

Prediction of Iron Deficiency by Red Cell Distribution Width, Mean Corpuscular Volume and Haemoglobin Concentration in Pregnant Women

Sultana GS^a, Haque SA^b, Mishu FA^c, Muttalib MA^d, Rahman Q^e

Abstract

Background: Red cell distribution width (RDW) is a routine parameter in fully automated hematology auto analyzer, can give the idea of iron deficiency before haemoglobin and mean corpuscular volume in early iron deficiency or latent stage. Patient can be benefited by doing complete blood count including RDW for the diagnosis of early iron deficiency as a cheaper test than iron profile. This study was aimed to predict early iron deficiency by RDW, mean corpuscular volume and haemoglobin concentration in pregnant women.

Methods: In this study, 190 pregnant women were included from Gynae and Obstetric outdoor of Bangabandhu Sheikh Mujib Medical University from august 2008-2009. Complete blood count including haemoglobin percentage, mean corpuscular volume and RDW and iron profile were done. RDW was compared with haemoglobin concentration and mean corpuscular volume in various stages of iron deficiency.

Results: RDW was more significant than haemoglobin concentration in latent iron deficiency when haemoglobin level was normal ($p < 0.05$). In mild and moderate iron deficiency anemia, RDW was increased progressively though haemoglobin level was reduced. RDW was more significant than mean corpuscular volume level in latent iron deficiency, mild and moderate iron deficiency anemia. The difference of mean corpuscular volume and RDW was statistically significant ($p < 0.05$) in latent iron deficiency, mild iron deficiency anaemia and moderate iron deficiency anaemia (p value of 0.001, 0.001 and 0.011). In this study RDW had sensitivity 82.3% and specificity 97.4%. haemoglobin concentration and mean corpuscular volume had sensitivity 56.6% and 29.2% and specificity 90.9% and 98.7% respectively. Based on the receiver-operator characteristic (ROC) curves RDW had the best area (0.925) under curve compared to haemoglobin and mean corpuscular volume.

Conclusion: Latent iron deficiency without other existing disease like haemoglobinopathy, early folate / vit B12 deficiency could be predicted early by increased RDW when haemoglobin concentration and mean corpuscular volume were normal.

Key words: Iron deficiency anemia, red cell distribution width.

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Introduction

Iron deficiency anemia (IDA) is a common cause of anemia and one of the most important contributing factors to the global burden of the disease. ¹According to Center for Disease Control and Prevention, about 8 million American women during child bearing are iron deficient. ² Jamil et al found that the prevalence of anaemia in pregnant women of Bangladesh was 38.8%. ³ IDA is the predominant cause of anemia in pregnancy and early detection of iron deficiency (ID) at low cost is essential. ^{4,5} For detection of ID, some biochemical tests like iron profile, zinc protoporphyrin etc are used but those are costly and it is not advised to the pregnant women routinely. Red cell distribution width (RDW) is a quantitative measure of red cell size variation. It is a

routine parameter which is included in complete blood count (CBC) that can give the idea of early ID before other tests to become positive, as anisocytosis is the earliest morphologic changes in IDA. RDW can express the variation of different population of cells and assess the percentage of cells falling above or below the given mean corpuscular volume (MCV) threshold and flag the presence of an increased number of microcytes or macrocytes.⁶ Early ID only has high RDW because early ID is not associated with anemia or microcytosis.⁷ In prelatent and latent ID, haemoglobin concentration and MCV are normal.⁸ But in latent ID, RDW would be expected to increase because a microcytic population of cells appears in the blood.^{7, 9} RDW increases at minimum four weeks before MCV, thus leads to early detection of ID.⁸ RDW also increases before hemoglobin concentration falls.⁸ MCV is increased slightly in normal pregnancy, so may lead to misinterpretation of microcytosis. Mean corpuscular haemoglobin and mean corpuscular haemoglobin concentrations are reducing only when anemia is severe or established iron deficient women entered in pregnancy. During latent stage few microcytes may appear in peripheral blood film thus RDW would expect to increase during this period.^{7, 9}

During normal pregnancy the serum iron, percentage saturation and total iron binding capacity (TIBC) have less diagnostic value because during this period serum iron and percentage saturation falls and TIBC increases in an iron replete women like ID.^{5, 7} Serum ferritin is the gold standard for diagnosing IDA but it is costly, may give misinterpretation due to physiological reduction during normal pregnancy and falsely elevated as an acute phase reactant.² RDW is less explored in Bangladesh but Uddin et al showed the value of RDW as a diagnostic tool in IDA and various congenital haemoglobin disorders.¹⁰ But no study was done to see the role of RDW in detection of IDA during pregnancy in Bangladesh. The aim of this study was to evaluate whether RDW can predict iron deficiency before haemoglobin concentration and MCV during pregnancy.

Methods

This cross sectional study was conducted in Department of Clinical Pathology in Bangabandhu Sheikh Mujib Medical University, Dhaka from august 2008-2009. The aim of this study was to see whether RDW can predict iron deficiency before haemoglobin concentration and

MCV during pregnancy. Total 190 pregnant women were enrolled in the study. After taking ethical permission from BSMMU ethical board, all pregnant women attended in Obstetrics and Gynae outdoor during their prenatal visit were included after scrutinizing inclusion and exclusion criteria. About 2 ml blood was taken in ethylene diamine tetra acetic acid tube for CBC and another 2 ml in a plain tube for iron profile. Iron profile was done in all the cases and categorized as Group I/ iron deficient group (serum ferritin level < 12 ng/ml) and Group II / non iron deficient group (serum ferritin 12 to 200 ng/ml).^{11, 12} CBC including RDW was done in both groups. Then all the pregnant women of group I were categorized as prelatent ID, latent ID, mild and moderate IDA.^{9, 13} Pregnant women were identified as iron deficient (Group-I= 113) and non iron deficient (Group-II=77). Mean corpuscular volume level <76.0 fl and Hb <11.0 g/dl were considered as reduced and RDW coefficient of variation level >14.5% were considered as increased.¹⁴ Then all data were analyzed by standard statistical method using statistical package for social science.

Results

In this study age of the women was ranged from 18-38 years in both groups and mean was 27+ 5.4 (+SD) in group I and 27+4.0 (+SD) in group II.

Hb level was not reduced in pre-latent and latent ID groups, but reduced in 100% in mild IDA (n=38) groups and moderate IDA (26) groups and 9.1% in non ID (n=7) group. RDW-CV was increased 12.5% in pre-latent ID (n=1) groups, 82.9% were in latent ID (34) groups, 32(84.2%) were in mild IDA, 26(100%) were in moderate IDA and 2(2.6%) in non ID group (Table I).

MCV was not reduced in pre-latent ID, reduced in 4.9% in latent ID (n=2) groups, 28.9% in mild IDA (11), 76.9% in moderate IDA (20) and 1.3% in non ID (n=1) group. RDW-CV was increased 12.5% in pre-latent ID (n=1) groups, 82.9% were in latent ID (34), 32(84.2%) were in mild IDA, 26(100%) were in moderate IDA and 2(2.6%) in non ID group (Figure 1).

The difference of Hb level and RDW was statistically significant (p<0.05) in latent ID and mild IDA. p value of 0.001 in latent ID and 0.013 in mild IDA reached from chi square test. The difference of MCV and RDW was statistically significant (p<0.05) in latent ID, mild IDA and moderate IDA. p value of 0.001, 0.001 and 0.011 reached from chi square test.

Table I Difference of Hb and RDW in the diagnosis of IDA

Grade of iron deficiency	N	Hb g/dl		RDW-CV%		Chi value	P value
		n	%	n	%		
Group I							
Pre-latent iron deficiency	8	0	0.0	1	12.5	1.07	0.500 ^{ns}
Latent iron deficiency	41	0	0.0	34	82.9	58.08	0.001 ^s
Mild iron deficiency anaemia	38	38	100.0	32	84.2	6.51	0.013 ^s
Moderate iron deficiency anaemia	26	26	100.0	26	100.0	-	-
Group II							
Non Iron deficient	77	7	9.1	2	2.6	2.95	0.083 ^{ns}

Hb level: Normal: ≥ 11 g/dl, Reduced <11 g/dl RDW-CV level: Increased: >14.5 %

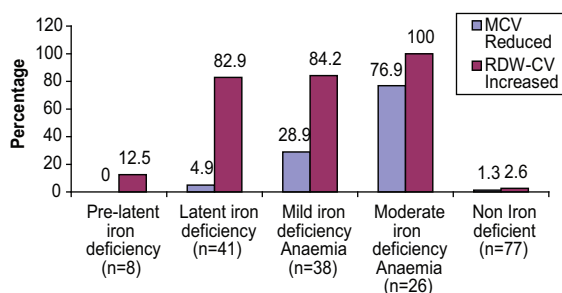


Figure 1 Bar diagram showing difference of MCV and RDW in the diagnosis of IDA

The validity test of Hb (g/dl), MCV (fl) and RDW (%) for detection of ID was confirmed by calculating sensitivity, specificity, accuracy, positive and negative predictive values by using the standard formula. The complete result is shown in Table II.

Table II Sensitivity, specificity, accuracy, positive and negative predictive values of the Hb (gm/dl), MCV (fl) and RDW (%) in diagnosis of IDA (n=190).

Validity test	Hb(gm/dl)	MCV (fl)	RDW (%)
Sensitivity	56.6	29.2	82.3
Specificity	90.9	98.7	97.4
Accuracy	70.5	57.4	88.4
PPV	90.1	97.1	97.9
NPV	58.8	48.7	78.9

Receiver-operator characteristic (ROC) curve of Hb, MCV and RDW for prediction of ID were plotted. The area under the ROC curves for the ID predictors is depicted in Table III.

Table III ROC curve of Hb, MCV and RDW for prediction of ID

	Area under the ROC curve	95% Confidence interval (CI)	
		Lower bound	Upper bound
Hb(gm/dl)	0.140	0.09	0.19
MCV (fl)	0.230	0.16	0.30
RDW(%)	0.925	0.89	0.97

Based on the ROC curves RDW had the best area under curve compared to Hb and MCV level. ROC were constructed using RDW value of the women among two groups, which gave a RDW cut off value of $>14.5\%$ as the value with a best combination of sensitivity and specificity for microcytic hypochromic anaemia. At this RDW cut-off value of $>14.5\%$, the sensitivity and specificity of RDW in diagnosing microcytic hypochromic anaemia was found to be 82.3% and 97.4%, respectively with correctly classified 88.4% of the women (Figure 2).

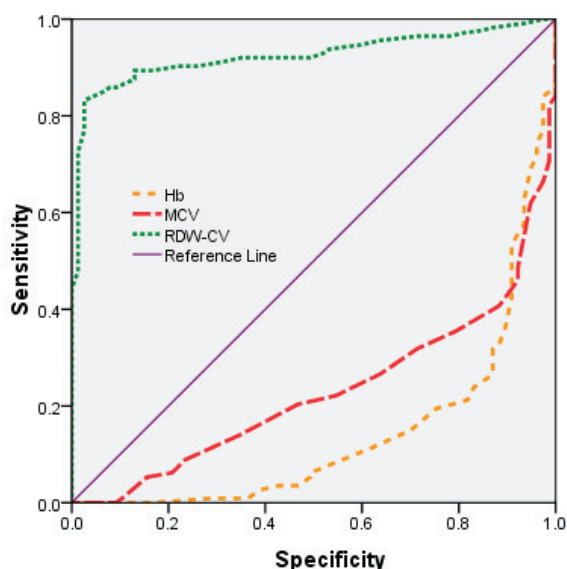


Figure 2 ROC of Hb, MCV and RDW for prediction of ID

Discussion

IDA in pregnancy produces various ill effects both for mother and child therefore early diagnosis of anemia during pregnancy is essential.¹⁵ Due to physiologic alteration of plasma volume and red cell mass in pregnancy, Hb levels are unreliable and mild to moderate ID may be misdiagnosed due to increased MCV.² Thus routine parameters are only useful in the detection of overt deficiency.¹¹

Levels of Hb, MCV were decreased progressively with the progression of ID while RDW was increased. In prelatent and latent ID, Hb levels were not reduced and mean Hb levels were 11.50 ± 0.34 g/dl and 11.61 ± 0.51 g/dl. In mild and moderate IDA mean Hb levels were 10.48 ± 0.30 g/dl and 8.94 ± 0.83 g/dl. In non ID, mean Hb level was 12.23 ± 1.03 g/dl. Difference was statistically significant between two groups that correspond to the study done by Thangaleela and Vijayalakshmi.¹⁶ Mean MCV reduced only in mild and moderate IDA but prelatent, latent and non ID groups MCV were normal. Uchida¹³ and Thompson et al¹⁷ also found more or less same MCV levels.

RDW was progressively increased in prelatent, latent, mild and moderate IDA. Mean RDW was $13.35 \pm 1.08\%$ in prelatent ID, $14.88 \pm 0.77\%$ in latent ID, $15.98 \pm 1.65\%$ in mild IDA, $18.03 \pm 2.22\%$ in moderate IDA,

whereas $13.21 \pm 0.70\%$ was found in non ID. Difference found between group-I and group-II were statistically significant ($p=0.001$). In prelatent and non ID, RDW were almost same and normal. Similar result was also observed by Uchida.¹³ Thompson et al¹⁷ also found mean RDW in ID group was $18.3 \pm 3.9\%$ but in non ID group $15.5 \pm 2.7\%$. Park and Kim found RDW was increased in women with early ID and iron therapy. They concluded that RDW could be used as a sensitive parameter of red cell anisocytosis.¹⁸

RDW was increased in 26 women (100%) of moderate IDA, 32 women (84.2%) of mild IDA and 34 women (82.9%) of latent ID but RDW increased only in 1 woman (2.5%) of prelatent and 2 women (2.6%) of non ID. In prelatent and non ID group RDW may be increased due to co-existence of other nutritional deficiency like folate or vit B12.¹⁹ Mean RDW in both pre latent and non ID groups were normal. The difference was statistically significant between two groups ($p = 0.001$). Uchida¹³ also found increased RDW in latent and IDA.

Hb level was not reduced in prelatent, latent ID pregnant women while RDW was increased in 1 pregnant woman (12.5%) and 34 women (82.9%) of prelatent and latent ID. In mild and moderate IDA 38 women (100%) and 26 women (100%) had reduced Hb level but RDW was increased in 32 women (84.2%) and 26 women (100%). Therefore RDW was more significant than Hb level in latent ID when Hb level was normal. In mild and moderate IDA, RDW was increased progressively though Hb level was also reduced. But Hb is less specific indicator of ID.²⁰ Uchida, 1989 also found normal Hb level with increased RDW in latent ID and reduced Hb level with increased RDW in IDA.¹³ In early ID without anemia and IDA was infrequently identified by increased level of RDW by Osborne et al.⁷ He also found RDW was increased in 4 out of 24 womens of ID without anemia and 15 out of 49 womens with anemia.

MCV was reduced in 2 women (4.9%) of latent ID, 11 women (28.9%) with mild IDA, 20 women (76.9%) with moderate IDA while RDW was increased in 34 (82.9%), 32 (84.2%) and 26 (100%) women with latent ID, mild and moderate IDA. The difference of MCV and RDW level was statistically significant ($p- 0.001, 0.001$ and 0.011) in latent, mild and moderate IDA. But not significant in prelatent and non ID group. Thompson et

al¹⁷ also found increased RDW with reduced MCV in 23 subjects out of 48 iron deficient patients. Osborne et al⁷ found RDW was increased in 7 patients with normal MCV. RDW was abnormal in 26% women and MCV was abnormal in 24% patient. Uchida¹³ also found MCV reduced only in IDA but RDW was increased in latent and IDA group.

In this study Hb level had sensitivity 56.6% and specificity 90.9% with accuracy 70.5%, PPV 90.1% and NPV 58.8% for diagnosis of iron deficiency. Casanova, Sammal and Macones also found low sensitivity (42.6%) and high specificity (86.2%) in IDA in pregnancy for Hb and classified 71.6% as ID, but the sensitivity and specificity was less than RDW, which was almost consistent with the present study.²¹

In the present study MCV had sensitivity 29.2% and specificity 98.7% for diagnosis of iron deficiency. Uchida also found low sensitivity (56.3%) and high specificity (91%).¹³ Thompson et al¹⁷ also concluded that MCV was neither sensitive to screen iron deficiency and found low (53%) sensitivity but high specificity (84). RDW had the highest sensitivity (82.3%) and specificity (97.4%) for diagnosis of iron deficiency. Accuracy, PPV and NPV was found 88.4%, 97.9% and 78.9% respectively. Aulakh et al²², found almost same sensitivity 81.0% and NPV 72.4% but the specificity and PPV was low 53.4% and 63.0%. Thompson et al¹⁷ also found RDW was not sensitive indicator of ID in pregnancy and found only 16.4% sensitivity. Whereas vanZeben et al²³ found sensitivity of RDW was 94% and specificity 59% and concluded that RDW was important than serum ferritin in infection, inflammation and tissue damage. Thompson et al¹⁷ found sensitivity of RDW was 71%. Mahu, Leclercq and Suquet found sensitivity and specificity was best for RDW and not good for MCHC for epidemiological survey of ID.²⁰ Casanova, Sammal and Macones found RDW more than 15% has sensitivity and specificity 85.1% and 46.8% and correctly classified 72.3% women with iron deficiency. They found area under ROC curve for RDW was 0.8. In this study area under curve was 0.90 that was almost same.

Limitation

Women with hemoglobinopathies, early folic acid / vit-B₁₂ deficiency and chronic disorder, where RDW also increases could not be excluded properly.

Conclusion

Most women in the developing country enter pregnancy with little or no iron reserve and are very prone to develop IDA. In this study RDW had the highest sensitivity (82.3%) and specificity (97.4%) for diagnosis of iron deficiency. Based on the ROC curves RDW had the best area (0.9) under curve compared to Hb and MCV level. In latent iron deficiency increased RDW was significant than other test like Hb and MCV. In mild and moderate iron deficiency anaemia RDW was significant than MCV. RDW is one of the parameter of CBC that first becomes abnormal then Hb% and MCV in IDA. If RDW is requested with all other parameter of CBC then physicians can correlate RDW with other parameter and get the idea of IDA by reducing costly investigation like iron profile.

Conflict of interest: Nothing to declare.

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