

ROLE OF CBC WITH SPECIAL REFERENCE TO RDW-CV IN DETECTING EARLY IRON DEFICIENCY ANAEMIA IN PREGNANCY

Sumita Tripathy¹, Bagmi Mishra²

¹Assistant Professor, Department of Pathology, M.K.C.G. Medical College, Berhampur.

²Resident, Department of Pathology, M.K.C.G. Medical College, Berhampur.

ABSTRACT

BACKGROUND

Anaemia appears to be the rule rather than exception in our population. Females are most vulnerable and in pregnancy a woman is further pushed to an edge in this regard. Iron deficiency a preventable cause is the most common factor. Screening of the pregnant woman as early as possible and correcting anaemia is the priority of every clinician. Evaluation of CBC with the help of an automatic cell counter is immensely helpful in mass screening, much so in pregnant women where early detection with appropriate treatment will avoid many untoward effects both in mother and newborn.

MATERIALS AND METHODS

This is a Prospective study of pregnant women up to 20 weeks gestation. The Haematological evaluation done in Dept. of Pathology using 5-part cell counter, System XT-2000i. In all cases PS study done along with iron profile wherever possible. All the data were statistically analysed.

RESULTS

A total of 187 cases were analysed. Very strong association were observed between RDW-CV, Hb, MCV, MCH, MCHC & TRBC with IDA, in decreasing order of significance. RDW-CV was raised in 82.3% cases with iron deficiency and 22% cases in non-iron deficient cases.

CONCLUSION

Though Iron Profile is gold standard for detection of iron deficiency anemia, RDW-CV is a reliable and useful parameter for screening and detecting early iron deficiency anemia during pregnancy.

KEYWORDS

RDW-CV, Pregnant Women, Iron Deficiency Anaemia.

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BACKGROUND

WHO estimates the number of anaemic people worldwide to be a staggering two billion and that approximately 50% of all anaemia can be attributed to iron deficiency. The most dramatic health effects of anaemia, i.e., increased risk of maternal and child mortality due to severe anaemia, have been well documented.¹ National family health survey data shows prevalence of anaemia among woman of reproductive age in India is 56.1% whereas in Odisha 62.8%.² Iron deficiency anaemia (IDA) is the predominant cause of anaemia in pregnancy and early detection of anaemia at low cost is essential. Red cell distribution width (RDW) is a new, routine parameter in fully automated haematology analyser, which is included in complete blood count (CBC). RDW can give the idea of early changes in RBC, which is accompanied

in iron deficiency anaemia.³ Usually CBC is advised by the physician to all pregnant women for their antenatal checkup, which is less costly than iron profile. 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.⁴ Whereas RDW-CV can express the small variation of different population of red cell size.⁵ In pre-latent and latent iron deficiency, Hb% and MCV are normal. In latent iron deficiency, RDW-CV would be expected to increase because a microcytic population of cells appears in the blood.⁶ MCH and MCHC are reducing only when anaemia is severe or established iron deficient women entered in to pregnancy.⁷ As anisocytosis is less prominent in early iron deficiency anaemia, Peripheral Blood Smear (PBS) examination gives less information though it needs expert's opinion.^{8,9} Though Iron profile is the gold standard, it is expensive and time consuming and falsely elevated as an acute phase reactant.⁸ So, RDW-CV is better guide than those tests in early Iron deficiency. The aim of this study is to determine the role of RDW-CV in diagnosing early IDA in pregnancy.

Aims and Objectives

Haematological evaluation of women in first 20 weeks of pregnancy using automated haematologic analyser with

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Corresponding Author:

Dr. Sumita Tripathy,

Qr. No. 3R/18,

MKCG Medical Campus,

Berhampur-760004, Odisha.

E-mail: sumitatripathy1969@gmail.com

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special reference to RDW-CV in screening Iron Deficiency Anaemia (IDA).

MATERIALS AND METHODS

The cross-sectional prospective study includes all pregnant women below 20th gestational week attending ANC on outpatient basis in the Department of Obstetrics & Gynaecology, MKCG Medical College & Hospital during September 2013 to August 2016. About 2 ml blood was collected through from antecubital vein in EDTA tube for complete blood count. Iron profile and PBS examination done in each case and categorized as test group (Hb level <11 gm%) and control group (Hb>11 gm%).

Case Selection-

Inclusion Criteria-

All pregnant women below 20th gestational age attending OPD for antenatal check-up.

Exclusion Criteria-

Patient refusing iron study, associated haemoglobinopathy, bleeding diathesis or history of blood transfusion within 3 months of ANC visit, with co-existing chronic illnesses or anaemia of chronic disorder or with features of acute infection. Data were evaluated by standard statistical methods.

RESULTS

Patients in first 20 weeks of pregnancy, attending A.N.C accounted for 41.9% of total cases. In present study a total

of 292 ANC cases recorded, out of which 105 cases excluded taking into account the exclusion criteria. 50 out of 187 cases (26.7%) had Hb \geq 11 gm/dl, which is the control group and 137 cases had Hb<11 gm/dl that is the study group. Maximum cases in study group were in the age group of 20-25 years (31.4%) and in control group of 25-30 years (40%). Minimum cases were encountered in the age group of >35 years with percentage of cases in study and control group, been 1.4% and 2% respectively.

Severity of anaemia has been graded as mild, moderate, severe and very severe according to their Hb levels, 10-10.9 gm/dl, 7-9.9 gm/dl, 5-6.9 gm/dl and <5 gm/dl respectively. Maximum number of patients present with moderate degree of anaemia (52.6%) and minimum with very severe degree (2.2%). Based on iron profile out of 137 cases 96 (70.1%) shows IDA but in control group 28 cases shows low iron level (latent/prelatent anaemia).

Iron Study	Hb decreased	Hb normal	Total
Iron deficiency	96	28	=124
Normal	41	22	=63
Total	=137	=50	187

Table 1. Iron Study and Haemoglobin Level

Table 1 shows relationship between Hb with iron study. In present study, level of haemoglobin was found to have a sensitivity and specificity of 71.6% & 34.9% in detecting IDA.

In Study Group, n=137				In Control Group, n=50		
Iron Studies	MCV ↓	MCV-Normal	Total	MCV ↓	MCV-Normal	Total
Iron deficiency	57	39	=96	14	14	=28
Normal	10	31	=41	4	18	=22
Total	=67	=70	137	=18	=32	50

Table 2. Iron Study and MCV

Table 2 shows relation of iron studies and MCV amongst study and control group. Cases with low MCV and low iron were "True Positive", i.e., 57 of 137 cases in test group whereas in control group it is 14 out of 50 cases. Cases with low MCV and normal iron were "False Positive", here, 10 of 137 cases in study group but in control group it is 4 of 50 cases. Cases with normal MCV and low iron were "False

Negative", i.e. 39 of 137 in study group and in control group it is 14 of 50. Cases with normal MCV and normal iron were "True Negative", i.e., 31 of 137 in study group and it is 18 of 50 in control group. Thus 71 of 124 iron deficiency cases had low MCV values whereas only 14 of 63 non-iron deficiency cases had low MCV values.

Cases	Total Cases	Iron Deficient			% + ve	Non-iron Defiant Cases			% + ve	
		No. of cases	MCV ↓	MCV-N		No. of cases	MCV ↓	MCV-N		
Normal	--	--	--	--	--	22	4	18	18	Hb>11gm/dl
Pre/latent	28	28	14	14	50	--	--	--	--	
Mild	54	30	16	14	53.3	24	12	12	50	Hb<11gm/dl
Mod.	72	55	32	23	56.4	17	10	7	59	
Severe	8	8	7	1	87.5	--	--	--	--	
V. severe	3	3	3	--	100	--	--	--	--	
	=187	=124	=72	=52		=63	=26	=37		

Table 3. Distribution of Cases according to their MCV Values in Iron Deficient and Non-iron Deficient Group

The above table denotes distribution of cases according to their MCV values in iron deficient and non-iron deficient groups. MCV can detect iron deficient cases with a sensitivity of 100% in cases with Hb<5 gm%, however MCV is not a sensitive parameter in detecting IDA in cases with mild and moderate anaemia.

In Study Group, n= 137				In Control Group, n= 50		
Iron Studies	RDW-CV Raised	RDW-CV Normal	Total	RDW-CV Increased	RDW-CV Normal	Total
Iron deficiency	79	17	=96	21	7	=28
Non-IDA	9	32	=41	6	16	=22
Total	=88	=49	137	=27	=23	50
Table 4. Iron Studies and RDW-CV						

Table. 4 shows relation of iron studies and RDW-CV in study group and in control group. Cases with raised RDW-CV and low iron were "True Positive", i.e., 79 of 137 in study group and 20 of 50 in control group while raised RDW-CV and normal iron were "False Positive", here, 9 of 137 cases in study group but 66 of 50 in control group. Cases with normal RDW-CV and low iron were "False Negative", i.e., 17 of 137 cases in study group and 7 of 50 in control group. And normal RDW-CV and normal iron were "True Negative", i.e., 32 of 137 cases in study group whereas 16 of 50 in control group. Above data shows 100 (79+21) of 124 (96+28) (80.6%) iron deficient cases had raised RDW-CV, whereas only 15 of 63 (23.8%) non-iron deficient cases had raised RDW-CV.

Cases	Total Cases	Iron deficient			% + ve	Non-iron defiant cases			% + ve	
			RDW-CV	RDW-CV-N		No. of cases	RDW-CV	RDW-CV-N		
Normal	--	--	--	--	--	22	6	16	27.7%	Hb>11 gm/dl
Pre/latent	28	28	21	7	75	--	--	--	--	
Mild	54	30	25	5	83.3	24	4	20	16.7%	Hb≤11gm/dl
Mod.	72	55	52	3	94.5	17	5	12	29.4%	
Severe	8	8	8	8	100	--	--	--	--	
V. severe	3	3	3	3	100	--	--	--	--	
Total	=187	=124	=109	=15		=63	=15	=48		

Table 5. Distribution of Cases According to their RDW-CV Values in Iron deficient and Non-iron Deficient Cases

Table 5 denotes distribution of cases according to their RDW-CV values in iron deficient and non-iron deficient groups. With increase in severity of anaemia, sensitivity of RDW-CV in detecting IDA increases. RDW-CV can detect iron deficient cases in latent and prelatent group with a sensitivity of 75%. Sensitivity in moderate, severe and very severe anaemic cases approaches 100%. Sensitivity is poorer in non-IDA cases.

Iron Study	RDW-CV ↑ MCV ↓	RDW-CV-N MCV-N	RDW-CV ↑ MCV-N	MCV ↓ RDW-CV-N	Total
Iron deficient (n=124)	63	6	46	9	=124
Non-iron deficient cases (n=63)	4	26	11	22	=63
Total	=67	=32	=57	=31	

Table 6. Variation of RDW-CV and MCV in cases

The above table shows 69 of 99 cases were iron deficient and 30 were non-iron deficient cases. 63 cases had raised RDW-CV and low MCV with abnormal iron studies (true positive). 4 cases had raised RDW-CV and low MCV with normal iron studies (false positive). 26 cases had normal RDW-CV and normal MCV with normal iron studies (true negative). 6 cases had normal RDW-CV and normal MCV with abnormal iron studies (false negative). Statistically analysing the above data of RDW-CV & MCV shows sensitivity, PPV, NPV and accuracy of automated haematology analyser was found to be 91.3%, 86.7%, 94%, 81.25% & 89% respectively.

Parameters	Sensitivity	Specificity	PPV	NPV	Accuracy
RDW-CV	80.6	76.2	87	66.7	79.1
MCV	57.3	77.8	83.5	48	64.17
HGB	71.6	34.9	70	44	63.1
RDW-CV CV+MCV	91.3	86.7	94	81.25	89
TRBC	20.2	65	53.2	29.2	35.3
MCHC	25.8	88.9	82	37.8	47
MCH	33	68.2	80.3	34	44.9

HCT	70.16	44.4	71.3	43.1	60.43
RET	16.13	84.1	66.7	33.76	39

Table 7. Statistical comparison of all CBC Parameters

The above table shows of other CBC parameters HCT had highest sensitivity of 70.16% and reticulocyte count had the minimum sensitivity of 16.1%. MCHC had highest specificity of 88.9% and HCT had the minimum specificity of 44.4%. MCHC had highest PPV of 82% followed by HCT (71.3%). TRBC had the minimum PPV of 53.2%. HCT had the highest accuracy of 60.43%. And also, it shows out of all CBC parameters RDW-CV & MCV together had the highest sensitivity, specificity, PPV, NPV & accuracy.

DISCUSSION

Anaemia is an under diagnosed condition with serious negative consequences including bringing down an individual's productivity, affecting the quality of life and thereby affecting the nation's economy. Women are vulnerable to malnutrition and anaemia throughout their life cycle for both biological and social reasons. Anaemia begets anaemia. But it is largely a preventable and easily treatable, warranting an intensified screening effort. By performing more systematic laboratory testing and obtaining interpretive test reports, can aid physicians in better understanding of the aetiopathology of anaemia.

Though iron study has high accuracy and specificity and also can detect early latent and prelatent states, its major disadvantage is high cost, time consuming and available at select centers.

Use of automated cell counter in haematological investigation plays a pivotal role in giving early clue in less time, reduced cost with high precision and accuracy.¹⁰ It is very sensitive in giving RBC indices, mild variation in sizes that usually missed in routine microscopy. RDW is an index of variation in cell size. RDW is a quantitative, not subjective, measure of anisocytosis viewed in complete blood count. Whereas, microscopic classification of erythrocyte size variation, on other hand, is semi quantitative.

In patients with iron deficiency anaemia in treatment, sequential histograms may early evidence the gradual appearance of a new erythrocyte population. Reduced MCV with high RDW CV is consistent with iron deficiency anaemia, where as normal MCV with high RDW CV points towards early iron deficiency.

All the cases in the study group were subjected to thorough history taking and clinical examination. 2 ml of EDTA blood was collected from each subject and was analysed using automated analyser Sysmex XT 2000,¹¹ simultaneously a peripheral blood smear study was also done. Various blood cell parameters were obtained to study the morphological classification of anaemia. Specific tests were conducted to ascertain the aetiology of anaemia whenever required.

In present study a total of 292 ANC cases recorded, out of which 32 cases excluded taking into account the exclusion criteria. Out of 260 cases, 65% cases had Hb% less than 11 gm%. Whereas, 70% of anaemic cases had iron deficiency

anaemia. In aggregate, 66.3% cases were iron deficient, values were comparable with Tiwari et al (2013).¹²

In present study, maximum number of cases belonged to the age group 20-25 years, mean age in present study was 25-26 years. Which, was comparable to studies by Abdelrahman et al (2012),¹³ the mean age in their study was 25.6 years.

Amongst anaemic cases, maximum cases i.e. 52.6% were recorded to have moderate anaemia (Hb% 7-9.9 gm%). In studies by Sultana et al,¹⁴ they registered most cases with mild anaemia i.e. 59.4%.

In this study RDW-CV has the highest sensitivity (80.6) and specificity (76.2%). Accuracy, PPV and NPV was found 87%, 66% and 79.1% respectively which was consistent with Tiwari et al, Sultana et al, Aulakh et al¹⁵ and Sazawal et al¹⁶ shows sensitivity of 82.4%, 82.3%, 81% and 76.5% respectively. However, specificity was more comparable to Tiwari et al, Abdelrahman et al, Sazawal et al and Alquaiz et al¹⁶ i.e. 75.8%, 73.7%, 73.1% and 71% respectively.

Sensitivity of RDW-CV in iron deficient anaemia increases with severity of case. Table 5 shows severity of RDW-CV as high as 75% in prelatent and latent cases as compared to 69.4% in studies done by Sultana et al. the sensitivity increases with degree of anaemia reaching 100% in severe and very severe cases. Sultana et al found 84.2% and 100% cases with raised RDW-CV in mild & moderately anaemic patients respectively, which was comparable to present study, which came out to be 83.3 & 100% respectively. The gradation in sensitivity values suggest that it is a very good screening parameter for IDA. The 'p-value' of RDW-CV in detecting IDA was evaluated using Person's Chi square which is highly significant with 'p-value≤0.01'.

Several cases were encountered in which haemoglobin level was ≤11 gm/dl with abnormal iron studies but RDW-CV was not raised (false negative), these are the cases which are in the compensatory iron deficiency state and degree of anaemia has not severely affected the size of RBCs.

False positive cases in study group is also alarming and a simultaneous peripheral smear study is always recommended along with a repeat CBC at an interval of 7-10 days. False positive cases in control group can again be explained by transient recovery or in a convalescence from prolonged compensatory iron deficient state.

In present study, MCV had sensitivity of 57.3% which was similar to Uchida et al and Thomson et al. specificity in this study was 77.8% which was close to Wian et al and Thomson et al. This gives an impression that automated analysers are not sensitive enough to detect early changes in RBC volume accompanied with microcytic anaemias because the mean values remain undisplaced until the anaemia is severe enough to affect most of the red cells and hence, MCV values may be misleading.

Table 3 shows sensitivity of MCV increases with degree of anaemia. Sensitivity of MCV in prelatent/latent, mild and

moderate anaemia were poor with no gross difference in sensitivity values. Sultana et al found 76.9% cases with reduced MCV in cases with moderate anaemia, however, in present study we found 56.4% cases in this group. The 'p-value' of MCV in detecting IDA is ≤ 0.001

In this study Hb level had sensitivity of 71.6% and specificity of 34.9% with and accuracy of 63% respectively. Sultana et al found sensitivity of 56.6% and specificity 90.9% with accuracy 70.5% for iron deficiency.

Table 6 shows, RDW-CV and MCV when considered together had a better statistical correlation with IDA. The 'p-value' of \uparrow RDW-CV and \downarrow MCV in IDA was found ≤ 0.01 .

Table. 7 shows the comparison of other CBC parameters in relation to iron deficiency anaemia. PCV though has a better sensitivity compared to MCV, its significance in relation to IDA was to be low in present study. (P-value-0.029)

All CBC parameters are important and very strong association were observed between RDW-CV, Hb, MCV, MCH, MCHC & TRBC with IDA, in decreasing order of significance. Sensitivity of RDW-CV was maximum of all the parameters in prelatent/latent cases & gradual increase in sensitivity, from mild to very severe anaemic cases. RDW-CV and MCV together were better parameters for screening early IDA in pregnant women in first 20 weeks of pregnancy.

CONCLUSION

In an era of hope by awesome scientific advances, we in India are still battling with the paradox of high maternal morbidity and mortality, much of it due to anaemia. What a doubly distressing is that the most common cause of anaemia of pregnancy in India is nutritional anaemia.

Though iron profile study is gold standard for detecting IDA in pregnancy, it has several limitations and is not available at every centre. CBC in these instances can be a powerful diagnostic tool for mass screening purpose. CBC is a simple, powerful diagnostic tool. Sensitivity of RDW-CV is maximum of all the parameters in prelatent/latent cases. There was gradual increase in sensitivity, from mild to very severe anaemic cases. RDW-CV and MCV taken together were better parameters for screening early IDA in pregnant woman.

Appropriate evaluation of all aspects of the CBC can lead to specific diagnosis and assist in ruling out many diseases. To gain the full benefit of CBC in detecting iron deficiency anaemia it must be used in conjunction with a good history, physical examination, peripheral smear examination as well as biochemistry panel wherever possible.

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