using a standard automated hematology analyzer. Red cell distribution width is calculated from a histogram of red blood cell volumes, showing the variation in size (anisocytosis). It uses techniques like electrical impedance and laser light scatter to classify cells and generate this data. C-reactive protein (CRP) levels were also analyzed by fully automated Biochemistry analyzer BA400 (biosystem) in all three phases by turbidimetry method. Biosystem uses an advanced LED optical system to measure light absorption/scattering for clinical chemistry tests. It precisely dispenses samples and reagents, then uses LEDs to detect color changes. Blood samples were processed immediately after collection to ensure accuracy. Data were analyzed using ANOVA for repeated measures and Pearson correlation. Correlation between RDW and CRP analyzed using Pearson or Spearman method. $p<0.05$ considered significant.

Statistical Analysis and Results

The parameters were statistically analyzed using descriptive statistics, i.e., mean and standard deviation. Data were analyzed using SPSS software version 29.0. This study involved a total of 50 young, healthy female subjects, in which red cell distribution width and C-reactive protein levels were evaluated for the intended objectives. This study involved a comprehensive analysis of 50 female patients. The demographic profile of these patients showed that they were in different age groups and belonging to different age ranges (within age 18 to 30 years). As indicated in Table 1 and Graph 1, a detailed statistical breakdown of the age based distribution shows that out of the total 50 patients, Maximum 12 patients were noticed in the age range of 18-20 and 27-28 each. P value was highly significant for these patients (0. 01). Minimum 8 patients were noticed in the age range of 21-23 and 29-30 each. P value was not significant for these patients (0.40). Among these 50 participants, the red cell distribution width exhibited variability throughout all three studied phases. There was a moderate increase in width observed from the follicular phase to the Luteal phase. Additionally, in most of the studied cases the C-reactive protein levels showed an increasing trend from the Follicular phase to the Luteal phase. Temporal Variation of RDW: RDW increased progressively from Follicular→Ovulatory→Luteal phase. Statistical testing showed this rise to be significant ($p<0.05$, Table 2 and Graph 2). Table 3 showed the significant statistical findings observed during the study using the Pearson Chi-Square test, which is a reliable method for evaluating the relationship between categorical variables. Temporal Variation of CRP: CRP fluctuated across phases but without any clear upward or downward trend. CRP differences across phases were not statistically significant ($p<0.05$, Table 4 and Graph 3). Table 5 showed the significant statistical findings observed during the study using the Pearson Chi-Square test, which is a reliable method for evaluating the relationship between categorical variables. Values remained within normal physiological limits. Table 6 demonstrated about the Estimation amongst all studied patients for RDW Variation using one-way ANOVA (For repeated measures and Pearson correlation). The Pearson correlation and associated p value was highly significant (0.02). Table 7 demonstrated about the Estimation amongst all studied patients for CRP Variation using one-way ANOVA (For repeated measures and Pearson correlation). The Pearson correlation and associated p value was highly significant (0.01).

Table 1: Age based statistical description of contributing patients

Age Group (Yrs)	Female	Total	P value
18-20	12	12	0.01*
21-23	8	8	0.40
24-26	10	10	0.02*
27-28	12	12	0. 01*
29-30	8	8	0.40
Total	50	50	*Significant

Graph 1: Patients Graphical distribution and associated statistical details

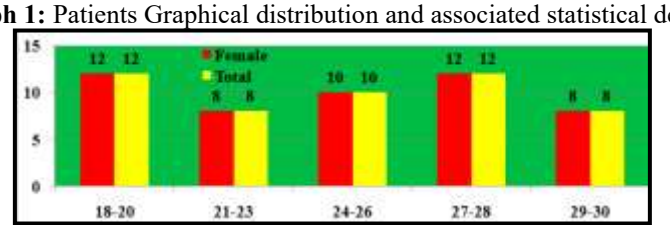

Table 2: Temporal Variation of RDW

Phase	Mean	Median	SD	Minimum	Maximum
Follicular	13.5	13.4	0.9	12.0	15.0
Ovulatory	14.2	14.1	0.8	12.8	15.6
Luteal	15.1	15.0	0.9	13.5	16.8

Table 3: To assess the significance of the findings observed during the study, a rigorous statistical analysis was performed using the Pearson Chi-Square test, which is a reliable method for evaluating the relationship between categorical variables

Phase	Std. Error	95% CI	Pearson Chi-Square Value	df	p value
Follicular	1.07	1.05	1.09	1.10	0.06
Ovulatory	1.03	1.01	1.03	1.06	0.02*
Luteal	1.02	1.02	1.04	1.04	0.08

Graph 2: RDW Variation

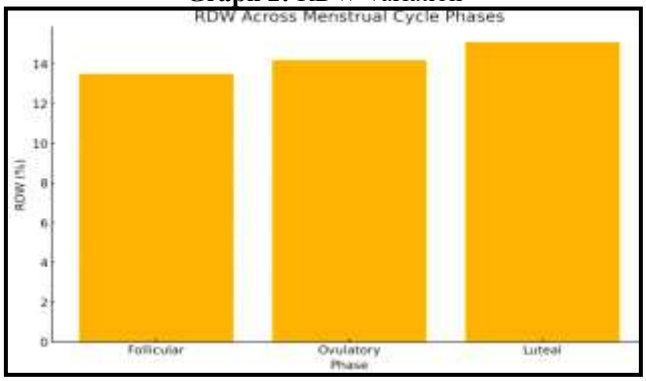

Table 4: Temporal Variation of CRP

	Phase	Mean	Median	SD	Minimum	Maximum
CRP	Follicular	2.89	2.10	2.21	0.300	10.10
	Ovulatory	2.57	2.00	1.82	0.400	8.70

**Author for Correspondence: Dr. Naushi Mujeeb*

	Luteal	2.81	2.00	2.48	0.000	10.30

Table 5: To assess the significance of the findings observed during the study, a rigorous statistical analysis was performed using the Pearson Chi-Square test, which is a reliable method for evaluating the relationship between categorical variables

Phase	Std. Error	95% CI	Pearson Chi-Square Value	df	p value
Follicular	1.07	1.05	1.09	1.10	0.06
Ovulatory	1.03	1.01	1.03	1.06	0.02*
Luteal	1.09	1.07	1.05	1.09	1.10

Graph 3: CRP Variation

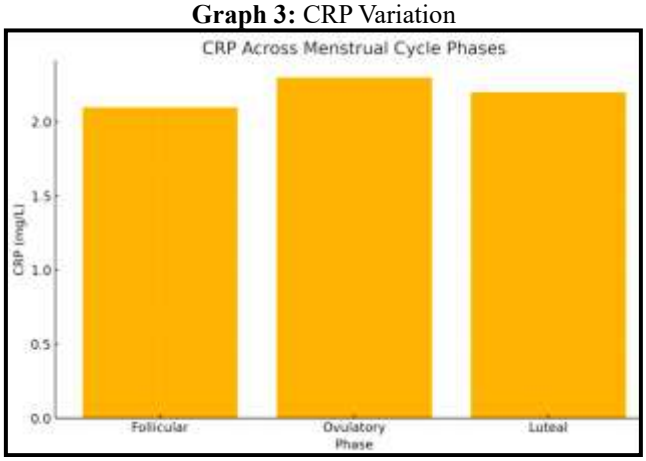

Table 6: Estimation amongst all studied patients for RDW Variation using one-way ANOVA (For repeated measures and Pearson correlation)

Variables	Degree of Freedom	Sum of Squares ∑	Mean Sum of Squares m∑	F	Level of Sig. (p)
Between Groups	5	2.235	2.237	1.2	0.02*
Within Groups	17	2.246	2.413	_	
Cumulative	125.09	5.98	*p<0.05 significant		

Table 7: Estimation amongst all studied patients for CRP Variation using one-way ANOVA (For repeated measures and Pearson correlation)

Variables	Degree of Freedom	Sum of Squares ∑	Mean Sum of Squares m∑	F	Level of Sig. (p)
Between Groups	4	2.765	1.217	1.6	0.01*
Within Groups	14	2.556	2.113	_	
Cumulative	115.02	2.93	*p<0.05 significant		

Discussion

This study demonstrates a distinct pattern of RDW variation across the menstrual cycle, with increasing values toward the luteal phase. RDW measures the variation in the size and volume of red blood cells (RBCs). Normal, healthy RBCs are typically uniform in size. The typical RDW range is 11.5% to 14.5%, but this may vary slightly by laboratory. Elevated levels are seen usually in cases of Iron, vitamin B12, or folate deficiency anemias, Chronic conditions such as liver disease, kidney disease, or cardiovascular disease, Bone marrow disorders.[8] Fluctuating sex hormones may influence erythropoiesis, iron metabolism, or red cell turnover, explaining this rise. CRP is a sensitive, widely used biomarker of inflammation. Elevated levels indicate systemic inflammation due to various causes, including infection, injury, or chronic disease. Some of the pioneer researchers have shown that CRP levels can sometime

fluctuate during the menstrual cycle in healthy women.[9,10] In contrast with our results, CRP did not show meaningful temporal variability, indicating that low-grade systemic inflammation remained stable throughout the cycle. The absence of a cyclical pattern in CRP also corroborates the idea that the menstrual cycle acts more as a regulator of local uterine inflammation rather than systemic inflammation. Therefore, systemic markers like CRP may not reliably capture menstrual-phase–related inflammatory changes in otherwise healthy young females. The lack of correlation between RDW and CRP further reinforces that RDW behaves independently of inflammation in this context.

Conclusion

This study unveiled significant insights into the relationship between red cell distribution width (RDW) and C-reactive protein (CRP) levels among young female patients. The findings indicated a notable elevation and rising pattern in RDW among female subjects showing its sensitivity to cyclical hematological and hormonal fluctuations. However, CRP remains relatively stable, with no clear upward or downward trend across the follicular, ovulatory, and luteal phases. These results show the importance of monitoring RDW for understanding the health dynamics in young females. Additionally, RDW may serve as a useful hematological indicator of physiological variations across menstrual phases, whereas CRP is not significantly influenced by menstrual-cycle dynamics in healthy individuals. Furthermore, RDW may serve as a more sensitive indicator of menstrual cycle–related physiological variations than CRP.

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