Spectrum of Non Haematological Diseases in Patients with Increased RDW - An Institutional Observational Study

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ABSTRACT

Introduction: Red blood cell distribution width (RDW) is the coefficient of variation of the mean corpuscular volume (MCV). RDW is used as an auxiliary index to help diagnose different types of anemia. 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. RDW can be made as a predictor of mortality in patients with cancer, chronic lung disease or acute renal failure.

Materials & methods: The present cross sectional study was conducted in the Department of Pathology, Adesh Institute of Medical Sciences (AIMSR), Bathinda, from January 2017 to December 2017 on 271 patients as per the inclusion and exclusion criterias after taking ethical clearance.

Results: In this study 50.25% of the patients were males and 49.75% were females with male to female ratio of 1.01:1, hence no relationship between RDW and gender is noted. The mean age was 44.78±18.31 years and 20.5% of the patients were aged between 51 to 60 years. Hypertension was the common non haematological diagnosis noted in 10.70% of the patients followed by rheumatoid arthritis (8.86%). The grouping of diseases according to body organ systems, cardiovascular diseases (27.31%) were common followed by liver disease (17.71%), autoimmune diseases (11.07%).

Conclusion: Patients presenting with increased RDW are likely to have other non haematological diseases other than haematological disease alone. The present study showed that diseases related to cardiovascular system were most common (especially hypertension) followed by liver disease, and autoimmune diesases. 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.

Keywords: Non Haematological, Red Blood Cell Distribution Width, Hypertension

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). Higher RDW values reflect greater variation in MCV (anisocytosis), which is usually caused by perturbation in erythrocyte maturation or degradation. RDW is used as an auxiliary index to help diagnose different types of anemia.[3-5] National Health and Nutrition Examination Survey III study showed the upper and lower limits of the RDW values to be 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]

Many researchers 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] RDW can be made as a predictor of mortality in patients with cancer, chronic lung disease or acute renal failure.[7]

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.[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.[8-12]

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),

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liver and kidney failure as well as in other acute and chronic conditions.[13]

RDW has been evaluated as a potential screening marker for colon cancer and celiac disease. Recent researches have shown higher mortality risk associated with higher RDW in patient populations with cardiovascular disease (CVD).[14-17]

This study was aimed to evaluate spectrum of non-haematological diseases in patients with increased red blood cell distribution width (RDW). The objective was to study increased RDW in non haematological diseases.

MATERIAL AND METHODS

The present cross sectional study was conducted in the Central Clinical Laboratory Department of Pathology, Adesh Institute of Medical Sciences (AIMSR), Bathinda, from January 2017 to December 2017. Ethical Clearance was obtained for the study from the Institutional Ethics Committee, Adesh Institute of Medical Sciences (AIMSR), Bathinda. A total of 271 patients of all age groups and sex with increased RDW for the respective age group and sex were included in the study after taking informed consent. Patients with decreased or normal RDW and those who were not willing to participate in the study were excluded from this study.

Sample Size and sample size calculation

Since the present study was time bound study, all the patients with increased red blood cell distribution width confirmed by haematological report were enrolled. A total of 271 patients had increased red blood cell distribution and were enrolled.

Inclusion criteria

Patients of all age groups and sex with increased RDW for the respective age group and sex.

Exclusion criteria

Patients with decreased or normal RDW and those not willing to participate in the study.

Blood sample and Data collection

Blood samples were collected in haematology lab of central laboratory of Adesh Hospital. Samples were collected through venipuncture, drawing the blood into a test tube containing an anticoagulant (EDTA) to prevent it from clotting. 2ml of blood was used in BD (Becton Dickinson) vacutainer. All samples were run for complete blood count on automated cell counter 5 part differential Mindray BC-5380. Sample 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.

On the basis of clinical findings and investigations, provisional diagnosis was recorded in a clinical performa sheet. Relevant other investigations for confirmation of systemic diseases were also performed and final diagnosis was made after necessary investigations. Selective patients were also followed up.

STATISTICAL ANALYSIS

The data obtained was coded and Microsoft Excel spread sheet (Appendix-1). Categorical data was expressed in terms of rates, ratios and percentages and continuous data was expressed as mean ± standard deviation. The comparison of continous data was done by independent sample t test assuming unequal variance

On the basis of clinical findings and investigations, provisional diagnosis was recorded in a clinical performa sheet. Relevant other investigations for confirmation of systemic diseases were also performed and final diagnosis was made after necessary investigations.

RESULTS

This one year cross-sectional study was conducted from January 2017 to December 2017. Patient referred to the haematological investigations in the section of Central Clinical Laboratory, Adesh Institute of Medical Sciences and Research, Bathinda (Punjab) were evaluated for the underlying diseases.

In 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.

The distribution of the patients according to the non haematological diseases is as shown in Table 1. Hypertension was the non haematological diagnosis noted in 10.70% of the patients followed by rheumatoid arthritis (8.86%) and pneumonia and Myocardial infarction (5.13% each).

The mean age, RDW, haemoglobin and MCV in patients with non haematological disease is as shown in table 2 and graph 1.

In the present study cardiovascular diseases (27.31%)

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

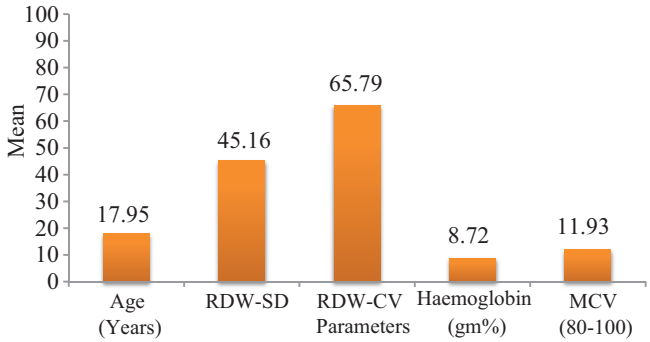
Table-1: Distribution of the patients according to the non haematological diseases

Parameters	Non Haematological (n=273)	
	Mean	SD
Age (Years)	44.54	17.72
RDW-SD (fL)	66.10	10.22
RDW-CV (Percent)	17.50	4.08
Haemoglobin (gm%)	12.86	0.91
MCV (fL)	82.40	14.14

Table-2: Comparison of mean age, RDW, MCV, haemoglobin and MCV levels in non haematological diseases

Non haematological diseases type	Distribution (n=271)	
	Number	Percentage
Cardiovascular disease	74	27.31
Liver disease	48	17.71
Autoimmune disease	30	11.07
Others	25	9.23
Lung disease	21	7.75
Infections	19	7.01
Gastrointestinal tract (GIT) cause	13	4.80
Diabetes mellitus	9	3.32
Cancer	7	2.58
Obstetrics related causes	5	1.85
Peripheral vascular disease	5	1.85
Cerebrovascular disease	4	1.48
Neonatal sepsis	3	1.11
Renal disease	3	1.11
Venous thromboembolism	2	0.74
Orthopaedic cause	1	0.37
Benign tumour	1	0.37
Recent haemorrhage	1	0.37
Total	271	100.00

Table-3: Systemic distribution of the patients according to the types of non haematological diseases



Graph-1: Showing the comparison of Age, RDW, Hb and MCV levels in relation to Mean in non haematological diseases.

were common among the patients with non haematological diseases followed by liver disease (17.71%), autoimmune disease (11.07%). The other uncommon types are as shown in table 3.

DISCUSSION

RDW has been used as diagnostic or prognostic marker in some of the clinical studies. Highly significant associations have been described between RDW value and patients with myocardial and peripheral artery diseases.

The present study was done so as to evaluate spectrum of non haematological diseases in patients who presented with increased RDW.

Increased RDW did not show any sex predilection with males (50.25%) and females (49.75%) (male to female ratio of 1.01:1) which was similar to the study by Borne Y et al[18].

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%) with the mean age being 44.78±18.31 years and the median age 45.50 years. Our observations are in concordance with study of Braun et al[20] in which his patients were 60 years or above. Lippi et al[19] showed increased RDW with advancing age. His study showed 11% higher RDW in subjects aged 60 years or older compared to those aged less then 60 years.

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. Detail of other diseases has been described in table 1.

Recently Bilal A. et al.[21] 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.

Rheumatoid arthritis was the second common condition diagnosed in 10.7% of the patients. This observation was in agreement with the findings reported by He Y. et al.[22] 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 our study the third common non haematological diseases were pneumonia and myocardial infarction comprised of 5.13% of the patients each.

Braun E. et al.[20] retrospectively analyzed the data of 637 consecutive patients aged 60 years old or younger, who were diagnosed with CAP, and reported that a RDW value[4] 14.5% was significantly associated with complicated hospitalization in multivariate analysis. 2 of our cases were diagnosed with pneumonia (RDW-SD value of 66 fL & RDW-CV value of 18%) and chronic renal disease (RDW-SD value of 78 fL and RDW-CV value of 18%) died critically. Study done by Solak et al[23] reported RDW values significantly increased in patients with impaired Glomerular filtration rate.

RDW has been reported to be increased in liver diseases.[24,25,26] It has been shown 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.[24] In addition, RDW increased with worsening of Child–Pugh grade in hepatic cirrhosis.[27] 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.

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.[28,29] 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.[27] Wen *et al.*[30] 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.[10]

The persistent RDW increase in cardiovascular diseases has been attributed to the effective stimulation of erythropoiesis by erythropoietin (EPO), a hormone secreted during hypoxic events, which promotes the release of enlarged RBCs from bone marrow. Another hypothesis is that elevated RDW may be due to a slight reduction of RBC turnover. More specifically, since the size of RBCs gradually reduces with ageing of the cells, a decreased rate of RBC turnover would allow smaller cells to persist for longer into the circulating. It has been speculated that the chronic inflammatory state which often accompanies acute and chronic cardiovascular diseases may be another powerful erythropoiesis modulator. In line with this hypothesis, a number of proinflammatory cytokines are effective to inhibit EPO secretion and RBC maturation, thus enhancing anisocytosis.[10]

The second most common group of disease was liver disease. Total of 43 cases of liver disorder including hepatocellular carcinoma had increased RDW. Interestingly RDW was marginally increased in hepatocellular carcinoma whereas it was markedly increased in hepatitis patients. Lou et al.[24] 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. Study by Chen et al.[31] 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.

Overall in the nutshell, erythropoiesis is substantially influenced by the concentration of many inflammatory cytokines, oxidative stress, poor nutritional status, dyslipidemia and increased RBC turnover. Hence patients presenting with increased RDW are likely to have other non haematological diseases other than haematological disease alone. The present study showed that, maximum number of patients had non haematological disease and disease related to cardiovascular system being common (especially hypertension) followed by liver disease, and autoimmune diesases. However the findings from the present study need careful interpretation due to potential limitations of

this study. viz. single centre study involving relatively smaller sample size which limits the generalization of the observations to the entire population. Hence further multicentric studies involving large sample size may provide the true usefullness of RDW. 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.

CONCLUSION

The mean RDW-SD levels were noted as 66.01±11.18, the mean RDW-CV levels were noted as 17.32±4.06 and the mean MCV was 82.47±13.99.

50.25% of the patients were males and 49.75% were females with male to female ratio of 1.01:1, hence no relationship between RDW and gender is noted.

The mean age was 44.78±18.31 years and 20.5% of the patients were aged between 51 to 60 years.

Hypertension was the common non haematological diagnosis noted in 10.70% of the patients followed by rheumatoid arthritis (8.86%).

The grouping of diseases according to body organ systems, cardiovascular diseases (27.31%) were common followed by liver disease (17.71%), autoimmune diseases (11.07%).

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.

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