Original Research Article

Indian Journal of Pathology: Research and Practice
Volume 6 Number 3, July - September 2017 (Part-II)
DOI: http://dx.doi.org/10.21088/ijprp.2278.148X.6317.50

Evaluation of Red Cell Distribution Width (RDW) Parameter in the Diagnosis of Erythrocyte Disorders

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Abstract

Context: The initial classification of anemia can be improved substantially by including RDW and histograms of the red cell volume as these variable become part of the routine blood counts. *Aims:* To evaluate the effectiveness of the RDW parameter in the diagnosis of the erythrocyte disorders. *Settings and Design:* A hospital based cross sectional diagnostic evaluation study, Department of Pathology, Lt. BRKM Government Medical College. *Methods and Material:* 250 randomly selected cases of anemia were studied. All patients having hemoglobin value of less than 12.5 gm were included in the present study. Initially all patients were screened by automated cell counter. Those with hemoglobin of less than 12.5 gm were included in the present study. A possible pathophysiologic entity was assigned. Now the peripheral smear was screened and a specific etiology (category or cases) was assigned. *Statistical Analysis:* Chi square test was used wherever appropriate. P value of less than 0.05 was taken as statistically significant. *Results:* Decreased MCV and mild increase in RDW was seen in thalassemia trait. Serum iron was found to be normal in IDA patients. Low MCV and high RDW was found to be a good predictor of IDA. Single parameter of high MCV was found to be of poor diagnostic value in B_{12} deficiency anemia. Very high RDW was a consistent feature of sickle cell disease. Fairly deciding heterogeneity was observed with decrease to normal MCV in cases of various types of hemolytic anemia. *Conclusion:* RDW is a fairly sensitive and specific diagnostic approach and can eliminate unnecessary expensive and invasive investigations.

Keywords: Sickle Cell Disease; Iron Deficiency Anemia; Beta Thalassemia; MCV; RDW; MCH.

Introduction

Erythrocyte disorders are traditionally divided into two main groups: anemia and polycythemia and are characterized respectively by a decreased (erythrocytopenia) or increased (erythrocytosis) size of the red cell mass. Anemia is functionally best characterized by hemoglobin concentration below normal and polycythemia by hematocrit above normal. The use of two different erythroid parameters in the characterization of anemia and polycythemia is based on clinical consideration. Anemia is a disorder in which the patient suffers from tissue hypoxia, as a consequence of a low oxygen carrying capacity of the blood. Polycythemia on the other hand is a disorder in which the clinical manifestations are related to the increased whole blood viscosity and increased blood volume both the consequences of a high hematocrit [1].

The red cell disorders especially anemia, which is wide spread in our country mostly affects women and young children causing long term deleterious effect. Nutritional anemia (especially iron deficiency anemia) is the most wide spread clinical nutritional deficiency and accounts for 90% of all anemia. Prevalence of anemia in India ranges from 38-88% [2].

Automated analysis of the blood has made the erythrocyte indices more accurate, reproducible and readily available even without experienced morphologists. In the past, poor intra observer and inter observer reproducibility and lack of skilled in blood smear interpretation limited their use. There are

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(Received on 26.06.2017, **Accepted on** 11.07.2017)

three absolute values: mean corpuscular volume (MCV), mean corpuscular Hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) of which MCV tends to be the single most useful value. Anemia is classified as microcytic if MCV is less than 76 and macrocytic when MCV is more than 96. Anemia is normocytic when the indices are within normal limits (MCV = 76-96) [3].

An additional parameter obtained by analysis of blood sample in fully automated cell counters is red cell distribution width (RDW). The RDW is an estimate of erythrocyte anisocytosis or heterogeneity. The RDW is the coefficient of variation (CV) of the distribution of individual red cell volume. The RDW-CV is calculated as a ratio of the width of the curve at a one standard deviation divided by the MCV. The RDW-SD is simply the width of the curve measured at 20% frequency level. The RDW-CV is less sensitive to early macrocytosis. In contrast, the RDW-SD is very sensitive to the small proportion of microcytes or macrocytes [4].

Use of an automatic procedure for determination of cell count and indices has enabled us to obtain erythrocytes size and its distribution. In iron deficiency anemia (IDA) there is marked dispersion in the cell volume (size), so that the RDW increases whereas it generally remains within normal limit in anemia or chronic disease (ACD). Bessman et al (1983) had proposed a system of classification of anemia based on the RDW and the MCV [5]. They evaluated how RDW complements the MCV to improve the classification of anemia and also suggests the physiologic basis of the classification [5].

The initial classification of anemia can be improved substantially by including RDW and histograms of the red cell volume as these variable become part of the routine blood counts. Hence present study has been attempted to evaluate the effectiveness of the RDW parameter in the diagnosis of the erythrocyte disorders.

Material and Methods

Study Design

Hospital based cross sectional diagnostic evaluation study

Settings

Department of Pathology, Lt. BRKM Government Medical College, Jagdalpur, Chhattisgarh, India.

Study Period: January 2013 to October 2014

Sample Size

A total of 250 randomly selected cases were the sample size for the present study

Sampling Technique

Systematic random sampling technique was used for the present study. First case was taken randomly. Then every 10th case was selected till the sample size was completed. If the selected case was found to be not eligible as per inclusion and exclusion criteria, then immediately next eligible case was taken.

Inclusion Criteria

1. Hemoglobin value less than 12.5 gm%
2. Willing to participate in the study.

Exclusion Criteria

1. Hemoglobin value more than 12.5 gm%
2. Not willing to participate in the study
3. Having any severe systemic disease

Ethical Considerations

Institutional Ethics Committee permission was taken before the start of the study. Individual patient informed consent was obtained.

Methodology

A hospital based cross sectional diagnostic evaluation study was carried out for a period of more than one year from January 2013 to October 2014 among 250 randomly selected cases of anemia at department of Pathology. All patients having hemoglobin value of less than 12.5 gm% were included in the present study.

Initially all patients coming to the hematology lab of the hospital were screened by automated cell counter. Those with hemoglobin of less than 12.5 gm were included in the present study. A possible pathophysiologic entity was assigned. Now the peripheral smear was screened and a specific etiology (category or cases) was assigned as follows:

The sample was divided into two parts: one part was taken into 2 ml EDTA bulb and one part was sent for peripheral smear preparation. The EDTA sample was processed with fully automated cell counter and the data was processed. The peripheral smear was

stained with Leishman stain and examined under light microscope. Both the part results were compared and a probable etiology was assigned. After excluding the chronic systemic illness on clinical ground, any history of blood transfusion, and any history of anemia treatment, additional diagnostic work up was requested.

Investigations like complete blood count and peripheral smear examination test for sickling, Hb electrophoresis, serum iron, serum B_{12} assay was done with appropriate techniques and standard guidelines.

Statistical Analysis

Data was entered in the Microsoft Excel Worksheet and analyzed using proportions. Chi square test was used wherever appropriate. P value of less than 0.05 was taken as statistically significant.

Table 1: Comparison of variation in values of RDW (cut off at 16%) in different degrees of anemia in cases of IDA

Hemoglobin (gm %)	RDW (%)		Total
	13-16	> 16	
< 6	00	15 (100%)	15
6-9	00	32 (100%)	32
9-12	18 (60%)	12 (40%)	30
> 12	01 (100%)	00	01
Total	19 (24.4%)	59 (76.6%)	78

Table 2: Comparison of variation in values of RDW (cut off at 14%) in different degrees of anemia in cases of IDA

Hemoglobin (gm %)	RDW (%)		Total
	12-14	> 14	
< 6	00	15 (100%)	15
6-9	00	32 (100%)	32
9-12	02 (6.7%)	28 (93.3%)	30
> 12	00	01 (100%)	01
Total	02 (2.5%)	76 (97.5%)	78

Table 3: Correlation of serum vitamin B_{12} with MCV, MCH and RDW

Vitamin B_{12} (pg/ml) (< 157)	MCV (fl)			MCH (pg)			RDW (%)		Total
	< 76	76-96	> 96	< 27	27-32	> 32	13-16	> 16	
	00	10 (40%)	15 (60%)	00	00	25 (100%)	05 (20%)	20 (80%)	25

Table 4: Correlation of sickle positive cases with MCV, MCH and RDW

Sickling phenomenon positive	MCV (fl)			MCH (pg)			RDW (%)		Total
	< 76	76-96	> 96	< 27	27-32	> 32	13-16	> 16	
	21 (61.8%)	13(38.2%)	00	23 (67.6%)	08(23.5%)	03 (8.8%)	02 (5.8%)	02(5.8%)	34

Table 5: Correlation of beta thalassemia trait with MCV, MCH and RDW

Beta thalassemia trait	MCV (fl)			MCH (pg)			RDW (%)		Total
	< 76	76-96	> 96	< 27	27-32	> 32	13-16	> 16	
	18 (94.7%)	00	01 (5.3%)	18 (94.7%)	01 (5.3%)	00	13 (68.4%)	06(31.6%)	19

Table 6: Major classes of anemia based on MCV and RDW

Low MCV (N = 133)		Normal MCV (N = 101)		High MCV (N = 16)	
Normal RDW (N = 88)	High RDW (N = 162)	Normal RDW (N = 88)	High RDW (N = 162)	Normal RDW (N = 88)	High RDW (N = 162)
43 (17.2%) Microcytic non-heterogeneous	90 (36%) Microcytic heterogeneous	44 (17.6%) Normocytic non-heterogeneous	57 (22.8%) Normocytic heterogeneous	01 (0.4%) Macrocytic non-heterogeneous	15 (6%) Macrocytic heterogeneous

Results

Table 1 shows comparison of variation in values of RDW (cut off at 16%) in different degrees of anemia in cases of IDA. All cases with moderate and severe degree of anemia (Hb < 9 gm %) showed the increased width of red cells of more than 16%. In case of mild anemia, (Hb = 9-12 gm %) 40% of cases had shown increased RDW of more than 16%. But cases with normal hemoglobin, all were having normal RDW.

Table 2 shows comparison of variation in values of RDW (cut off at 14%) in different degrees of anemia in cases of IDA. When cut off value of RDW was lowered at 14%, it was found that the proportion of cases with moderate and severe degree of anemia (Hb < 9 gm%) remained unaffected as compared to cut off of RDW at 16%. But in case of mild anemia, (Hb = 9-12 gm %) the proportion of cases with abnormal RDW increased from 40% to 93.3%.

Table 3 shows correlation of serum vitamin B_{12} with MCV, MCH and RDW. Serum B_{12} assay was done in 75 cases. One third of them (25/75) had shown low serum B_{12} levels. Macrocytosis was seen in 60% of the cases of B_{12} deficiency. 40% had normocytic RBCs. Increased MCH was seen in all these cases. Increased RDW was present significantly in 80% of cases.

Table 4 shows correlation of sickle positive cases with MCV, MCH and RDW. In the present study, out of 250 cases, 34 (13.6%) cases of sickle cell anemia were seen. Slightly more than half of the cases (61.8%) were microcytic and hypochromic. Nearly 40% had normocytosis. Heterogeneity (i.e. increased RDW) was a feature of majority of cases (94%). Only 5.8% of cases had normal RDW. Less than a quarter had normal MCH. 26 cases were of sickle cell disease and 8 cases were of sickle cell trait. A comparison among them showed that proportion of microcytosis among them was almost equal but red cell heterogeneity was more in sickle cell disease and also high MCH value was seen in them compared to trait cases.

Table 5 shows correlation of Beta thalassemia trait cases with MCV, MCH and RDW. Microcytosis was seen in all cases of beta thalassemia trait cases except one. Similarly hypochromia was seen in all cases of beta thalassemia trait cases except one. RDW however in contrast to sickle cell anemia was normal in large majority (68.4%). Increased RDW was seen in only 32% of cases.

Table 6 shows major classes of anemia based on MCV and RDW. It was found that majority (36%) had Microcytic heterogeneous anemia followed by Normocytic heterogeneous anemia in 22.8% of cases. Microcytic non-heterogeneous anemia and Normocytic non-heterogeneous anemia was present in 17.2% of cases each. Macrocytic non-heterogeneous anemia was seen in only one case.

Discussion

A hospital based cross sectional diagnostic evaluation study was carried out among 250 randomly selected cases of anemia. We observed that serum iron was not very good predictors of nutritional anemia as one third of cases of nutritional anemia were found to have normal hemoglobin. Kim SK et al [2] demonstrated that serum iron as a single assay had 60% sensitivity in the diagnosis of IDA. Vishwanath D et al [3] also concluded that transferring saturation had a better correlation with degree of anemia as compared to serum iron. Thus serum iron has a limited role in further evaluation of nutritional anemia when suspected by hemoglobin testing and clinical presentation.

Evaluation of MCV and RDW with peripheral smear is more useful in this regard [3]. Uchida T [4] had studied RDW in relation to iron deficiency anemia in 1648 samples. He had recommended increased RDW as a screening test for iron deficiency over serum iron or ferritin. Seward SJ et al [5] in their study found that 83% cases of low serum iron had low MCV as opposed to 75% in the present study. Though sensitivity was good, specificity of MCV in cases of low serum iron or low serum ferritin was below 50%. The author also showed that 5% cases of IDA had high MCV. Thus MCV alone is poor in suggesting further diagnostic work up [5].

Vishwanath D et al [3] also demonstrated increased RDW in more than 80% of the cases. Bessman JD et al [1] noted that RDW appear to be the first parameter affected in IDA. They concluded that low MCV and high RDW can predict IDA. Ghionni A et al [5] also pointed out that increased RDW is a feature of IDA as opposed to beta thalassemia which also shows microcytosis.

Kim SK et al [2] observed that MCV had a sensitivity of 90% for detecting IDA if cut off was less than 70 fl. In the present study the cut off was less than 76 fl and we found the sensitivity of 75%. We found that increased RDW was present in 75% of cases similar to the finding of Burk M et al [7].

In the present study, in cases of IDA, microcytosis was seen in 83% of cases of mild anemia, 81% of cases of moderate anemia and 53.3% cases of severe anemia. Only theoretical explanation for this change from

microcytosis to normocytosis is development of concomitant B_{12} / folate deficiency. This is due to social factors like poverty, vegetarianism, bad food habits, alcoholism, etc.

Kim SK et al [2] noted that with RDW more than 15% gave a sensitivity of 83% and a specificity of 57.7%. They also observed that combination of RDW and MCV gave a positive predictive value of 97.8% in IDA. In the present study the cut off for RDW was 16% and hence we got a lower sensitivity of 76.5%. We also noted that MCV and RDW were equally sensitive. Uchida T [4] had noted a sensitivity of 77% when he used mean RDW value of 15.6±1.7. We also had a higher cut off value and had lower sensitivity. Thus it can be concluded that higher the cut off for RDW, lower the sensitivity. Das Gupta A et al [8] found the value of RDW as 15.1±1.2 in beta thalassemia trait cases. In IDA, this value was 18.2±3.8. However a cut off of 16% in the present study excluded 93% of people with normal hemoglobin. This figure is nearly equal to 2 SD limits of 95.5%. Thus the cut off limit was kept at 16% in the present study. Baqar MS A et al [9] used the range of 12.5 to 15.5% as a normal range of RDW in their study. Ghionni A et al [6]also found that increased RDW was a feature of IDA. Bessman JD et al [1] showed that decreased MCV and increased RDW both had 90% sensitivity for IDA when considered alone. Significantly though, increased RDW appear well before decreased MCV. Thus RDW is more sensitive. Helleman PW et al [10] concluded that RDW increase in IDA is less than other diseases and that greater overlap with normal population occur in this range.

In the present study we found that 60% of cases of B_{12} deficiency had increased MCV and 80% had increased RDW. Monzon CM et al [11] observed that increased MCV and increased RDW was a feature of B_{12} deficiency. Gupta PK et al [12] also found that increased MCV and increased RDW was a feature of B_{12} deficiency. Davidson RJ et al [13] noted that MCV was normal in 12% of cases with B_{12} deficiency. Thus these findings point that MCV correlate poorly with B_{12} deficiency. Bessman JD et al [1] observed that increased RDW was a constant feature of nutritional anemia.

We found no significant differences while comparing MCV, MCH and RDW in cases of sickle cell disease and sickle cell trait. Robert GT et al [14] concluded that patients of hemoglobinopathy had increased red cell turnover and erythropoietic activity even when hemoglobin was normal. Thus they observed highest and earliest changes in RDW in cases of hemolytic anemia. Monzon CM et al [11] observed that increased RDW was a feature of sickle cell disease only.

Thus our finding of usefulness of RDW as a parameter in the diagnosis of erythrocyte disorders was supported by various studies.

Key Messages

Evaluation of cut off value for RDW in a particular population is mandatory for maximum utilization of this parameter in the diagnosis of the disease.

Conclusion

Evaluation of cut off value for RDW in a particular population is mandatory for maximum utilization of this parameter in the diagnosis of the disease. With availability of automation in hematology and possibility of proper evaluation of MCV and RDW, that RDW is a fairly sensitive and specific diagnostic approach and can eliminate unnecessary expensive and invasive investigations for classification, evaluation and monitoring of various types of anemia in large number of cases.

References

1. Bessman JD, Glimer PR Jr, Gardner FH. Improved classification of anemias by MCV and RDW. Am J Clin Pathol 1983;80(2):322-6.
2. Kim SK, Cheong WS, Jun YH et al. Red blood cell indices and iron status according to feeding practices in infants and young children. Acta Pediatr 1996;85(2):139-44.
3. Vishwanath D, Hedge R, Murthy V et al. Red cell distribution width in the diagnosis of iron deficiency anemia. Indian J Pediatr 2001;68(12):1117-9.
4. Uchida T. Change in red blood cell distribution width with iron deficiency. Clin Lab Hematol 1989;11(2): 117-21.
5. Seward SJ, Safran C, Marton KI et al. Does the mean corpuscular volume help physicians evaluate hospitalized patients with anemia? J Gen Intern Med 1990;5(3):187-71.
6. Ghionni A, Miotti TC, Cammandona U. [Differential erythrocyte parameters in thalassemia minor and hyposideremic syndromes]. [Article in Italian]. Minerva Med 1985;76(24):1143-8.
7. Burk M, Arenz J, Giagomnidis AA et al. Erythrocyte indices as screening tests for the differentiation of microcytic anemias. Eur J Med Res 1995;16(1):33-7.
8. Das Gupta A, Hegde C, Mistri R. Red cell distribution width as a measure of severity of iron deficiency in iron deficiency anaemia. Indian J Med Res 1994;100:177-03.

9. Baqar MS, Khurshid M, Molla A. Does red blood cell distribution width (RDW) improve evaluation of microcytic anaemias? J Pak Med Assoc 1993;43(8): 149-51.

10. Helleman PW, Bartels PC, van Waverin GD. Screening for thalassemia using the width of the Technicon H6000/H601 erythrocyte size histograms. Scand J Clin Lab Inv 1988;48(7):697-704.

11. Monzon CM, Beaver BD, Dillon TD. Evaluation of erythrocyte disorders with mean corpuscular volume (MCV) and red cell distribution width (RDW). Clin Pediatr (Phila) 1987;26(12):632-8.

12. Gupta PK, Saxena R, Karan AS et al. Red cell indices for distinguishing macrocytosis of aplastic anaemia and megaloblastic anaemia. Indian J Pathol Microbiol 2003;46(3):375-7.

13. Davidson RJ, Hamilton PJ. High mean red cell volume: its incidence and significance in routine hematology. J Clin Pathol 1978;31(5):493-8.

14. Robert GT, El Badawi SB. Red blood cell distribution width index in some hematologic diseases. Am J Clin Pathol 1985;83(2):222-6.

15. el Sayed HL, Tawfik ZM. Red cell profile in normal and sickle cell disease children. J Egypt Soc Parasitol 1994;24(1):147-54.

16. Webster P, Castro O. Red cell distribution width in sickle cell disease. Ann Clin Lab Sci 1986;16(4):274-7.

17. Flynn MM, Reppun TS, Bhagvan NV. Limitations of red blood cell distribution width (RDW) in evaluation of microcytosis. Am J Clin Pathol 1986;85(4):445-9.