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## Original Research Article

# Correlation between red cell indices and serum ferritin level in pregnant women with latent iron deficiency

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## ABSTRACT

**Background:** Latent iron deficiency (LID), defined as iron depletion without anemia, frequently precedes iron deficiency anemia in pregnancy and is associated with adverse maternal and fetal outcomes. Serum ferritin is the gold standard for assessing iron stores but is often unavailable in low-resource settings. Readily obtainable red cell indices may serve as practical alternatives for identifying early iron deficiency. This study aimed to evaluate the relationship between red cell indices and serum ferritin levels among pregnant women with latent iron deficiency.

**Methods:** This cross-sectional analytical study was conducted at Sir Salimullah Medical College Mitford Hospital, Dhaka, including 205 non-anemic pregnant women in their second trimester. Complete blood count and serum ferritin were assessed using automated analyzers. Participants were categorized as latent iron-deficient (ferritin <30 µg/l) or non-deficient (≥30 µg/l). Group differences were compared using independent t-tests, and correlations between red cell indices and ferritin levels were analyzed using Pearson's test.

**Results:** Mean MCV and MCH were lower in the latent iron-deficient group, though not significantly ( $p>0.05$ ). RDW-CV% was significantly higher in LID women ( $15.3\pm1.6$  vs  $14.1\pm1.6$ ,  $p<0.001$ ). A significant negative correlation was observed between RDW-CV% and serum ferritin ( $r=-0.347$ ,  $p<0.001$ ).

**Conclusions:** RDW-CV% demonstrates a strong negative correlation with serum ferritin and may be used as a sensitive hematologic marker for early detection of latent iron deficiency in pregnancy. Integrating RDW interpretation into routine antenatal blood count assessments can improve screening and management of iron deficiency in resource-limited settings.

**Keywords:** Latent iron deficiency, Pregnancy, Red cell indices, Serum ferritin

## INTRODUCTION

In pre-eclampsia, there is increased uteroplacental resistance and reduced fetal perfusion due to inadequate invasion of spiral arterioles by trophoblast cells. This

causes impaired fetal growth and fetal hypoxia. Pre-eclampsia contributes to 25% perinatal morbidity and mortality and optimal evaluation of fetus is necessary to ensure a good outcome.<sup>1</sup> Ultrasonography is done to evaluate fetal well-being by biophysical profile and recently Doppler ultrasound has emerged as a vital tool for

antenatal surveillance Iron deficiency remains one of the most widespread nutritional deficiencies affecting women of reproductive age, particularly during pregnancy, when physiological demands for iron increase substantially. During gestation, the maternal blood volume expands to support fetal growth, increasing iron requirements for both erythropoiesis and placental function.<sup>1</sup> When these increased demands are not met through dietary intake or supplementation, iron depletion ensues. The depletion of iron stores without a decline in hemoglobin concentration is termed latent iron deficiency (LID). LID precedes the development of iron deficiency anemia (IDA) and is clinically significant, as it may contribute to adverse maternal and fetal outcomes if not detected early.<sup>2</sup>

Serum ferritin is considered the most reliable biochemical indicator of iron stores and the gold standard for diagnosing iron deficiency. However, ferritin measurement is costly and not routinely available in all healthcare settings, particularly in low-resource environments.<sup>3,4</sup> Consequently, attention has turned to identifying more accessible hematological markers that can predict early iron deficiency. Red cell indices, including mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and red cell distribution width (RDW), are derived from complete blood count (CBC) analyses, which are widely available, cost-effective, and routinely performed in antenatal screening.<sup>5</sup> These indices may reflect subtle alterations in erythropoiesis before the onset of overt anemia and are therefore promising indicators of latent iron deficiency.

Previous studies have demonstrated variable associations between red cell indices and serum ferritin levels. Rabindrakumar et al reported that MCV, MCH, and MCHC correlated positively with serum ferritin in pregnant women, suggesting their potential diagnostic utility.<sup>6</sup> In contrast, Tiwari et al found a significant correlation only between serum ferritin and RDW, but not with other red cell indices.<sup>7</sup> Similarly, Sultana et al highlighted that RDW increased significantly in latent iron deficiency and exhibited higher sensitivity and specificity than other indices for early detection of iron-deficient erythropoiesis.<sup>8</sup> These inconsistencies underscore the need for additional research to clarify which red cell parameters are most predictive of early iron depletion, particularly in non-anemic pregnant women.

Given that latent iron deficiency often precedes the clinical manifestation of anemia, its early identification can facilitate timely intervention through iron supplementation, thereby preventing progression to IDA and its associated complications.<sup>9</sup> In developing countries, including Bangladesh, routine ferritin testing remains limited, and many women with early iron depletion go undiagnosed until anemia develops. Establishing the relationship between red cell indices and ferritin levels could therefore provide a practical approach for screening pregnant women at risk of latent iron deficiency using readily available tests.

This study aims to evaluate the correlation between red cell indices specifically MCV, MCH, and RDW and serum ferritin levels among pregnant women with latent iron deficiency in their second trimester. The findings may assist in identifying reliable, cost-effective hematological markers to detect LID in antenatal settings where advanced biochemical testing is not routinely feasible.

## METHODS

This cross-sectional analytical study was conducted in the Department of Obstetrics and Gynecology, Sir Salimullah Medical College Mitford Hospital (SSMCMH), Dhaka, Bangladesh, over 12 months. A total of 205 pregnant women in their second trimester (13-28 weeks) with normal hemoglobin levels were included.

### Inclusion criteria

Pregnant women in the second trimester (13–28 weeks of gestation), confirmed by the last menstrual period or early ultrasound examination, with a singleton pregnancy and a hemoglobin concentration  $\geq 10.5$  g/dL (non-anemic) were eligible for inclusion in the study.

### Exclusion criteria

Participants were excluded from the study if they had known hematological disorders or active infections; liver disease, malignancy, or chronic connective tissue disorders; use of medications that interfere with micronutrient metabolism (such as antiepileptics or aspirin); or preeclampsia or multiple pregnancies.

### Study procedure

Participants meeting the inclusion criteria were selected purposively following informed consent. Data were collected via interviewer-administered questionnaires, supplemented by review of medical records. Blood samples were drawn for complete blood count (CBC) and serum ferritin estimation. CBC was analyzed using an automated hematology analyzer, and serum ferritin was measured using chemiluminescence immunoassay on a Liaison XL automated analyzer. Respondents were categorized as: Group I: Latent iron deficiency present (serum ferritin  $< 30$   $\mu$ g/l) and Group II: Latent iron deficiency absent (serum ferritin  $\geq 30$   $\mu$ g/l).

Strict quality control procedures were followed for laboratory assays. Data were cross-checked for consistency and completeness after each collection session.

### Ethical consideration

Ethical approval was obtained from the Institutional Review Board of Sir Salimullah Medical College Mitford Hospital. Written informed consent was collected from all participants, confidentiality was strictly maintained, and

no financial incentives were offered. Participants were free to withdraw at any stage.

### Statistical analysis

Data were analyzed using SPSS version 26. Descriptive statistics were presented as mean  $\pm$  standard deviation (SD) for continuous variables and frequencies with percentages for categorical variables. Group comparisons were performed using independent sample t-tests for continuous variables and chi-square tests for categorical

variables. Pearson's correlation test assessed the relationship between red cell indices and serum ferritin levels. A p value  $<0.05$  was considered statistically significant.

### RESULTS

Participants with latent iron deficiency were significantly younger, had more advanced gestational age, and were less likely to have taken iron supplementation compared to those without LID (Table 1).

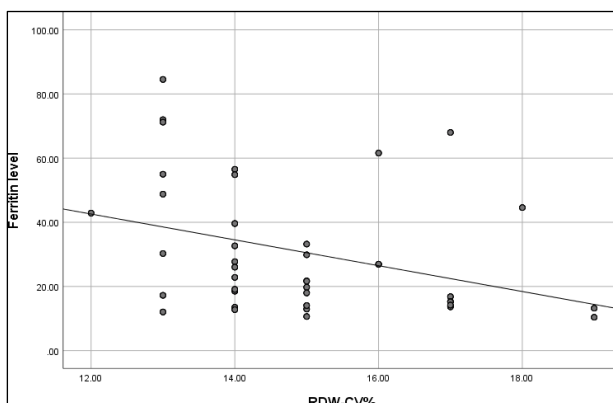
**Table 1: Baseline characteristics of the study participants (n=205).**

Characteristics	Group I (Ferritin $<30$ $\mu\text{g/l}$ ) n=130, N (%)	Group II (Ferritin $\geq 30$ $\mu\text{g/l}$ ) n=75, N (%)	P value
Age (years, Mean $\pm$ SD)	22.5 $\pm$ 3.9	25.1 $\pm$ 6.3	$<0.001$
Gravidity (%)	Primigravida 45 (56.3)	35 (43.8)	0.088
	Multigravida 85 (68.0)	40 (32.0)	
Gestational age (weeks, Mean $\pm$ SD)	21.6 $\pm$ 3.1	18.7 $\pm$ 4.0	$<0.001$
Iron supplementation (%)	Not taken 70 (73.7)	25 (26.3)	0.005
	Taken 60 (54.5)	50 (45.5)	

Mean MCV and MCH values were slightly lower among women with latent iron deficiency, although not statistically significant. RDW-CV was significantly higher in the LID group ( $p<0.001$ ), indicating greater variability in red cell size and suggesting early iron depletion (Table 2).

**Table 2: Comparison of red cell indices between Group I and Group II (n=205).**

Red cell indices	Group I (Ferritin $<30$ $\mu\text{g/l}$ ) Mean $\pm$ SD	Group II (Ferritin $\geq 30$ $\mu\text{g/l}$ ) Mean $\pm$ SD	P value
MCV (fl)	88.6 $\pm$ 7.3	89.9 $\pm$ 5.9	0.183
MCH (pg)	30.1 $\pm$ 3.6	30.8 $\pm$ 2.1	0.091
RDW-CV (%)	15.3 $\pm$ 1.6	14.1 $\pm$ 1.6	$<0.001$



**Figure 1: Scatter diagram showing the relationship between RDW-CV% and serum ferritin level (n=205).**

Significant negative correlation present between mean RDW-CV% and serum ferritin level as  $r = -0.347$ ,  $p<0.001$  (Pearson correlation coefficient test) (Figure 1).

### DISCUSSION

This study investigated the relationship between red cell indices and serum ferritin levels among pregnant women with latent iron deficiency. The findings demonstrate a significant negative correlation between RDW-CV% and serum ferritin, indicating that RDW increases as ferritin decreases. This observation supports the hypothesis that RDW is a sensitive and early hematologic marker for iron depletion even before the onset of anemia. In contrast, MCV and MCH values were only slightly lower in the latent iron-deficient group, with no statistically significant difference, suggesting their limited sensitivity in the early stages of iron deficiency.

The results align with previous research highlighting the diagnostic value of RDW as an early indicator of iron-deficient erythropoiesis. Sultana et al found that RDW increased significantly in latent iron deficiency compared with both pre-latent and overt anemic conditions, with sensitivity and specificity rates of 82.3% and 97.4%, respectively.<sup>8</sup> Similarly, De Silva et al reported that RDW was the most sensitive red cell parameter indicating latent iron deficiency among Sri Lankan pregnant women.<sup>10</sup> These findings collectively emphasize RDW's potential as a cost-effective screening tool for detecting early iron deficiency in antenatal settings where biochemical assays are unavailable or unaffordable.

The current study's observation that MCV and MCH values were lower among latent iron-deficient women but

not significantly different from the non-deficient group is consistent with earlier studies. Rabindrakumar et al observed a positive correlation between serum ferritin and MCV, MCH, and MCHC, suggesting that these indices decrease progressively with worsening iron depletion.<sup>6</sup> However, the changes may not reach statistical significance in latent deficiency, when hemoglobin synthesis is not yet compromised. Tiwari et al also found no significant association between ferritin levels and MCV or MCH in pregnant women but reported a significant negative correlation with RDW-CV%, reinforcing RDW's diagnostic superiority in early iron depletion.<sup>7</sup>

The physiological basis for these findings lies in the gradual depletion of iron stores, which initially affects the uniformity of erythrocyte production. As iron becomes insufficient for consistent hemoglobin synthesis, erythropoiesis yields red cells of variable size, reflected as increased RDW. Only with sustained deficiency do MCV and MCH decline significantly. Therefore, RDW elevation precedes microcytosis and hypochromia, marking the transition from latent to overt iron deficiency.<sup>11</sup> This early variability in red cell morphology may serve as a practical indicator of compromised iron supply to the marrow.

The present findings also demonstrate that younger maternal age, advanced gestational age, and lack of iron supplementation were significantly associated with LID, which corroborates earlier literature. Studies from Bangladesh and other low- and middle-income countries have identified short inter-pregnancy intervals, insufficient antenatal supplementation, and increasing gestational age as predictors of iron depletion during pregnancy.<sup>12</sup> These demographic trends reflect the physiological demands of repeated pregnancies and inadequate iron replenishment between gestations.

RDW's value as a diagnostic parameter extends beyond anemia detection. Park et al and Lee et al showed that RDW not only identifies subclinical iron deficiency but also predicts clinical outcomes in various conditions, suggesting its potential as a broader marker of systemic iron status and erythropoietic function.<sup>13,14</sup> In obstetric care, this finding has critical implications: integrating RDW interpretation into routine antenatal blood count assessments could enable earlier identification of women at risk, facilitating prompt dietary counselling or supplementation.

Despite strong evidence for RDW's predictive role, its clinical application requires caution. Variability in instrumentation, reference ranges, and population characteristics can influence RDW interpretation. Fava et al emphasized the necessity of establishing laboratory-specific reference intervals due to inter-laboratory variability.<sup>15</sup> Hence, local validation of cutoff thresholds is essential before RDW can be routinely used for diagnostic decision-making.

Overall, the study reinforces the notion that latent iron deficiency is common even among non-anemic pregnant women, and that RDW provides a simple, inexpensive, and effective means of early detection. Incorporating RDW into antenatal screening protocols could improve iron deficiency management, particularly in resource-limited settings where ferritin assays are unavailable.

This study has few limitations. This study's cross-sectional design restricts causal inference between red cell indices and iron depletion. Serum ferritin was the sole biochemical marker used, which, although reliable, can be influenced by inflammation or infection. Additionally, dietary intake and compliance with iron supplementation were not thoroughly quantified. Finally, as the study was conducted in a single tertiary hospital, the findings may not be generalizable to all pregnant populations in Bangladesh.

## CONCLUSION

The study establishes a significant inverse correlation between RDW-CV% and serum ferritin levels among pregnant women with latent iron deficiency, underscoring RDW's potential as a simple and cost-effective screening tool for early iron depletion. While MCV and MCH showed limited diagnostic sensitivity, RDW exhibited consistent predictive value, supporting its incorporation into routine antenatal hematological evaluations. Early detection of LID through such hematologic indices may facilitate timely supplementation and prevent progression to overt anemia, thereby improving maternal and fetal outcomes.

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