To Study the Spectrum of Diseases with Increased Red Blood Cell Distribution Width (RDW) in Patients Attending Tertiary Care Hospital

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ABSTRACT

Introduction: Red blood cell distribution width (RDW) is the coefficient of variation of the mean corpuscular volume (MCV). RDW can be reported statistically as coefficient of variation (CV) and/or standard deviation (SD); RDW-CV and/or RDW-SD respectively. The role of RDW is well established in haematological diseases but not much research has been done in relation to non haematological diseases. Hence the present study was undertaken to evaluate spectrum of non haematological and haematological diseases in patients who presented with increased RDW. Current research aimed to study increased RDW in haematological and non haematological diseases.

Material and methods: The present study was conducted in the Department of Pathology, Adesh Institute of Medical Sciences (AIMSR), Bathinda, from January 2017 to December 2017.

Results: Most of the patients had non haematological diseases (67.25%) and 32.25% of the patients had haematological diseases. Iron deficiency anaemia was the common haematological diagnosis noted in 52.75% of the patients followed by megaloblastic anaemia (21.13%) while hypertension was the common non haematological diagnosis noted in 10.70% of the patients. Cardiovascular diseases (27.31%) were common followed by liver disease (17.71%), autoimmune diseases (11.07%).

Conclusion: Patients with increased RDW are having several non haematological disease presentations. Therefore, RDW alone cannot be used as single specific marker for any disease, but nevertheless it cannot be ignored in hematology reporting.

Keywords: RDW, Haematological Diseases, Anaemia, Non-Haematological Diseases, Cardiovascular Diseases, Liver Diseases, Autoimmune Diseases.

INTRODUCTION

Red blood cell distribution width (RDW) is the coefficient of variation of the mean corpuscular volume (MCV). RDW can be reported statistically as coefficient of variation (CV) and/or standard deviation (SD); RDW-CV and/or RDW-SD respectively.[1,2] depending on the types of hematology analyzer instruments. RDW is calculated by dividing the standard deviation of mean cell volume (MCV) by the MCV and multiplied by 100 and yields RDW percentage.[1-3] It is routinely assessed as part of the complete blood count (CBC) to gather information on the heterogeneity in the size of circulating erythrocytes. Higher RDW values reflect greater variation in MCV (anisocytosis), which is usually caused by perturbation in erythrocyte maturation or degradation because of its responsiveness to subtle nutrient deficiency. RDW is used as an auxiliary index to help diagnose different types of anemia.[3-5]

From a National Health and Nutrition Examination Survey III study, the upper and lower limits of the RDW values were set at the 5th (11.0%) and 95th (14.0%) percentiles in a population.[6] The RDW is used as an auxiliary index to help diagnose different types of anemia.[5]

In hemolytic anemia and some other hematological diseases, because of the release of immature red blood cells into the blood stream, RDW would increase.[7-9] Early indication of iron deficiency appears, when RDW value increases than the decline of mean corpuscular volume (MCV). Iron studies may still be normal. When iron therapy is given, RDW would elevate first and then gradually reduce to the normal level. Many researches suggested that RDW was closely related to the mortality in cardiovascular events such as acute coronary syndrome, ischaemic cerebrovascular disease, peripheral vascular disease, atrial fibrillation (AF), heart failure (HF) and hypertension.[5,8,10-14] RDW can be made as a predictor of mortality in patients with cancer, chronic lung disease or acute renal failure.[8] RDW has also been thought as one of the strongest predictors of poor survival in patients with established heart failure[8-10] and coronary artery disease.[11-15]

It is only used clinically for diagnosis of subtyping of anemia. The links between increased RDW and negative health outcomes could provide clues to improve prognosis in those with high RDW who are not anemic, particularly in elderly people.[16]

Iron or folate deficiencies,[17] dyslipidemia[18] and other metabolic abnormalities, and inflammation[19] are the established clinical causes of increased RDW. Various mechanisms for increased RDW also include impaired erythropoiesis (the generation of new RBC) perhaps due to effects of inflammation or senescence of erythropoietic cells

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in the bone marrow along with variation in RBC survival.[20] Recent evidence suggests that, elevated RDW is associated with sarcopenia, particularly in people who are overweight and obese persons.[21]

Recent evidence attests that anisocytosis is common place in human disorders such as cardiovascular disorder, venous thromboembolism, cancer, diabetes, community acquired pneumonia, chronic obstructive pulmonary disease (COPD), liver and kidney failure as well as in other acute and chronic conditions. Increased RDW may also convey an important information of short and long term prognosis. The value of RDW is now being regarded as a short and independent risk for death in the general population.[22]

An increased RDW shows a profound deregulation of red cell homeostasis involving both impaired erythropoeisis and abnormal red blood cell survival, which may be attributed to a variety of underlying metabolic abnormalities such as shortening of telomere length, oxidative stress, inflammation, poor nutritional status, dyslipidemia, hypertension, erythrocyte fragmentation and alteration of erythropoietin function.[22] Because of its responsiveness to subtle nutrient deficiency, RDW has been evaluated as a potential screening marker for colon cancer and celiac disease and is used as an auxiliary index to help to diagnose different types of anaemia.[23]

Recent researches have shown higher mortality risk associated with higher RDW in patient populations with cardiovascular disease (CVD).[24-27] However, none of these prospective studies had taken into account the nutritional status or any inflammatory process.[28]

In the past role of RDW is well established in haematological diseases but not much research has been done in relation to non haematological diseases. RDW was incorporated in haematological analysers in year 1980, hence less of literature is available.

From the above facts it is clear that the role of RDW in not only limited to anaemia but also related to other diseases. Hence the present study was undertaken to evaluate spectrum of non haematological and haematological diseases in patients who presented with increased RDW.

MATERIAL AND METHODS

The present study was conducted in the Department of Pathology, Adesh Institute of Medical Sciences (AIMSR), Bathinda, from January 2017 to December 2017. Patients with increased red blood cell distribution width confirmed by haematological report were studied. Blood samples were collected in haematology lab of central laboratory of Adesh Hospital. All samples were run for complete blood count on automated cell counter 5 part differential Mindray BC-5380. Samples were run on the counter and reports having increased RDW were segregated before delivery to the patients. At the time of handing over the report to the patient, complete clinical and investigative performa was filled up.

RESULTS

The data obtained was tabulated and analysed and the final results and observations were tabulated and interpreted as below.

The present study, 50.25% of the patients were males and 49.75% were females with male to female ratio of 1.01:1.

In this study, 20.5% of the patients were aged between 51 to 60 years. The mean age was 44.78±18.31 years. The median age was 45.50 years and ranged between 05 months to 90 years.

In the present study, 32.25% of the patients had haematological diseases and 67.25% of the patients had non haematological diseases.

Iron deficiency anaemia was the common haematological diagnosis noted in 52.75% of the patients followed by megaloblastic anaemia (21.13%).

Hypertension was the non haematological diagnosis noted

Gender	Distribution (n=400)	
	Number	Percentage
Male	201	50.25
Female	199	49.75
Total	400	100.00

Table-1: Distribution of patients according to the gender

Age group (Years)	Distribution (n=70)	
	Number	Percentage
≤ 18	28	7.00
19 to 30	75	18.75
31 to 40	61	15.25
41 to 50	76	19.00
51 to 60	82	20.50
> 60	78	19.50
Total	400	100.00

Table-2: Distribution of patients according to the age

Type of disease	Distribution (n=400)	
	Number	Percentage
Haematological	129	32.25
Non haematological	271	67.75
Total	400	100.00

Table-3: Distribution of the patients according to the type of disease

Haematological diseases	Distribution (n=127)	
	Number	Percentage
Iron deficiency anemia	67	52.75
Megaloblastic anemia	35	27.13
Dimorphic anemia	15	11.63
Hemolytic anemia	6	4.65
Sickle cell anemia	2	1.55
K/C/O CML	1	0.78
Beta thalassemia minor	1	0.78
Thalassemia intermedia	1	0.78
Thalessemia minor	1	0.78
Total	129	100.00

Table-4: Distribution of the patients according to the haemato-logical diseases

Non haematological diseases	Distribution (n=271)	
	Number	Percentage
Hypertension	29	10.70
Rheumatoid arthritis	24	8.86
Myocardial infarction	14	5.17
Pneumonia	14	5.17
Alcoholic liver disease	13	4.80
Non alcohalic fatty liver disease	12	4.43
Acute appendicitis	7	2.58
Bronchial asthma	7	2.58
Chronic hepatitis C	7	2.58
Type 2 diabetes mellitus	7	2.58
Angina	6	2.21
COPD	6	2.21
Fatty liver	6	2.21
Cardiovascular disease	5	1.85
Inflammatory bowel disease	5	1.85
Preeclampsia	5	1.85
Depression	5	1.85
Chronic hepatitis B	4	1.48
Coronary artery disease	4	1.48
Fracture right elbow	4	1.48
Liver cirrhosis	4	1.48
Acute pancreatitis	3	1.11
Atherosclerosis	3	1.11
Bronchitis	3	1.11
Valvular heart disease	3	1.11
Deep vein thrombosis	3	1.11
Heart failure	3	1.11
Peripheral vascular disease	3	1.11
Neonatal sepsis	3	1.11
Bleeding peptic ulcer	2	0.74
Stroke	2	0.74
Systemic lupus erythematosus	2	0.74
Tuberculosis	2	0.74
Viral hepatitis	2	0.74
Fracture neck femur	2	0.74
Coeliac disease	2	0.74
Hashimoto's thyroiditis	2	0.74
Ischaemic heart disease	2	0.74
Fracture right leg	2	0.74
Colon and esophageal carcinoma	1	0.37
Community acquired pneumonia	1	0.37
Diabetic nephropathy	1	0.37
Fibroid uterus	1	0.37
Fracture Hip	1	0.37
Fracture left leg	1	0.37
Fracture right arm	1	0.37
Fracture right femur	1	0.37
Frature left femur	1	0.37
Frature right leg	1	0.37
Gangrenous foot (type 2 DM)	1	0.37
Gastric cancer	1	0.37
Hepatocellular carcinoma	1	0.37
Acute blood loss (RTA)	1	0.37
Interstial lung disease	1	0.37
Ishaemic stroke	1	0.37
acute coronary syndrome	1	0.37
Lung cancer	1	0.37
Asthma	1	0.37
Osteoarthritis	1	0.37
Acute renal failure	1	0.37
Ovarian cancer	1	0.37
Atrial fibrillation and hypertension	1	0.37
Pulmonary embolism	1	0.37
Pulmonary TB	1	0.37
Recent hemorrhage	1	0.37
Rheumatic heart disease	1	0.37
Bladder carcinoma	1	0.37
Systemic hypertension	1	0.37
Chronic lung disease	1	0.37
Chronic RENAL DISEASE	1	0.37
Carcinoma rectum	1	0.37
Bronchiectasis	1	0.37
Cerebral thrombosis	1	0.37
Cerebrovascular disease	1	0.37
Chronic bronchitis	1	0.37
Chronic glomerulonephritis	1	0.37
Ulcerative colitis	1	0.37
Viral pneumonia	1	0.37
Total	**271**	**100.00**

Table-5: Distribution of the patients according to the non haematological diseases

in 10.70% of the patients followed by rheumatoid arthritis (8.86%) and pneumonia and Myocardial infarction (5.13% each).

DISCUSSION

In the present study the RDW SD levels ranged from 43 to 183 fL and the mean RDW SD levels were 66.01±11.18 fL and median levels were noted as 63 fL. The RDW CV levels ranged between 12 to 57 percent and mean RDW CV levels were 17.32±4.06 percent and median levels were 16 percent. The MCV levels ranged between 57 to 130 fL and mean MCV was noted as 82.47±13.99 and median MCV levels were 78. These findings suggested that, the RDW SD and RDW CV were higher than the normal reference range. Also there was variation in MCV levels.

Increased RDW did not show any sex predilection with males (50.25%) and females (49.75%) (male to female ratio of 1.01:1). Borne Y et al[29] in his study did not show any significant sex difference with the patients having malignancies. However in one of the study by Chen et al[30] showed statistically significant male preponderance.

In our study, the age ranged between 5 months to 90 years. Most of the patients were aged between 51 to 60 years (20.5%). The mean age was 44.78±18.31 years and the median age was 45.50 years. Our observations are in concordance with study of Braun et al[31] in which his patients were 60 years or above. Lippi et al[32] showed increased RDW with advancing age.

In the present study nearly one third (32.25%) of the patients had haematological diseases and two thirds (67.25%) of the patients had non haematological diseases.

Among haematological diseases, most common diagnosis was iron deficiency anaemia (16.75%) followed by megaloblastic anaemia (8.75%) and dimorphic anemia (3.75%). It is difficult to discuss entire disease pattern due to the diversity of the underlying etiology. The common diagnosis of iron deficiency anaemia (IDA) noted in the present study can be explained by the fact that, the RDW is used as an auxiliary index to help to diagnose different types of anaemia.[3,4] Furthermore, an increased RDW mirrors a profound deregulation of erythrocyte homeostasis involving both impaired erythropoeisis and abnormal red blood cell survival, which may be attributed to a variety of underlying metabolic abnormalities such as shortening of telomere length, oxidative stress, inflammation, poor nutritional status, dyslipidemia, hypertension, erythrocyte fragmentation and alteration of erythropoietin function.[20]

Considering the heterogeneity of the non haematological diseases, in this study we further divided the diseases according to the different body systems and organ systems and it was observed that cardiovascular diseases including Hypertension (27.31%) were common followed by liver disease (17.71%) and autoimmune disease (11.07%) and pneumonia 5.13%. Hypertension alone was noted in 10.70% of our patients.

Recently Bilal A. et al.[33] showed that, RDW is directly related with hypertension and suggested the hypothesis that RDW and inflammation are directly linked and that chronic inflammation can lead to an increase in RDW. Being a relatively easy and readily available test to perform, it can be used as an early warning system for physicians to identify prehypertension and hypertension in patients and to identify those patients who are at a greater risk for adverse outcomes from cardiovascular disease. Despite methodological differences the present study is in agreement with the observations noted by Bilal A. et al.[33]

In our study 45 cases (16.60%) of non haematological diseases were of hypertension, myocardial injury and cerebral strokes. Earlier studies in the general population pinpointed the existence of an intriguing association between RDW and stroke or carotid atherosclerosis.[34,35] The common diagnosis of cardiovascular diseases in patients was consistent with the hypothesis that, many acute and chronic cardiovascular diseases are often associated with a high degree of anisocytosis.[36] Wen *et al.*[37] observed a close relationship between high RDW and ultrasound detection of advanced subclinical atherosclerosis, such as an increase of intimal-medial thickness (IMT) and the evidence of carotid plaques.[13]

In recent years, RDW has been reported to be increased in liver diseases. It has been claimed that elevated RDW values positively correlate with Model for End-Stage Liver Disease (MELD) scores in different disease statuses of hepatitis B virus (HBV) infection.[38] In addition, RDW increased with worsening of Child–Pugh grade in hepatic cirrhosis.[36] One of our case diagnosed with Chronic hepatitis B infection (RDW-SD value of 85 fL and RDW-CV value of 31%) had critical stay in hospital and died due to its complications.

The second most common group of disease was liver disease. Total of 43 cases of liver disorder including hepatocellular carcinoma had increased RDW. Interestingly showed RDW was marginally increased in hepatocellular carcinoma whereas it was markedly increased in hepatitis patients. Lou et al.[38] (2012) had conducted a study of Red cell Distribution Width (RDW) in hepatitis B patients, and the increase of Red cell Distribution Width (RDW) was significantly in accordance with the degree of severity of the liver. Another study by Chen et al.[39] (2013) tried to investigate by combining the ratio of Red cell Distribution Width (RDW) and platelet counts compared with liver biopsy. The results were found that the ratio of Red cell Distribution Width (RDW) and platelet counts can predict liver fibrosis and cirrhosis in chronic hepatitis B significantly with relatively high accuracy, and superior to other non-invasive methods ever studied in several studies earlier to predict liver fibrosis, such as aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ratios, AST and platelet Ratio Index, and FIB-4.

Rheumatoid arthritis was third most common condition diagnosed in 10.7% of the patients. This observation was in agreement with the findings reported by He Y. et al.[40] (2018) who concluded that, RDW was increased in patients with Rheumatoid arthritis (RA) which was associated with inflammation in RA, suggesting that RDW may be a potential auxiliary marker for indicating inflammation process in RA conveniently.

In a subsequent study Lee JH et al.[41] (2013) carried out a retrospective investigation of 744 patients with CAP. After stratifying the study population in quartiles of RDW, the values of several prognostic scales were found to gradually increase from the lowest to the highest RDW quartiles. Patients with a RDW value in the highest quintile also had a significantly higher 30-day mortality compared to those in the lowest quintile (OR: 2.37; 95% CI: 1.04–5.42).

Braun E. et al.[42] (2014) also carried out a retrospective analysis of 3815 patients aged 18 years or older who were diagnosed with CAP, and found that a RDW value 415% was a significant predictor of both complicated admission (OR: 2.10; 95% CI: 1.81–2.44) and 90-day mortality (OR: 3.04; 95% CI: 2.61–3.54).

CONCLUSION

Based on the results of this study it can be concluded that patients with increased RDW are having several non haematological disease presentations. Therefore, RDW alone cannot be used as single specific marker for any disease, but nevertheless it cannot be ignored in hematology reporting.

Clinicians and haematologists should take definite note increased RDW in routine reporting for any impending catastrophe.

To substantiate the importance of RDW as a prognostic marker, more research and follow up of the patients is required. Also the usefulness of RDW can be broadened beyond the conventional boundaries of erythrocyte disorders, in particular for assisting the diagnosis and prognostication of

patients with cardiovascular, liver and autoimmune diseases.

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