

## Role of red cell distribution width (RDW) in the detection of iron deficiency anaemia in pregnancy within the first 20 weeks of gestation

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### Abstract

Iron deficiency anemia is common problem during pregnancy. Red cell size variation (anisocytosis) is the earliest morphologic changes in iron deficiency anemia. Red cell distribution width is a quantitative measure of red cell size variation and it can give the idea of early iron deficiency before other test to become positive. 190 pregnant women were included in this study. Red cell distribution width was compared between iron deficient & non-iron deficient pregnant women. Red cell distribution width also compared with Hb level, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration and peripheral blood film in prelatent iron deficiency, latent iron deficiency, mild and moderate iron deficiency anemia. Red cell distribution width had sensitivity 82.3% and specificity 97.4%. Whereas Hb level, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration and peripheral blood film all had 56.6%, 29.2%, 68.1%, 15% and 38.9% sensitivity but specificity was 90.9%, 98.7%, 83.1%, 96.1% and 98.7% in the detection of iron deficiency. Red cell distribution width appears to be a reliable and useful parameter for detection of iron deficiency during pregnancy.

### Introduction

Anemia is a common problem during pregnancy and it affects 25% to 50% of the world population and 50% of pregnant women<sup>1</sup>. Iron deficiency anemia (IDA) is the predominant cause of anemia in pregnancy and early detection of anemia at low cost is essential. Red cell distribution width (RDW) is a new, routine parameter in fully automated hematology analyzer, which is included in complete blood count (CBC). RDW can give the idea of early changes in RBC, which is accompanied in iron deficiency anemia<sup>2</sup>. Women can be benefited by doing CBC including RDW for the diagnosis of early iron deficiency. Usually CBC is advised by the physician to all pregnant women for their antenatal checkup, which is less costly than iron profile. Physician can get the idea of early iron deficiency from RDW by advising CBC as a simple test. During pregnancy erythrocyte hypochromia and microcytosis are less prominent than non-pregnant, even in moderate iron deficiency<sup>3</sup>. Red cell indices (MCV, MCH and MCHC) are mean value, which cannot express the small variation of red cells size, which is accompanied in early iron deficiency<sup>4</sup>. Whereas RDW can express the small variation of different population of red cell size<sup>5</sup>. In prelatent and latent iron deficiency, Hb% and MCV are normal. In latent iron deficiency RDW would be expected to increase because a microcytic population of cells

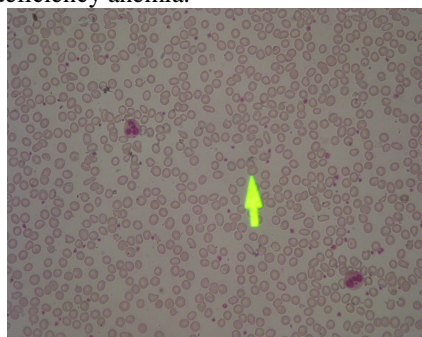
appears in the blood<sup>6</sup>. Again MCV is increased slightly in normal pregnancy, so may lead to misinterpretation of microcytosis. MCH and MCHC are reducing only when anemia is severe or established iron deficient women entered in pregnancy<sup>7</sup>. As anisocytosis is less prominent in pregnancy and also in early iron deficiency anemia, Peripheral Blood Film (PBF) examination gives less information though it needs expert's opinion<sup>3,8</sup>. Iron profile is expensive and time consuming. During normal pregnancy serum iron, serum ferritin and percentage saturation falls and TIBC increases physiologically<sup>3,7,8</sup>. Though serum ferritin is gold standard for iron deficiency anemia but it is costly, may give misinterpretation due to physiological reduction and falsely elevated as an acute phase reactant<sup>3</sup>.

For this RDW is better guide than those tests in early iron deficiency. RDW is less explored in Bangladesh but Uddin et al<sup>9</sup> showed the value of RDW as a diagnostic tool in IDA and various congenital haemoglobin disorders. The aim of this study is to determine the role of RDW in diagnosing early IDA in pregnancy.

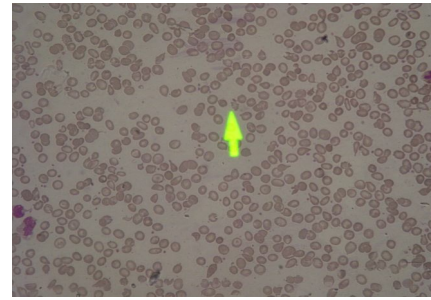
### Materials and Methods

This cross-sectional study was enrolled in dept of Clinical pathology and Obstetrics and Gynae outdoor, Bangabandhu Sheikh Mujib Medical University (BSMMU) from August 2008 to 2009.

190 pregnant women within the first 20 weeks of gestation were included after scrutinizing inclusion and exclusion criteria. About 6 ml blood was collected through an aseptic venepuncture from antecubital vein. 2ml blood was taken in EDTA tube for complete blood count including RDW and ESR. About 4 ml blood was taken in a clean, dry plain test tube for serum iron profile. A drop of blood was taken on a glass slide for PBF. Hb, MCV, MCH, MCHC, RDW, PBF and iron profile were done. Then all the pregnant women were categorized as Group I/iron deficient group (serum ferritin level <12 ng/ml) and Group II/non iron deficient group (serum ferritin 12 to 200ng/ml)<sup>10,11</sup>. Group II considered as control. Group I again categorized as pre-latent iron deficiency (Transferrin saturation  $\geq$ 16%, Hb normal), latent iron deficiency (Transferrin saturation <16%, Hb normal), mild iron deficiency anaemia (Transferrin saturation <16%, Hb 10-10.9 gm/dl), moderate iron deficiency anaemia (Transferrin saturation <16%, Hb 7-9.9 gm/dl)<sup>6,12</sup>. Women with severe anaemia were excluded. RDW >14.5% is considered as abnormal<sup>13</sup>. Serum ferritin level is the gold standard in the diagnosis of iron deficiency anaemia in pregnancy<sup>14</sup>. Women with serum ferritin normal (12-200ng/ml) or raised (>200ng/ml), serum iron low (<70 $\mu$ g/dl), TIBC normal (250-435 $\mu$ g/dl) or low (<250  $\mu$ g/dl) and ESR >40 mm/hr suggestive of anemia of chronic disorder were excluded<sup>15,16</sup>. Pregnant women with leucocytosis (TC>17.1 $\times$ 10<sup>9</sup>/L) considered as acute infection was also excluded<sup>17</sup>. In IDA, RBC became microcytic hypochromic, poikilocyte, particularly tailed and elongated elliptical form were found<sup>6,18</sup> (Figure 1 & 2). Then the findings of laboratory investigation were recorded in a predetermined data collection sheet. Data were evaluated by standard statistical methods. Analysis was done by SPSS (Statistical package for social science) by applying appropriate formula. Sensitivity, specificity, accuracy, positive predictive values (PPV) and negative predictive values (NPV) of RDW, unpaired t test, Chi square test and ANOVA test were calculated in diagnosing iron deficiency anemia.



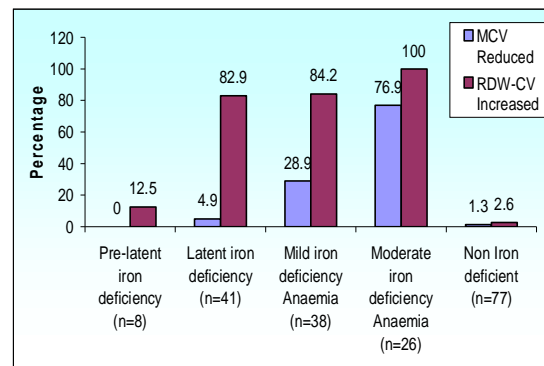
**Fig. 1:** PBF of case no 12 (Mild IDA) showing elongated and tear drop cells. Hb-10.3 gm/dl, MCV-78fl, RDW-18% (X 400).



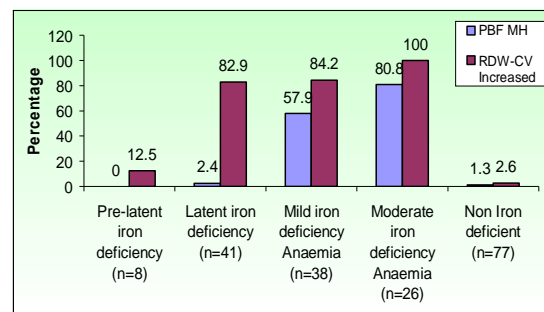
**Fig. 2:** PBF of case no 36 (Moderate IDA) showing some elongated cells. Hb-8gm/dl, RDW 19.5%, MCV-64fl (X 400).

## Results

RDW was compared between group I and group II. RDW also compared with Hb level, MCV, MCH, MCHC and PBF in prelatent iron deficiency, latent iron deficiency, mild and moderate IDA. RDW was statistically significantly ( $P<0.05$ ) increased in iron deficient then non iron deficient. Again RDW was statistically significantly increased ( $P<0.05$ ) than Hb level, MCV, MCH, MCHC and PBF in latent iron deficiency. In mild and moderate IDA, RDW was statistically significantly increased than MCV, MCHC and PBF (Figure 3&4). Validity of RDW, Hb, MCV, MCH, MCHC and PBF was done by calculating sensitivity, specificity, PPV, NPV and accuracy (Table I). In this study RDW had high sensitivity 82.3% than other test. But the specificity is slightly lower (97.4%) than PBF & MCV (98.7%).



**Fig. 3:** Bar diagram showing difference of MCV and RDW-CV in the diagnosis of Iron deficiency of anaemia.



**Fig. 4:** Bar diagram showing difference of PBF and RDW in the diagnosis of Iron deficiency of anaemia.

**Table I:** Sensitivity, specificity, accuracy, positive and negative predictive values of the Hb (gm/dl), MCV (fl), MCH(pg), MCHC (gm/dl), RDW (%) and PBF in diagnosis of IDA (n=190).

Validity test	Hb	MCV	MCH	MCHC	RDW	PBF
Sensitivity	56.6	29.2	68.1	15.0	82.3	38.9
Specificity	90.9	98.7	83.1	96.1	97.4	98.7
Accuracy	70.5	57.4	74.2	47.9	88.4	63.2
PPV	90.1	97.1	85.6	85.0	97.9	97.8
NPV	58.8	48.7	64.0	43.5	78.9	52.4

## Discussion

During pregnancy women are prone to develop iron deficiency. Detection of latent iron deficiency is important but usually difficult to detect. Routine parameters are only useful in the detection of overt deficiency<sup>18</sup>. During pregnancy even mild and moderate iron deficiency may be misdiagnosed due to increase MCV and less findings found in PBF<sup>3</sup>. Due to physiologic alteration of plasma volume and red cell mass in pregnancy, Hb level are unreliable<sup>3</sup>. Hb determination is neither sensitive nor specific as a screening test for iron deficiency<sup>19</sup>. During latent stage few microcyte may appear in PBF thus RDW would expect to increase during this period<sup>6,20</sup>.

In this study Hb level was not reduced in prelatent, latent iron deficient pregnant women while RDW was increased in 1 pregnant women (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.

MCV was reduced in 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 between prelatent and NID group (Figure 3).

In PBF study RBC morphology was seen in all grade of iron deficiency. Microcytosis and hypochromia was found in 21 pregnant women (80.8%) out of 26 moderate IDA and 22 women (57.9%) out of 38 in mild IDA. In latent iron deficiency only 1 women (2.4%) had MH. Whereas RDW was increased in 100% case of moderate IDA, 84.2% (32 cases) with mild IDA and 82.9%

(34) case of latent ID. So the difference of PBF study and increased RDW was significant in latent, mild and moderate IDA ( $p=0.001$ ,  $0.011$  and  $0.025$ ) (Figure 4).

In this study Hb level had sensitivity 56.6% and specificity 90.9% with accuracy 70.5% for iron deficiency. Casanova, Sammal and Macones<sup>1</sup> also found low sensitivity (42.6%) and high specificity (86.2%) in IDA in pregnancy for Hb and classified 71.6% as iron deficient, but sensitivity and specificity was less than RDW, which was almost consistent with the present study.

In this study MCV had sensitivity 29.2% and specificity 98.7%. Uchida<sup>12</sup> found low sensitivity (56.3%) and high specificity (91%). Thompson et al.<sup>21</sup> also found low (53%) sensitivity but high specificity (84%). In this study MCH, MCHC also had low sensitivity 68.1% and 15.0% with specificity of 83.1% and 96.1%.

Sensitivity of PBF in this study was low 38.9% but high specificity 98.7%. Viswanath et al.<sup>4</sup> also found low sensitivity (48.31%) of PBF and high specificity (90.9%). The result was almost similar with this study.

In this study RDW has the highest sensitivity (82.3%) and specificity (97.4%). Accuracy, PPV and NPV was found 88.4%, 97.9% and 78.9% respectively (Table I). Aulakh et al<sup>22</sup> found almost same sensitivity 81.0% and NPV 72.4% but the specificity and PPV was low 53.4% and 63.0%. vanZeben et al<sup>13</sup> 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 al.<sup>21</sup> found sensitivity of RDW was 71%. But Casanova, Sammal and Macones<sup>1</sup> found RDW more than 15% has sensitivity and specificity 85.1% and 46.8% and correctly classified 72.3% women with iron deficiency.

This study has some limitation. Haemoglobin electrophoresis, serum Vit B<sub>12</sub> or folate studies were not done to exclude hemoglobinopathies, early macrocytosis due to folic acid or Vit B<sub>12</sub> deficiency where RDW may increase. Anaemia of chronic disorder also could not be excluded properly by appropriate investigation where serum ferritin may misinterpret.

**Conclusion:** Iron deficiency anemia in pregnancy produces various ill effects both for mother and foetus. For prevention of iron deficiency early diagnosis is essential. Iron deficiency and IDA without other complicating disease could be screened out early by increased RDW when Hb, RBC indices and PBF were normal. RDW can give

the idea of iron deficiency but for final diagnosis serum ferritin should be done. In a mass examination in tertiary hospital where automated analyzer is available, RDW is a simple, cost effective and non invasive technique that should facilitate the detection of early iron deficiency anemia before expert's opinion of PBF or iron profile test are available.

### Acknowledgement

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