European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 10, Issue 2, Winter 2023

ORIGINAL RESEARCH

Assessment Of Red-Cell Distribution Width As Screening Tool For Different Types Of Anemia

[1]Dr.Vikram Singh, [2]Dr. V. N. Khanna, [1]Dr. Nidat Chothani, [1]Dr. Abuzar Daimay, [1]Dr. Kuldeep Mishra

[1]Resident, [2]Professor, Department of General Medicine, PCMS and RC, Bhopal, Madhya Pradesh, India

Corresponding author
Dr.Vikram Singh
Resident, Department of General Medicine, PCMS and RC, Bhopal, Madhya Pradesh, India

Received: 29 January, 2023 Accepted: 13 February, 2023

ABSTRACT

Background: There are various methods to diagnose different kinds of anaemia, but in developing countries many of the available investigation are also not feasible citing financial constraints. The present study was therefore conducted at tertiary care centre to assess RDW in different types of anemia; to investigate patients for peripheral smear picture, Iron Deficiency, Vitamin B12 Deficiency & Hemoglobinopathies wherever necessary; to determine efficacy of RDW in differentiating between Types of Anemia.

Methodology: The study was conducted as cross sectional study at Department of Medicine, PCMS and RC Bhopal during the study period of 18 months. A detailed history was obtained and examination was done. The study participates were then subjected to complete blood examination using hematology auto analyzer and RDW CV and RDW SD were recorded.

Results: This study included a total of 115 cases with anemia with mean age of 38.3±17.7 years. Mean RDW CV was lowest in hemolytic anemia, followed by anemia of chronic blood loss, dimorphic anemia and was highest in iron deficiency anemia ($p<0.05$). RDW SD was lowest in megaloblastic anemia, followed by anemia of chronic blood loss and hemolytic anemia ($p<0.05$). RDW CV as well as SD levels were significantly higher in severe anemia ($p<0.05$).

Conclusions: RDW is a simple and easily available screening tool helpful in screening of anemia as well as determining its severity. Red cell distribution width is increased in iron deficiency anemia and can be used routinely to differentiate iron deficiency anemia from other types of anemias with high accuracy. It can also be used in screening severe anemia irrespective of the type of anemia. RDW can be a cost effective tool for diagnosis of iron deficiency anemia as well as determining the severity of anemia.

Keywords: Iron deficiency anemia, Vitamin B12, RDW, complete blood picture, diagnosis

INTRODUCTION

Anemia is serious public health problem globally, that is often observed in young children and pregnant females.[1] According to World Health Organization, anemia is defined as reduction inhemoglobin or red blood cell count levels below the normal rangefor particular age and gender.[1] Hemoglobin plays an essential role in carrying oxygen to the peripheral

tissues and organs of the body, however, reduced hemoglobin levels are insufficient to meet the physiological needs of the body.[2] World health Organization (WHO) have described the cut off levels of hemoglobin to define anemia. Arbitrarily, hemoglobin level of less than 12 gram/dl and 13 gram/dl in females and males respectively is defined as anemia.[2]

Despite the fact that anemia is easily treatable and preventable condition, one third of women in reproductive age group and over 40% of children & pregnant women are anemic.[1] About one third of the population globally are estimated to be suffering from anemia of varying severity, and though the anemia can be observed in any age or gender, prevalence is more common in women of reproductive age group, pregnant females and among elderly.[3] The prevalence of anemia is documented to be much higher in low and middle income countries. According to National Family Health Survey 5 (2019-21) data, anemia is documented in 67.1% children in the age range of 6 month to 59 months, 57.2% in women of reproductive age group, 52.2% in pregnant women and 25% in men belonging to age range of 15 to 49 years.[4]

Anemia are mainly classified based upon the biological mechanisms such as nutritional deficiencies, chronic conditions, reduced erythropoiesis, hemolytic etc.[5] Nutritional deficiencies are most common cause of anemia in India. Among various nutritional deficiencies, iron deficiency anemia is the most common cause, which manifest as microcytic hypochromic anemia.[6,7] Other causes of anemia include chronic diseases, especially renal disorders which lead to reduce erythropoietin secretin and inefficient erythropoiesis, hemoglobinopathies, increased red cell destruction, lead poisoning etc.[8,9]

As the prognosis of anemia depend upon the cause of anemia, it is essential to identify its cause. The availability of hematology autoanalyser have provided an opportunity to study various blood components simultaneously in various diseases. Red cell distribution width (RDW) is a simple inexpensive screening tool measured on automated hematology analyzer as component of complete blood count which determine the distribution and broadness of erythrocyte size, i.e. it helps in assessment of degree of anisocytosis.[10]RDW is calculated as a ratio of the standard deviation of RBC volume to mean corpuscular volume (MCV) and is expressed as percentage.[11]Currently, two measurements of RDW are used. These are RDW-coefficient of variation (RDW-CV) and RDW- standard deviation (RDW-SD).

The RDW-CV is a measure of width of the red cell distribution curve and the mean cell size, which is calculated by ratio of standard deviation of the mean cell size to MCV of and multiplying by 100.[12] However, RDW-SD is considered as actual measurement of the red cell distribution curve width, which is measured at 20% above the baseline. This measure is unaffected by MCV and reflect the variation in red cell size more accurately as compared to RDW CV.[12]There are various methods to diagnose different kinds of anaemia, but in developing countries many of the available investigation are also not feasible citing financial constraints. The present study was therefore conducted at tertiary care centre to assess RDW in different types of anemia; to investigate patients for peripheral smear picture, Iron Deficiency, Vitamin B12 Deficiency & Hemoglobinopathies wherever necessary; to determine efficacy of RDW in differentiating between Types of Anemia.

METHODOLOGY

The present studywas conducted as an observational cross sectional study at Department of Medicine, People's College of Medical Sciences and Research Centre and associated People's Hospital Bhopal during the study period of 18 months i.e. from 1st December 2020 to 31st May 2022. All the patients presenting with anemia and diagnosed as per WHO criteria were included whereas patient with acute blood loss, with chronic diseases like CKD & CLD and pre diagnosed cases of Anemia were excluded from the study.

After obtaining ethical clearance from Institute's ethical committee, all the patients with anemia fulfilling the inclusion criteria were enrolled. A detailed data regarding their sociodemographic variables was obtained from all the study participants. A detailed clinical historywas obtained from all the study participants using the proforma. All the patients were then subjected to thorough clinical examination including general and systemic examination. The study participates were then subjected to complete blood examination using hematology auto analyzer and RDW CV and RDW SD were recorded. Apart from these, special Investigation such as Reticulocyte count, Serum ferritin, Serum B12, Sickling test, G-6-PD deficiency test,HB Electrophoresis, Stool Occult blood, Bone Marrow Biopsy were done as and when needed. Based upon serum hemoglobin level, patients were categorized as having mild, moderate or severe anemia according to WHO criteria.[2]

STATISTICAL ANALYSIS

Data was compiled using Ms Excel and analysis of data was done with the help of IBM SPSS software version 20. Categorical variables were expressed as frequency and proportions whereas continuous variables were expressed as mean and standard deviation. Association of RDW with severity and type of anemia was done using chi square test, whereas mean RDW in patients with varying severity of anemia and types of anemia was done using independent T test or ANOVA test. Correlation of RDW with hemoglobin levels was done using Pearson correlation coefficient. P value less than 0.05 was considered statistically significant.

RESULTS

This study was conducted on a total of 115 cases with anemia presenting at our hospital with mean age of 38.3±17.7 years.

Table 1: Distribution of patients according tobaseline variables

Baseline variables		Frequency(n=115)	Percentage
Age (years)	<20	31	27.0
	21-30	19	16.5
	31-40	18	15.7
	41-50	18	15.7
	51-60	7	6.1
	>60	22	19.1
Sex	Male	45	39.1
	Female	70	60.9
Marital Status	Unmarried	44	38.3
	Married	71	61.7
Clinical features	Easy fatigability	113	98.3
	Abdominal pain and easy fatigability	1	0.9
	Giddiness and Shortness of breath	1	0.9
History	Dysphagia	0	0.0
	Barefoot walking	10	8.7
	Burning sensation in feet	0	0.0
	History of pica	19	16.5
	History of upper or lower GI bleed	15	13.0
	Renal Disease	0	0.0
	Hypothyroidism	0	0.0

Examination	Pallor	112	97.4
	Icterus	0	0.0
	Clubbing	0	0.0
	Koilonychia	0	0.0
	Platynychia	26	22.6
	Pigmented Knuckles	42	36.5
	Purpura/ Petacchie	0	0.0
	Sternal Tenderness	0	0.0
	Haemic Murmur	31	27.0
	Splenomegaly	28	24.3

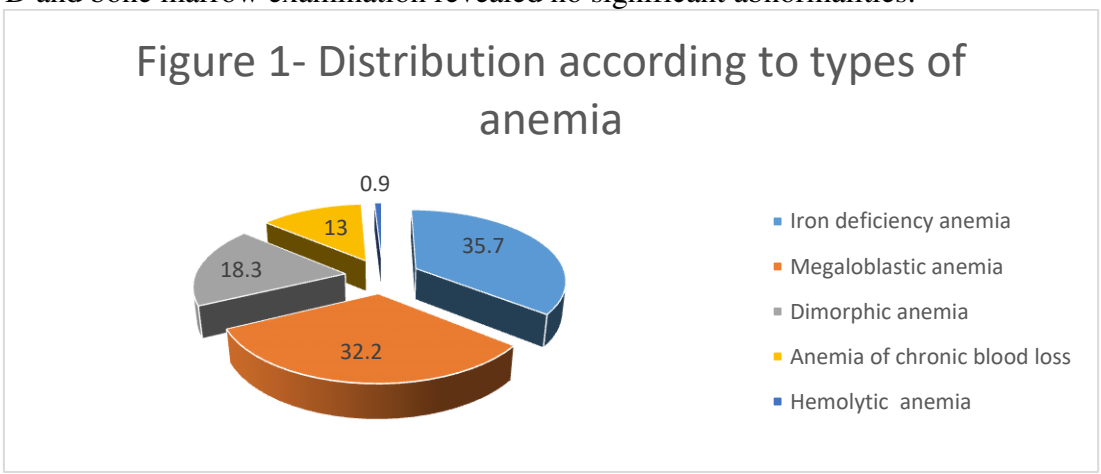
Majority of cases belonged to age range of less than 20 years (27%) and female predominance was observed with male: female ratio of 0.64:1. About 61.7% cases were married and most common complaint was easy fatigability (98.3%). History of pica was noted in 16.5% cases where as 13% cases had history of upper or lower GI bleed. History of barefoot walking was noted in 8.7% cases. Pallor was observed in 97.4% cases whereas pigmented knuckles was documented in 36.5% cases. Haemic murmur, splenomegaly and platynychia was noted in 27%, 24.3% and 22.6% cases respectively.

Table 2: Distribution according to the findings of investigations

Investigations		**Frequency (n=115)**	**Percentage**
Hemoglobin	Moderate anemia	40	34.8
	Severe anemia	75	65.2
	Mean±SD	5.98±2.3 (%)	
TLC	<4000	32	27.8
	4000-11000	76	66.1
	>11000	7	6.1
	Mean±SD	5960.52±2083.73	
Platelet	<1.5L	46	40.0
	1.5-4L	57	49.6
	>4L	12	10.4
	Mean±SD	216104.35±40296.76	
RDW CV	Mean±SD	21.4±9.5	
RDW SD	Mean±SD	59.69±28.57	
Peripheral smear	Anisopoikilocytes with abnormal cells	1	0.9
	Dimorphic Blood Picture	7	6.1
	Dimorphic Blood Picture with Microctyes as well as varied degree of Anisopoikilocytosis	5	4.3
	Dimorphic blood picture with Anisopoikilocytosis	2	1.7
	Macrocytic Blood picture	5	4.3
	Macrocytic blood picture with anisopoikilocytosis	32	27.9
	Microcytic Hypochromic Anemia	38	33.0
	Microcytic hypochromic Blood Picture with	2	1.7

	Anisopoikilocytosis with decreased Platelet count		
	Microcytic Hypochromic Blood picture with Anisopoikilocytosis with tear drop cells	5	4.3
	Microcytic Hypochromic blood picture with thrombocytopenia	1	0.9
	Microcytic Hypochromic Blood Picture with thrombocytosis	1	0.9
	Microcytic Hypochromic picture with Anisopoikilocytosis	1	0.9
	Multiple platelet aggregates	1	0.9
	Normocytic Normochromic Blood picture	12	10.4
	Normocytic Normochromic Blood picture, with thrombocytopenia	1	0.9
	Scanty Normocytic normochromic Cells with moderate anisopoikilocytosis	1	0.9
Other tests	Sickle Test	0	0.0
	G6PD	0	0.0
	Stool Occult	17	14.8
	BM Examination	0	0.0

In our study, mean hemoglobin was 5.98±2.3 gm%, with majority of cases having severe anemia (65.2%). Mean TLC count was 5960.52±2083.73, and leucocytopenia and leukocytosis was documented in 27.8% and 6.1% cases respectively. RDW CV and RDW SD levels in patients with anemia were 21.4±9.5 and 59.69±28.57 respectively. We reported microcytic hypochromic anemia in 33% cases and Macrocytic blood picture with anisopoikilocytosis in 27.9% cases. About 10.4% cases had normocytic normochromic anemia. Stool for occult blood was positive in 14.8% cases with anemia, whereas sickle test, G6PD and bone marrow examination revealed no significant abnormalities.



Our study documented iron deficiency anemia in majority of cases (35.7%), followed by megaloblastic anemia and dimorphic anemia in 32.2% and 18.3% cases respectively. About 13% cases had anemia due to blood loss and 0.9% cases had hemolytic anemia.

Table 3: RDW levels in different types of anemia

	Types Of Anemia					**ANOVA**	**P value**
	Iron deficiency anemia	Megaloblastic anemia	Dimorphic anemia	Anemia of chronic blood loss	Hemolytic anemia		
RDW CV	24.63±13.37	19.01±5.21	22.99±9.2	17.98±3.96	17.70±3.1	**2.518**	**0.045**
RDW SD	83.71±29.71	40.73±13.5	61.88±26.1	49.78±13.9	51.7±12.5	**18.749**	**0.001**

Mean RDW CV was lowest in hemolytic anemia, followed by anemia of chronic blood loss, dimorphic anemia and was highest in iron deficiency anemia ($p<0.05$).
RDW SD was lowest in megaloblastic anemia, followed by anemia of chronic blood loss and hemolytic anemia ($p<0.05$).

Table 4: Association of RDW levels with severity of anemia

	Severity Of Anemia		**T value**	**P value**
	Moderate	**Severe**		
RDW CV	18.82±6.22	22.77±10.64	4.671	0.033
RDW SD	52.01±17.45	63.80±32.37	4.587	0.034

In present study, RDW CV as well as SD levels were significantly higher in severe anemia ($p<0.05$).

Table 5: Area under the curve of RDW for diagnosis of different types of anemia

Anemia	**RDW**	**Area**	**P value**	**95% CI**		**Cutoff**	**Sensitivity**	**Specificity**
				Lower Bound	**Upper Bound**			
IDA	RDW CV	.629	**.026**	.517	.741	17.95	70.3	46.2
	RDW SD	.898	**.0001**	.840	.955	49.8	97.3	69.2
MA	RDW CV	.396	.064	.288	.503	16.1	68.3	34.3
	RDW SD	.126	**.0001**	.057	.195	30.45	80.5	3.7
DA	RDW CV	.585	.227	.457	.712	18.10	66.7	44.7
	RDW SD	.568	.334	.451	.684	47.95	71.4	44.7
CBL	RDW CV	.361	.083	.223	.498	16.5	66.7	31
	RDW SD	.402	.221	.280	.523	46.7	60	37
HA	RDW CV	.382	.684	.292	.471	17.65	100	38.7
	RDW SD	.513	.964	.421	.605	51.55	100	61

Area under the curve of RDW SD suggested good accuracy (AUC-0.989; $p<0.01$) for diagnosis of iron deficiency anemia with sensitivity and specificity of 97.3% and 69.2%

respectively. However, RDW CV had poor but significant area accuracy for diagnosis of iron deficiency anemia. RDW was not good predictor of other types of anemia (p>0.05).

DISCUSSIONS

Anemia is one of the most common and serious yet neglected public health problem worldwide and is characterized by reduced hemoglobin or red blood cell count levels.[1] It is essential to identify etiology of anemia as the prognosis as well as treatment largely depend upon the underlying cause. Literature suggest some role of various component of complete blood picture such as RDW, a marker of degree of anisocytosis may helps in determining underlying etiology of anemia.[10-12]

The present study was conducted on a total of 115 cases with anemia to study RDW in different types of anemia in patients reporting in medicine department and to determine efficacy of RDW in differentiating between types of Anemia. The mean age of patients was 38.3±17.7 years and about 60.9% cases were females. Complete blood picture was done in all the cases and based upon hemoglobin levels, patients were categorized according to severity of anemia. We reported moderate and severe anemia in 34.8% and 65.2% cases respectively. Red cell distribution width was documented in all the cases and we aimed to categorize anemia based upon RDW levels. Red cell distribution width (RDW) is a simple measure to determine the degree of anisocytosis reflecting the distribution and broadness of erythrocyte size. It can be easily obtained from the complete blood count on automated hematology analyzer.[10] In present study, RDW CV and RDW SD levels in patients with anemia were 21.4±9.5% and 59.69±28.57% respectively. Peripheral smear examination is helpful in determining the morphology of RBCs. In our study, most common finding on PS examination was microcytic hypochromic anemia in 33% cases and Macrocytic blood picture with anisopoikilocytosis in 27.9% cases. We included all the cases of anemia in our study based upon WHO cut off level for particular age and sex.[2]Pandya et al reported microcytic hypochromic anemia to be the most common findings on peripheral smear examination.[13]Zafar et al also reported microcytic hypochromic anemia in 92.1% cases.[14]Bhasin et al observed normocytic anemia in 62% cases whereas 30% cases had microcytic hypochromic anemia.[15]

We calculated RDW CV and RDW SD in all the cases and reported mean RDW CV to be lowest in hemolytic anemia and highest in iron deficiency (p<0.05) whereas RDW SD was lowest in megaloblastic anemia and highest in iron deficiency anemia (p<0.05). RDW increased with increasing in severity of anemia irrespective of type of anemia. RDW SD was found to be better predictor of iron deficiency anemia (AUC-0.989; p<0.01) with sensitivity and specificity of 97.3% and 69.2% respectively. However, RDW CV was also helpful in diagnosis of IDA but its diagnostic accuracy was in poor range.

The findings of present study were supported by the findings of Aulakh et al, where the authors reported significantly higher RDW levels in iron deficiency anemia as compared to anemia due to non iron deficiency (p<0.05) and RDW was significantly higher in severe anemia as compared to mild anemia (p<0.05). The authors reported sensitivity and specificity of RDW as 81% and 53.4% respectively at RDW cut off of 17.4%.[16] Sultana et al documented sensitivity of 82.3% and specificity of 97.4% for diagnosis of IDA using RDW.[17]Pandya et al used RDW to classify anemia and showed a sensitivity of 82.27% for diagnosis of iron deficiency anemia.[13]Our study findings were concordant with the findings of Choudhary et al, in which mean RDW was significantly higher in IDA and as the severity of anemia increased, RDW increased significantly (p<0.05).[18]

CONCLUSIONS

RDW is a simple and easily available screening tool helpful in screening of anemia as well as determining its severity. Red cell distribution width is increased in iron deficiency anemia and can be used routinely to differentiate iron deficiency anemia from other types of anemias with high accuracy. It can also be used in screening severe anemia irrespective of the type of anemia. RDW can be a cost effective tool for diagnosis of iron deficiency anemia as well as determining the severity of anemia.

REFERENCES

1. Anemia. World Health Organization. Available from https://www.who.int/health-topics/anaemia#tab=tab_1 Last accessed on 12th February 2022.
2. World Health Organization. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. World Health Organization; 2011. Available from https://apps.who.int/iris/bitstream/handle/10665/85839/WHO_NMH_NHD_MNM_11.1_eng.pdfLast accessed on 12th February 2022.
3. Turner J, Parsi M, Badireddy M. Anemia. [Updated 2022 Jan 9]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK499994/
4. Anemia among children and Adults. National Family Health Survey -5. India. Available from http://rchiips.org/nfhs/NFHS-5_FCTS/India.pdfLast accessed on 12th February 2022.
5. Chaparro CM, Suchdev PS. Anemia epidemiology, pathophysiology, and etiology in low- and middle-income countries. Annals of the new York Academy of Sciences. 2019 Aug;1450(1):15-31.
6. Aulakh R, Sohi I, Singh T, Kakkar N. Red cell distribution width (RDW) in the diagnosis of iron deficiency with microcytic hypochromic anemia. Indian J Pediatr. 2009;76(3):265-7.
7. Nadeem R, Ahmed N, Qureshi GR. Automated measurement of red blood cell microcytosis and hypochromia in iron deficiency and beta thalassemia trait. Pak J Med Health Sci. 2012;6(1):20-3.
8. Nesa A, Tayab A, Sultana T, Khondker L, Rahman Q, Karim A, et al. RDWI is better discriminant than RDW in differentiation of iron deficiency anemia and beta thalassaemia trait. Bangladesh J Child Health. 2009;33(3):100-3.
9. Van ZD, Bieger R, Van WRKA, Castel A, Hermans J. Evalution of microcytosis using serum ferritin and red blood cell distribution width. Eur J Haematol. 1990;44:105-8.
10. Salvagno GL, Sanchis-Gomar F, Picanza A, Lippi G. Red blood cell distribution width: a simple parameter with multiple clinical applications. Critical reviews in clinical laboratory sciences. 2015 Mar 4;52(2):86-105.
11. Lippi G, Plebani M. Red blood cell distribution width (RDW) and human pathology. One size fits all. Clinical Chemistry and Laboratory Medicine (CCLM). 2014 Sep 1;52(9):1247-9.
12. Caporal FA, Comar SR. Evaluation of RDW-CV, RDW-SD, and MATH-1SD for the detection of erythrocyte anisocytosis observed by optical microscopy. JornalBrasileiro de Patologia e Medicina Laboratorial. 2013 Oct;49(5):324-31.
13. Pandya AN, Agarwal M, Dave D. Red cell distribution width as a screening tool in classifying microcytic hypochromic anemias. Journal of Evolution of Medical and Dental Sciences. 2014 Jun 9;3(23):6559-66.
14. Zafar M, Tabassum A, Cheema QA, Mazhar SB. Role of red cell distribution width and Mentzer index in differentiating iron deficiency anemia from anemia due to β thalassemia

trait. Journal of South Asian Federation of Obstetrics and Gynaecology. 2019 Sep;11(5):298

15. Bhasin A, Rao MY. Characteristics of anemia in elderly: a hospital based study in South India. Indian journal of hematology and blood transfusion. 2011 Mar;27(1):26-32.
16. Aulakh R, Sohi I, Singh T, Kakkar N. Red cell distribution width (RDW) in the diagnosis of iron deficiency with microcytic hypochromic anemia. The Indian Journal of Pediatrics. 2009 Mar;76(3):265-8.
17. Sultana GS, Haque SA, Sultana T, Rahman Q, Ahmed AN. Role of red cell distribution width (RDW) in the detection of iron deficiency anaemia in pregnancy within the first 20 weeks of gestation. Bangladesh Medical Research Council Bulletin. 2011;37(3):102-5.
18. Choudhary M, Sharma D, Shekhawat DS, Dabi D. Significance of red cell distribution width in the diagnosis of iron deficiency anemia: an observational study from India. J Pediatr Neonatal Care. 2015;2(6):102-6.