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ROLE OF RED CELL DISTRIBUTION WIDTH IN HEART FAILURE PATIENTS

General Medicine

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ABSTRACT

Background: There is a growing body of evidence over the last decade that higher red cell distribution width (RDW) has been associated with increased risk of mortality and morbidity outcomes in patients with heart failure. The present study is carried out with an aim to evaluate the clinical significance of RDW in predicting the severity of heart failure and also to assess whether it is positively correlated with the other cardiac markers such as NT-Pro BNP, (N-terminal pro B-type natriuretic peptide), LVEF (Left ventricular Ejection fraction) and NYHA (New York Heart Association classification). **Methods:** A total of 100 participants are recruited in the current Case Control Study. Out of 100 participants recruited, 50 are healthy controls and 50 are patients (cases) with heart failure fulfilling the inclusion criteria. Participants are randomly selected and the study is conducted over a period of 18 months from 1st January 2020 . **Results:** The mean age of the study population is 61.58±12.01 years among cases and 58.34±5.06 years among controls with a p value 0.278. The mean RDW is significantly more among patients with severe LVEF compared to moderate/mild LVEF. RDW is remarkably high when compared to subjects with normal LVEF with a p- value of <0.005. The mean MCV and RDW-SD is significantly correlated with NT- Pro BNP, NYHA class and LVEF with Pearson correlations of 0.467, 0.442, and 0.489 and with a significant p-values of 0.026, 0.033, and 0.032 respectively. **Conclusion:** In the present case control study, RDW is emerged as an independent biomarker in predicting the severity of heart failure. Also significantly correlated with the clinical, biochemical and cardiac imaging parameters in assessing the severity of heart failure.

KEYWORDS

RDW, hs-CRP, NT-Pro BNP, 2D ECHO, LVEF, NYHA.

INTRODUCTION:

Heart failure is a complex clinical syndrome resulting from structural and functional impairment of ventricular filling or ejection of blood. It may result from abnormalities or disorders involving all aspects of cardiac structure and function. [1] Ischemia is the chief aetiology for heart failure worldwide.[2] Over the last decade, several biomarkers have been emerged in heart medicine like uric acid, **high-sensitivity C-reactive protein (hs-CRP),** cardiac neurohormone such as NT-Pro BNP and many other pro-inflammatory cytokines which help in the diagnosis as well as the prognosis of heart failure. The prognosis of acute heart failure (AHF) remains generally but not uniformly poor with all-cause mortality (ACM) rising to 10–20% at 2–3 months. [3]

Moreover, almost 25% of patients are readmitted within 30 days, and up to 46% within 6 months after discharge from hospitalization for AHF, which contributes to premature mortality and morbidity outcomes. [4,5] Biomarkers like NT-Pro BNP have been shown to improve prediction on top of clinical assessment in patients with chronic heart failure. N-terminal pro B-type natriuretic peptide (NT-proBNP) is an inactive peptide released along with the active peptide hormone BNP when the walls of the heart are stretched or there is pressure overload on the heart e.g. by fluid overload. An NT-proBNP level less than 400 pg/ml in an untreated person makes a diagnosis of heart failure less likely. An NT-proBNP level greater than 400 pg/ml is elevated and Heart Failure cannot be excluded. An NT proBNP >2000 pg/ml requires urgent referral for ECHO Left ventricular hypertrophy, right ventricular overload, ischemia, tachycardia, hypoxemia, PE, sepsis, COPD, diabetes, liver cirrhosis,age>70, and e GFR<60ml/min can all cause increase NT-proBNP[7]

The red cell distribution width (RDW) blood test measures the amount of red blood cell variation in volume and size. The red blood cell distribution width (RDW) is a rather simple measure of RBC size heterogeneity, which is calculated by dividing the standard deviation (SD) of erythrocyte volumes for the mean corpuscular volume (MCV) (i.e., RDW = SD/MCV). The normal range of RDW-CV is 11.5-14.5%. When the levels of oxygen are low, the body tends to increase the production of the red blood cells so as to compensate for the health condition causing it, such as heart failure. [8] Recent studies have reported a strong independent association between increased RDW and the risk of adverse outcomes in patients with heart failure and in patients with stable coronary disease.[9,10] Patients living in resource poor settings may not be able to access advanced technological investigations like NT pro BNP, 2D Echocardiography routinely. RDW is an integral component of Complete blood count (CBC), which is also a simple and affordable haematological investigation that can provide comprehensive, yet reliable, information regarding the disease progression. Specialised investigations like 2D ECHO and, NT-Pro BNP can be considered later to confirm the heart failure and also to quantify the severity of disease progression as indicated. The present study is carried out with an aim to evaluate the clinical significance of RDW in predicting the severity of heart failure and also to assess whether it is positively correlated with the other cardiac markers such as *NT-pro BNP*, (N-terminal pro B-type natriuretic peptide), LVEF (Left ventricular Ejection fraction) and NYHA (New York Heart Association classification).

Aims and Objectives:

Aim:

To evaluate the clinical significance of RDW in predicting the severity and prognostication of heart failure

Objectives:

- Primary objective is to study whether RDW as a robust marker of heart failure in cardiac patients.
- Secondary objective is to correlate RDW with the Left ventricular ejection fraction and NT-Pro BNP
- To correlate RDW with the severity of heart failure. (NYHA functional classification)

MATERIALS AND METHODS:

This prospective randomized clinical study entitled "Role of Red Cell Distribution Width in Heart Failure Patients" is conducted after obtaining the clearance from Board of Studies and Ethical committee in the Department of General Medicine, School of Medical Sciences & Research, Sharda University during the period, from 1st January 2020

for a period of 18 months.

Study Design: Case control study

Study population:
50 patients with heart failure fulfilling the inclusion criteria and 50 healthy controls were randomly selected for the study. Informed written consent was obtained.

Inclusion and Exclusion criteria:
The study subjects were chosen as per the inclusion and exclusion criteria:

Inclusion criteria
Adult patients of heart failure
Previously diagnosed patients of heart failure.
Newly detected patients of heart failure.

Exclusion criteria
Primary Liver disease
Primary Renal disease
Anaemia with haemoglobin < 12 g/dl
Blood transfusion within past 3 months
Haematological malignancy

Study procedure:
CBC including RDW was performed using a SYSMEX XN1000 automated hematology analyzer (Sysmex, Kobe, Japan) in all the patients.

Routine biochemical tests (including LFT, KFT, and Lipid profile) in all the patients. ECG, CXR PA view, 2D ECHO cardiography was performed in all cases. BNP and hs-CRP was done in acute and chronic heart failure patients

Statistical Analysis:
The data was entered into the Microsoft excel and the statistical analysis was performed by statistical software SPSS version 21.0. The Quantitative (Numerical variables) were present in the form of mean and SD and the Qualitative (Categorical variables) were present in the form of frequency and percentage. The student t-test was used for comparing the mean values between the 2 groups whereas chi-square test was applied for comparing the frequency. The p-value was considered to be significant when less than 0.05.

RESULTS:
Table 1 depicts the data about gender distribution, there were 55 (55.0%) males and 45 (45.0%) females among study population. Table 2, shows the mean age of the study population 61.58±12.01 years among cases and 58.34±5.06 years among controls with a p-value of 0.278. Table: 3 shows that 50% of heart failure is contributed by ischemic heart diseases. Table: 4 depicts, Alcohol is the predominant risk factor with a significant p-value of 0.009.

Table 1: Distribution of type of heart disease in study population according to gender

	Gender		Total	Chi-square value	p-value
	Male	Female			
Ischemic heart disease	14	11	25	0.082	0.774
	48.3%	52.4%	50.0%		
Rheumatic heart disease	6	3	9	0.338	0.561
	20.7%	14.3%	18.0%		
Cor pulmonale	3	4	7	0.766	0.381
	10.3%	19.0%	14.0%		
Dilated cardiomyopathy	3	2	5	0.009	0.924
	10.3%	9.5%	10.0%		
Alcoholic	0	0	0	0.000	1.000
	0.0%	0.0%	0.0%		
Calcific AS/AR	0	0	0	0.000	1.000
	0.0%	0.0%	0.0%		
Peripartum	0	0	0	0.000	1.000
	0.0%	0.0%	0.0%		
Right Ventricular Dysfunction	0	0	0	0.000	1.000
	0.0%	0.0%	0.0%		
Eisenmenger's	0	0	0	0.000	1.000
	0.0%	0.0%	0.0%		
Myocarditis	3	0	3	2.311	0.128
	10.3%	0.0%	6.0%		

Table 2: Distribution of study population according to Risk factors

	Gender		Total	Chi-square value	p-value
	Male	Female			
Hypertension	17	14	31	0.335	0.563
	58.6%	66.7%	62.0%		
Diabetes Mellitus	11	9	20	0.123	0.726
	37.9%	42.9%	40.0%		
Dyslipidaemia	9	5	14	0.315	0.574
	31.0%	23.8%	28.0%		
Smoking	20	10	30	2.313	0.128
	69.0%	47.6%	60.0%		
Alcohol	8	0	8	6.897	0.009*
	27.6%	0.0%	16.0%		
BMI > 30	9	4	13	0.910	0.340
	31.0%	19.0%	26.0%		

Table 3: Distribution of study population according to history & examination.

	Gender		Total	Chi-square value	p-value
	Male	Female			
Previous h/o heart failure	4	3	7	0.002	0.960
	13.8%	14.3%	14.0%		
Previous h/o myocardial infarction	4	4	8	0.250	0.617
	13.8%	19.0%	16.0%		
Paroxysmal Nocturnal Dyspnoea (PND)	12	8	20	0.055	0.815
	41.4%	38.1%	40.0%		
Orthopnoea	20	17	37	0.910	0.340
	69.0%	81.0%	74.0%		
Jugular Venous Pressure (JVP)	14	12	26	0.384	0.536
	48.3%	57.1%	52.0%		
Rales	18	16	34	1.116	0.291
	62.1%	76.2%	68.0%		
Third Heart sound (S3)	2	2	4	0.114	0.735
	6.9%	9.5%	8.0%		
Oedema	16	11	27	0.038	0.845
	55.2%	52.4%	54.0%		

Table 4: Distribution of study population according to hemogram.

	Groups	Mean	Std. Deviation	t-test value	p-value
Haemoglobin	Case	13.41	1.38	-0.667	0.507
	Control	13.59	1.32		
HCT	Case	40.85	4.02	-0.878	0.382
	Control	41.56	4.10		
MCV	Case	91.24	3.88	2.044	0.044*
	Control	89.49	4.68		
RDW-SD	Case	49.89	12.54	2.042	0.044*
	Control	45.14	3.36		

Table 5: Correlation of RDW-D with NT-Pro BNP, NYHA class and LVEF.

	RDW – SD	
NT Pro BNP	Pearson Correlation	0.467
	p-value	0.026*
New York Heart Association class	Pearson Correlation	0.442
	p-value	0.033*
LVEF	Pearson Correlation	0.489
	p-value	0.023*

Table 6: Correlation of RDW-D with different LVEF groups.

	Red cell distribution width				
LVEF	Mean	Std. Deviation	F-value	p-value	Post-hoc comparisons
Normal	45.79	14.13	4.712	0.005*	Severe > Moderate >Mild > Normal
Mild	49.00	12.57			

Moderate	50.22	9.35			
Severe	60.00	17.41			

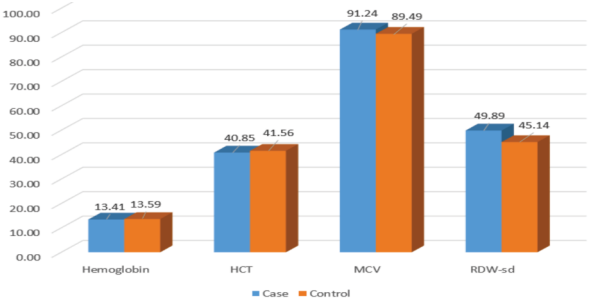

Figure 1

Table: 4 and Figure: 1 shows that the mean MCV and RDW-SD was significantly more among heart failure patients compared to controls.

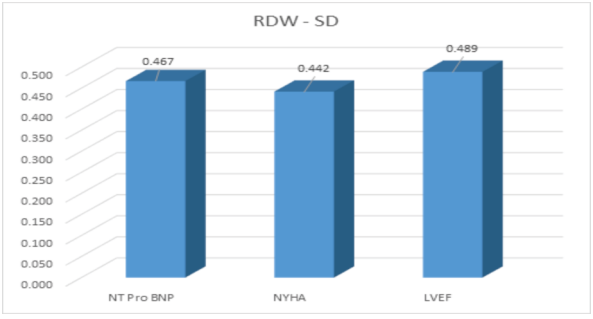

Figure 2

Table:5, and Figure: 2 demonstrates that the mean MCV and RDW-SD is significantly correlated with NT- Pro BNP, NYHA class and LVEF with a Pearson correlations of 0.467, 0.442 and 0.489 with a significant p-values of 0.026, 0.033 and 0.032 respectively.

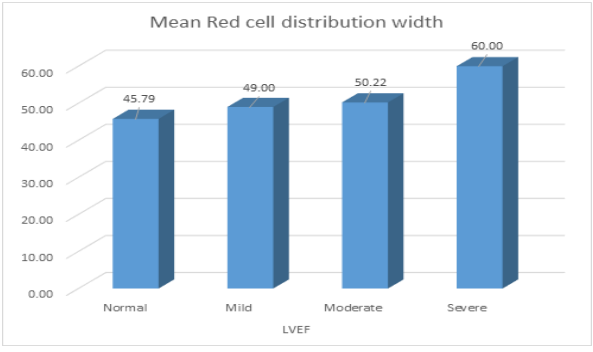

Figure:3

Table:6 and Figure:3 depicts the data on the mean red cell distribution width which is notably high among subjects with Severe LVEF compared to subjects with Moderate/Mild LVEF and also significantly high in comparison to subjects with normal LVEF.

DISCUSSION:

The goal of this study is to independently validate the recent observations on the predictive role of red cell distribution width (RDW) for outcomes in chronic heart failure and also to evaluate whether the other cardiac markers correlate with RDW in assessing the severity of heart failure (HF). Our study results demonstrate that mean MCV and RDW-SD is significantly more among heart failure patients compared to controls. While there can be many reasons for the occurrence of high RDW, the common reason is the low oxygen levels in the patient's body. Our study denotes that mean RDW is significantly more among patients with severe LVEF compared to moderate/mild LVEF and remarkably high when compared to subjects with normal LVEF with a p- value of <0.005. A cross-sectional study conducted by *Rudresh et al*[11] proven that the RDW was higher in the cases compared to controls with p value of <0.001. Our study shows that 50% of heart failure is contributed by ischemic heart diseases and predominant risk factor is found to be alcohol. *Rudresh et al* [11] found that 60% had ischemic heart disease, 27.14% had hypertensive heart disease. This is consistent with the study by Al-Najjar et al.[12] where the aetiology of the HF was mostly ischemic (70%). In India coronary artery disease, diabetes, hypertension, valvular heart diseases and primary muscle diseases are the leading causes for heart failure. Rheumatic heart disease is still a common cause of heart failure in India. Our study included all of the above aetiologies.

Heart failure can reduce tissue perfusion, and may cause dysfunction of kidneys, liver, worsens oxygen and carbon dioxide exchange in the lungs. Chronic inflammation is also common in heart failure and the presence of anisocytosis may be interpreted as a homeostatic response to the disease, thus reflecting the existence of a potential link between ineffective erythropoiesis and chronic inflammation. Förhécz et al.[13]

The current study demonstrates that the mean MCV and RDW-SD is significantly correlated with NT- Pro BNP, NYHA class and LVEF with a Pearson correlations of 0.467, 0.442, and 0.489 with a significant p-values of 0.026, 0.033 and 0.032 respectively. Another retrospective study done in 2016 by *Liu et al* to evaluate the value of baseline RDW for predicting the severity of chronic heart failure and to compare with NT-ProBNP and other haematological parameters, substantiated that RDW was potential marker for mortality during hospitalization but had a less predictive value compared to NT-pro BNP in congestive heart failure. Therefore, their study demonstrates that a combination of RDW and validated cardiac markers such as NT-pro BNP can help the earlier and targeted management of patients with CHF .[14] Our study also demonstrates that mean RDW is notably high among subjects with Severe LVEF compared to subjects with Moderate/Mild LVEF and also significantly high in comparison to subjects with normal LVEF. In a study conducted by Alexandra Holmström et al to study the role of RDW in heart failure and its relation to cardiac function and biomarkers demonstrated that RDW levels were higher in patients with SHF and HFNEF. Moreover, NT-pro BNP levels were independently linked with elevated RDW.[15]

Strengths of Study:

RDW, emerged as an independent predictor in assessing the severity of heart failure. RDW is an easily attainable bio-marker and also predicts the prognosis before and after developing the heart failure.

Limitations of study:

Multi-centric large scale studies are needed to testify its validity whether it can be successfully applied in clinical practice.

CONCLUSION:

In the current study, Red cell distribution width is emerged as an independent prognostic biomarker for heart failure. RDW is also significantly correlated with the other clinical, biochemical and cardiac imaging parameters such as NYHA, NT- Pro BNP and LEVF. Hence, RDW can be considered as an initial bio marker in predicting the severity of heart failure before considering the other specialised investigations. Treating physicians also need be aware of the underlying chronic diseases which may have been concomitantly contributing to anaemia and impaired LVEF. Elevated RDW may certainly alert the physicians to search for the underlying comorbidities that alter heart failure prognosis. Timely risk stratification of patients with congestive heart failure (CHF) is crucial for their targeted management.

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Conflict Of Interest: NIL

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