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Original Research Article

STUDY OF RELATION BETWEEN RED CELL DISTRIBUTION WIDTH (RDW) WITH AGE, SEVERITY AND DURATION OF HEART FAILURE

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Abstract:

Background: Recently RDW is getting studied in relation to heart failure and its elevated values seems significant in prediction of mortality and morbidity in heart failure patients. RDW is an easily available parameter as most of the CBC analysers give RDW.

Material and method: 300 patients of heart failure were studied for relation of RDW with their clinical, biochemical, hematological, echocardiographic parameters. Patients were followed up till the end of 3 months. Data were collected accordingly with predesigned proforma and appropriate statistical analysis was done to find out interrelations of parameters and association with mortality.

Results: Male to female ratio was 3:1with mean age of 57.13 years. Out of 300 patients of heart failure 27.7% patient had raised RDW while 74.3 % patients had RDW with in normal limit. Among 300 patients included in the study, 77 patients succumbed. The mean RDW of the patients on the basis of outcome was derived and found to be higher in patients who died at the end of 3 month that was 15.43 having a significant P value (<0.01). Among those who succumbed, out of young age group 2 patients were diabetic status and 6 patients were non-diabetics; out of older age group 20 patients were diabetic while 49 patients were non-diabetics. Out of 182 patients with raised RDW, 55 (30.2%) patients had raised CRP as well. Mean RDW was higher in the group with EF < 30%, when compared with moderate and mild LV dysfunction and was normal in the group where EF> 54% which was found to be statistically significant as evident by P value (<0.01).

Conclusion:

Red blood cell distribution width is an easy to measure, widely available and low-cost marker that is showing prognostic significance both in the diabetic and non-diabetic HF patients.

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Key words: C-Reactive Protein (CRP), Diabetes, Echocardiography, Heart failure, Red cell distribution width (RDW)

1. Introduction:

Heart Failure is a clinical syndrome characterised by symptoms such as shortness of breath, persistent coughing or wheezing, ankle swelling and fatigue, that may be accompanied by jugular venous pressure, pulmonary crackles, increased heart rate & peripheral oedema. [1] However, these signs may not be present in the early stages and in patients treated with diuretics. Initial workup should include clinical history, physical examination, laboratory assessment, chest radiography and electrocardiography.

Beyond detecting myocardial abnormality, abnormalities of the valves, pericardium, endocardium, heart rhythm, and conduction may be found. [2, 3] The identification of the underlying aetiology is pivotal for the treatment [4].
Red cell distribution width (RDW): is a maesurment of variation in the volume and size of the RBCs. Recently RDW was found to be elevated in many heart failure cohorts. It is represented in 2 forms- RDW-CV (coefficient of variation) or RDW-SD (standard deviation). It is an easily available parameter as most of the CBC analysers give RDW. An elevated RDW can predict mortality and morbidity in heart failure. Various postulates and theories have been put forth by many researchers for the cause for elevated RDW in the context of heart failure.

The aim of this study was to evaluate the association of RDW with severity, clinical outcome, diabetic status, C-reactive protein (CRP), Hb1AC, and echocardiography parameters in young (less than 40 years of age) and elderly (more than 40 years) patients with heart failure.

2. Material and methods

This observational study was conducted at department of medicine, Sri Aurobindo medical college & postgraduate institute, Indore (M.P.) in India during 2017 to 2019. Institutional ethical and research committee approval was obtained.
300 newly diagnosed and follow up cases of heart failure coming in decompensated state, of age group 18 years and above with their informed consent were included in the study.

Cases of COPD, congenital heart disease, rheumatic heart disease, anemia (Hb less than 11gm/dl in female and Hb less than 12 gm/d in male), malignancy (primary/metastasis), pregnancy and lactation, connective tissue disorder, haematological disorder, CKD, septic shock, blood transfusion, vit B12 and folic acid within 6-month, patient taking steroid therepy, pulmonary thromboembolism, pericardial diseases, and refusal to participate in study were excluded.

Data collected with appropriate predesigned proforma. All the cases were subjected to detailed history, thorough clinical examination and investigations (CBC, RDW, corrected ESR, peripheral smear, FBS, PPBS, HBA1C, serum creatinine, BUN, LFT, lipid profile, TSH, CRP, chest x ray PA view and echocardiography).

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Descriptive statistics, parametric test, correlation coefficient, chi square test to identify the association between variables and logistic regression to find out the predictive value of RDW were used for statistical analysis.

3. Results

30 patients (10%) were of <40 years age and 270 patients (90%) of >40 years with male predominance (75.3%). 182 patients (60.7%) had raised RDW and 39.3% had normal RDW. It was observed that 25.7% (77 patients) died within 3 months. 30% heart failure patients found to have diabetes mellitus while 70 % were non diabetic. 25.7% patients had raised CRP and 74.3% had normal CRP. Age range and diabetic status of survivors and non survivors are portrayed in table 1. Out of 300 patients of heart failure, 77 patients died within 3 months. Comparison between mortality at 3 months with RDW and diabetic status in heart failure patients is shown in table 2. Comparison between mortality at 3 months with CRP and diabetic status in heart failure patients is shown in table 3. LVEF and diabetic status in heart failure patients who died within 3months is shown in table 4. Table 5 shows correlation between different variables in heart failure patients. Table 6 shows group statistics between RDW and 3 months mortality in patients of heart failure

Table 1: Comparison between mortality at 3 months with age group and diabetic status in heart failure patients

Mortality at 3 months	**Age**	**Diabetics**	**Non diabetics**	**Total**
No	<40 year (young)	5(22.73%)	17(77.27%)	22
	>40 year (Old)	63(31.34%)	138(68.66%)	201
Yes	<40 year (young)	2(25.00%)	6(75.00%)	8
	>40 year (Old)	20(28.99%)	49(71.01%)	69

Table 2: Comparison between mortality at 3 months with RDW and diabetic status in heart failure patients

Mortality at 3 months	RDW	Diabetics	Non diabetics	Total
Yes	Raised	18 (32.14%)	38 (67.86%)	56
	Normal	4 (19.05%)	17 (80.95%)	21
No	Raised	38 (30.16%)	88 (69.84%)	126
	Normal	30 (30.93%)	67 (69.07%)	97

Table 3: comparison between mortality at 3 months with CRP and diabetic status in heart failure patients

Mortality at 3 months	CRP	Diabetics	Non diabetics	Total
Yes	Raised	9 (27.61%)	24 (72.73%)	33
	Normal	13(29.55%)	31 (70.45%)	44
No	Raised	15 (34.09%)	29 (65.91%)	44
	Normal	53 (29.61%)	126 (70.39%)	179

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Table 4: LVEF and diabetic status in heart failure patients who died within 3 months.

Mortality at 3 months- yes (77 cases)	LVEF	Diabetics	Non diabetics	Total
	<45%	4 (10.25%)	35 (89.74%)	39
	>45%	20(52.63%)	18 (47.36%)	38

Table 5: Correlation between different variables in heart failure patients

	Descriptive Statistics	
	Mean	Standard deviation
Age	57.13	12.12
RDW	15.44	8.44
cESR	13.17	4.48
HBA1C	8.57	31.74
Total cholesterol	135.53	40.54
LDL	108.90	40.06
HDL	41.85	11.87
Triglyceride	172.65	107.37

Table 6: Group statistics between RDW and 3 months mortality in patients of heart failure

3 months mortality	RDW			
	No. of Patients	Mean	Standard deviation	P<0.001 (Sig)
YES	77	15.59	1.97554	
NO	223	14.75	1.62933	

Group statistics between RDW and 3 Months mortality in patients of heart failure. It was observed that mean RDW was 15.59 in mortality group. While the mean RDW in non mortality group was 14.75. the p value was <0.001 which is statistically significant.
Out of 182 patients with raised RDW, 17 patients was < 40 years of age and 165 patients was in the group of > 45 year of age. While. Out of 118 patients with Normal RDW, 13 patients was in <40 year of age and 105 patients with Normal RDW. Comparisons were made among 2 groups using pearson chi-square test and the P value was 0.636 (i. e. >0.05, not significant).

Out of 182 patients with raised RDW, 55 patients had raised CRP and 127 patients had normal CRP.While out of 118 patients with Normal RDW, 22 patients had Raised CRP and 96 patients had normal CRP. Comparisons were made among 2 groups using pearson chi-square test and the P value was 0.025 which is statistically significant.

Out of 182 patients with raised RDW, 28 patients had raised HBA1c >8 and 154 patients had HBA1C level <8. While out of 118 patients with Normal RDW, 21 patients had Raised HBA1C >8 and 97 patients had HBA1C level <8. Comparisons were made among 2 groups using pearson chi-square test and the P value was 0.581 which is statistically not significant.

Table 7 shows comparison of levels of RDW with 3 months mortality in heart failure patients. Table 8 shows the LVEF range in patients with heart failure.

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Table 7: Comparison of levels of RDW with 3 months mortality in heart failure patients

RDW	3 Months mortality			P value 0.012 [<0.05(sig)]
	Yes	NO	Total	
Raised	56 (30.8%)	126 (69.2%)	182 (100%)	
Normal	21 (17.8%)	97 (82.2%)	118 (100%)	

Table 8: LVEF range in patients with heart failure

			Gender		Total	
			Male	Female		
LVEF	< 30 % Severe	N	52	4	56	P value 0.005 [<0.05(sig)]
		%	23.2%	5.3%	18.7%	
	31-44% Moderate	N	81	36	117	
		%	36.2%	47.4%	39.0%	
	45-54% Mild	N	73	27	100	
		%	32.6%	35.5%	33.3%	
	> 54 % Normal	N	18	9	27	
		%	8.0%	11.8%	9.0%	
Total		N	224	76	300	
		%	100.0%	100.0%	100.0%	

4. Discussion

Elevated red cell distribution width has been found to be associated with increased risk of adverse cardiovascular event in heart failure patients. Although the exact mechanism behind this is not clearly known, several postulates have been contemplated by researchers across the globe.

Inflammation and oxidative stress have been considered as the principal reason behind the alteration in erythrocyte homeostasis.

Pro-inflammatory cytokines [5] like IL-6, TNF α and IL-1β erythropoietin mediated RBC maturation leading to increase in RDW. [6]

Bone marrow resistance to erythropoietin, deranged iron metabolism, hemodilution and anemia of chronic disease have been proposed as mechanism for anemia [7] and increased mortality in Patients with Heart Failure. Although many studies have successfully elucidated the prognostic role of RDW in heart failure, no clear insights into the mechanisms behind the same have been arrived till date.

CHARM data and Duke Databank were used to study the role of RDW as a prognostic marker in heart failure [8]

Increased RDW is associated with metabolic syndrome, carotid artery atherosclerosis, renal impairment, older age and in a critically ill patients. Including natriuretic peptides and few other costly markers along with the cheaper RDW has helped in establishing the role of RDW as an independent marker in the prognosis of heart failure.

In our study we found that 90% patients belong to older age group while 10% patients were in the younger age group; mean age was 57.13 years. Mean age in studies of Elif Eroglu et al [9] and Marcello Tonelli et al [10] is 57 year and 56.7 year respectively.

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Fadi T. Alattar et al. found 79% of cases were males and 21 % females [11]. Emeline van et al. also found 72% cases were males [12]. Our study also clearly demonstrated male predominance with 75.3% males and 24.7% females.
Table 9 shows comparison of RDW and mortality across studies. Table 10 shows comparison across studies, of mortality at 3 months with age group and diabetic status in heart failure patients.

Table 9: Comparison of RDW & Mortality across studies

Study	Mean RDW	Mortality
Felker at el [13]	15.5%	31%
Kimmenade et al [5]	15.1%	31%
Tonellim et al [7]	15.91%	26%
In our study	15.43%	25.7%

Table 10: Comparison across studies, of mortality at 3 months with age group and diabetic status in heart failure patients

Study	Diabetic	Mortality	Mean Age	Mean RDW
Xanthopoulos et al [14]	32.6%	21%	73	15.2%
Roland R.J.et al [15]	39%	31%	56.15	15.1%
In our study	30%	26.66%	57.13	15.43%

ICARIA (Ibermutuamur Cardiovascular Risk Assessment study) observed that RDW is associated with metabolic syndrome. They stated that a cut-off of 13.5 for RDW-CV in metabolic syndrome.
A retrospective study conducted by Yusuke Uemura et al on 265 consecutive patients, revealed mean RDW of 15.0% and mean CRP 0.75 (p value <0.001) hence statistically significant [16]. A study done by Avci et al in 328 patients revealed mean RDW 15.65%, mean CRP 1.6 with a statistically significant p value of <0.001[17]. However, in one study conducted by Lippi' et al demonstrated that RDW is associated with chronic inflammation with no significant increase in CRP [18].

In the present study, out of 182 patients with raised RDW, 55(30.2%) patients had raised CRP while 127(69.8%) patients had normal CRP level. The study also revealed that out of 118 patients with Normal RDW, 22(18.6%) patients had raised CRP and 96(82.4%) patients had normal CRP. Comparisons were made among the 2 groups using pearson chi-square test and found to have a statistically significant P value (0.025) i.e. <0.05.
Previous epidemiological studies have reported that increased CRP levels or RDW levels are strongly related to adverse clinical outcomes In HF patients.
Persistent increase in the CRP and RDW may reflect unfavourable and uncontrollable disease conditions, which expose patients to higher risk and poor outcome.

Echo revealed 56 (18.7%) patients having EF less than 30%, 117 (39%) patients having EF between 31% - 44%, 100 (33.3%) patients having EF between 45% -54% while 27 (9%) patients had EF above 54%.

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The mean RDW among the 4 different groups based on EF values were compared. Mean RDW was higher in the group with EF <30%, when compared with moderate and mild LV dysfunction and was normal in the group where EF> 54% which was found to be statistically significant as evident by P value (<0.01).
Hence, we concluded that there is strong correlation between RDW and LV ejection fraction.
Red blood cell distribution width is an easy to measure, widely available and low-cost marker that showed in our study, similar prognostic significance both in the diabetic and non-diabetic group of HF patients with respect to the combined outcome of death from any cause or hospitalization for HF.
The longitudinal RDW changes shows significant statistical difference in diabetic and non-diabetic patients. These findings might be due to the higher inflammatory burden that patients with concomitant DM and HF may carry against the population of HF without DM and may provide new insights to the understanding of the pathophysiological mechanism of RDW increase in HF.

5. Conclusion

Red Cell Distribution Width (RDW) levels are increased in heart failure patients. RDW levels correlated with severity of LV dysfunction. RDW not just a marker but a strong predictor of mortality in heart failure patients. The changes in RDW showed significant statistical difference in diabetic and non-diabetic patients. These findings might be due to the higher inflammatory burden that patients with concomitant DM and HF may carry against the population of HF without DM and may provide new insights to the understanding of the pathophysiological mechanism of RDW increase in HF and other pathological states. Measurement of the serial RDW and especially the combination of Admission value with subsequent changes in RDW during in-hospital or home care, may be seen as an efficient and affordable tool to help assessing the prognosis of patients with HF and for reliably predicting the risk of adverse events. Combining RDW with other biomarkers and NYHA functional class can indeed be a very good predictor of morbidity and mortality. Heart failure patients with low LV ejection fraction and diabetic patients, have elevated RDW levels and had high mortality compared with normal LV ejection fraction and in non-diabetics. Therapy of anaemia in patients with heart failure with resultant changes in RDW can aid in the prediction of favourable outcome which further requires prospective studies.
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Conflict of intrest: Nil.

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