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Study of Relationship between Red Cell Distribution Width and Severity of Heart Failure in Tertiary Care Centre, Mysuru

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ABSTRACT:
BACKGROUND:
There has been growing attention given to the relationship between RDW andcardiovascular disorders. Red celldistribution width (RDW) has recently beendiscovered to be a novel prognostic marker in patients with heartfailure.

OBJECTIVES:
• To study and compare red cell distribution width between patients of heart failureand healthy subjects.
• To study relationship between Red Cell Distribution Width and severity of heartfailure.

METHODS:
The study was a cross sectional study including 100 subjects (70 Heart failurecases and 30 healthy controls). Datawas obtained from history, biochemical tests andechocardiographic tests.

RESULTS:
Mean RDW in cases was 16.177±3.247 and in controls was 13.67 ± 2.156.
RDW is higher in cases compared to controls (p value <0.001). RDW is >14.5 in 32cases (73%) of HFrEF group compared to 13 cases (50%) in HFpEF (p value0.003).
RDW is >14.5 in 13 patients with HFpRF (50%)where asRDW is >14.5 only in 6 controls (20%)(p value <0.001). Increasing trend of RDW was also found as per NYHA class.

INTERPRETATION AND CONCLUSION:
RDW values increase with severity of heart failure. Hence can be used as aprognostic marker at admission. However, follow up studies should be done in thefuture to further support the data.

KEY WORDS: Heart failure; Red cell distribution width; Heart failure withpreserved ejection fraction; Heart failure with reduced ejectionfraction; New York Heart Association class

I. INTRODUCTION:

Heart failure (HF) is a common cardiovascular disease which causes a large morbidity and mortality. AHA guidelines define Heart Failure as a complex clinical syndrome that results from structural or functional impairment of ventricular filling or ejection of blood which in turn leads to cardinal symptoms of dyspnea and fatigue and signs of heart failure namely edema and rales.[7]

The prevalence of heart failure in adult population in developed countries is nearly 1–2%.[1]

RDW is a quantitative measure of anisocytosis, i.e., the variability in size of the circulating red cells. It is used in finding the cause of anemia.[2]

In the recent past, more attention has been given to the relationship between RDW and cardiovascular disorders, such as heart failure and coronary artery disease. Red cell distribution width (RDW) has been found to be a prognostic marker in patients with heart failure.[3]

NT-proBNP (a marker of heart failure) is costly and difficult to be done in poor resource centres. RDW is reported in a complete blood count result. Extra test/cost is not required in knowing it and can be done even in primary health centres.[4]

II. OBJECTIVES OF THE STUDY

- To study and compare red cell distribution width between patients of heart failure and healthy subjects.
- To study relationship between Red Cell Distribution Width and severity of heart failure

III. METHODOLOGY:

Source of data: Primary source of information- observational study was done on data obtained from the venous samples of Heart failure patients admitted in the medical wards of the K. R Hospital, Mysuru as well as HF patients who came to OPD for follow up.

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Secondary source of information is from published articles and journals, books, related websites and were used as supporting documents.
Sample size: 100 (cases – 70, controls- 30)
Duration of study: 18 months – January 2018 to June 2019

INCLUSION CRITERIA
1. Subjects who are 18 years and above
2. Follow up cases of heart failure.
3. Newly diagnosed cases of heart failure- ischemic heart disease, valvular heart disease, non ischemic cardiomyopathy, Hypertensive heart disease.

EXCLUSION CRITERIA:
i. Chronic obstructive pulmonary disease
ii. Anemia
iii. Bone marrow neoplasms
iv. Pregnancy
v. Hypothyroidism
vi. Chronic liver disease
vii. Patients on chemotherapeutic drugs
viii. Chronic kidney disease
ix. Patients on antifolate drugs, vitamin supplements.

IV. MATERIALS AND METHODS:

Approximately 10ml of blood was drawn from the patient after informed consent for carrying out biochemical tests like complete blood counts, liver function tests, renal function tests, random blood glucose, thyroid function tests within 24hrs of admission/consultation. ECG and chest X-ray was also done.

RDW: 3ml sample was collected in EDTA vial. Using SYSMEX KX 21 automated hematology analyser, various indices of the blood cells were computed. RDW was noted from CBC report.

2DECHO: Echocardiography was done after stabilising the patient. Left ventricular ejectionfraction and cause for heart failure was assessed and grouped as
1. Heart failure with reduced ejection fraction (HFrEF) and
2. Heart Failure with preserved ejection fraction (HFpEF).

The criteria for diagnosis of HFREF and HFPRF are specified. Three criteria (symptoms typical of HF + signs typical of HF+ reduced LVEF) are required for HFREF, and four criteria (symptoms typical of HF + signs typical of HF+ normal/ mildly reduced EF+ relevant structural heart disease and/or diastolic dysfunction).[3]

Severity of heart failure as per NYHA classification was also noted within 24hrs of admission/consultation.

Statistical analysis: It was addressed with histogram, sample mean, standard deviation, chi square test, ANOVA test, Pearson's correlation and t test. A p value of <0.05 was considered as statistically significant.

V. RESULTS:

A total of 70 patients of heart failure and 30 healthy subjects were included and following results and observations made.

Of the 70 cases of heart failure 44(62.86%) had HFrEF and 26 (37.14%) had HFpEF.

The mean age was 57.4±13.48 among cases and in controls. 64.3% of the cases belonged to the age group of 40-65 years.48% were males and 52% were females in the study (p value: 0.963). Proportion of males and females in cases and controls are almost equal.

Most of the cases belong to IHD (52.8%) and HHD (25.7%).In age group of 20-39yrs, 55.6% were RHD subjects. In age group of 40-65yrs, 53.3% were IHD subjects. In the age group >40yrs, IHD and HHD are more in number. In the age group of 20-40yrs, RHD and DCM are more in number, in the age group >65yrs 75% were IHD subjects.

As per NYHA classification, 13 belonged to NYHA1, 22 to NYHA2, 14 in NYHA3, 21 in NYHA4.

Mean RDW in cases was 16.177±3.247 and in controls was 13.67 ± 2.156. RDW is higher in casescompared to controls. It is statistically significant with a p value of <0.001.

RDW is >14.5 in 45 subjects among cases (64.3%) and 6 subjects among controls (20%). (p value <0.001)

RDW is >14.5 among cases (64.3%) than among controls (20%).

Table 1: Mean RDW – cases vs controls

Group	Number	Mean	Standard deviation
Case	70	16.1771	3.24739
Control	30	13.6700	2.15617

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Subjects with RDW>14.5 were more in HFrEF group (91.7%) than HFpEF group (50%). Subjects with RDW >14.5 are more in HFrEF group when compared to HFpEFgroup and is statistically significant with p value: 0.003.

Subjects with RDW >14.5 are more in HFpEF (13) compared to controls (6). The difference between the two groups was found statistically significant with p value <0.001.

Table 2: RDW and NYHA class

NYHA	Number	Mean	Std.Deviation	Minimum	Maximum
1	13	13.5154	1.00486	11.40	15.60
2	22	15.4091	2.88789	12.00	25.80
3	14	16.4357	3.04495	12.30	25.20
4	21	18.4571	3.19900	11.50	23.50
Total	70	16.1771	3.24739	11.40	25.80

RDW values showed increasing trends with the NYHA class.The difference between the groups was found significant with p value <0.001.

VI. DISCUSSION

The hypothesis of the study was higher level of RDW is associated with HFrEF as well as HFpEF at the time of presentation to the hospital. RDW has been shown as a novel marker in predicting outcome in heart failure. The results of the present study add to theavailable data regarding predictive relevance of the elevated RDW in heart failure.

The age of the patients varied from 22 years to 77 yrs with a mean of 57 years. Mean age is comparable to other studies. Study on DHF patients by Atac Celik et al[5] had mean age as 57 years and study by Rudresh et al[3] on both HFrEF and HFpEF had mean age of 54.86 years among cases.

Heart failure can occur in any age. In the present study, IHD and HHD was found to be more above 40yrs of age especially 65yrs of agewhereas RHD and DCM was found more in younger age group (20-39yrs of age). This is because elderly ageitself is arisk factor for IHD and hypertension, rheumatic fever and substance abuse prevelance is more common in younger age group.

Of the 70 patients in the study, 34 were males and 36 were females. There is a slight female preponderance in the heart failure cases. This could be because of difference in admission pattern. This could also be because women at older age are at increased risk than men for IHD.

In our study IHD contributes to 52.9% of cases similar to study by Yahya Al Najar et al [4](70% of cases were IHD) and Rudresh et al [3](60% cases were IHD). In India, coronary heart disease, hypertension, rheumatic heart diseases are leading causes of heart failure.

RDW is a measure of variation of RBC size in the blood sample. Normal range is 11.5 - 14.5%. Hence 14.5 has been taken as cut off for RDW in the study. 14.5% has also been chosen as the cut off in the study by Andrew Xanthopoulos et al.[8]

Our study shows RDW is elevated in both HFrEF and HFpEF. RDW is significantly elevated in HFrEF group compared to HFpEF, similar to study by Rudresh et al.[3]

Table 3: Comparison of mean RDW in different studies with other studies

	MEAN RDW in cases
Our study	16.17±3.24%
Rudresh et al[3]	15.763 ±2.609%
Atack Celik et al[5]	14.33±1.53%
Eleni Tseliou et	18±3.5%

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al[9]	

Table 4: Significance of RDW in HFrEF and HFpEF with other studies

	HFrEF	HFpEF
Present study	Significant	Significant
Rudresh et al[3]	Significant	Significant
Atac Celik et al[5]	Did not include	Significant
Yahya Al Najjar et al[4]	Significant	Did not include
Konstantinos Sotiropolous et al[6]	Not significant	Significant
Eleni Tseliou et al[9]	Significant	Did not include

RDW as per NYHA class

Our study showed increasing values of RDW with the NYHA class and RDW >14.5 in NYHA class 2, 3, 4.

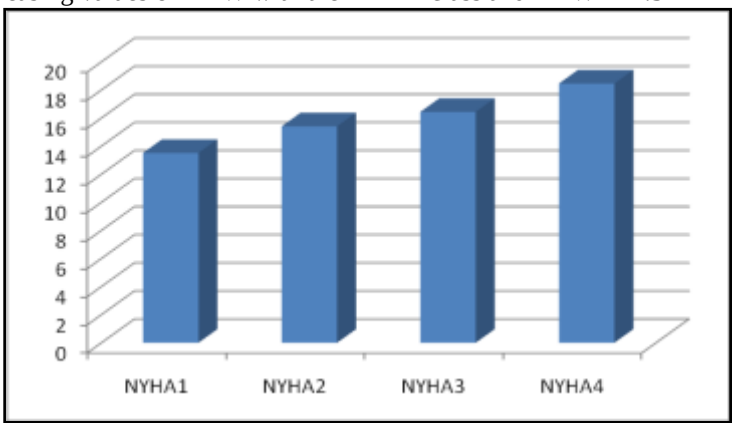

Figure 1: RDW and NYHA class

In a study by Sen Liu et al[10] it was found that RDW was elevated in NYHA 3 and 4.Study by Eiichi Akiyama et al[11] also found RDW levels to be higher in patients with NYHA 3 and NYHA 4 compared to NYHA1 and 2.

Various mechanisms have been suggested to underlie the association between the RDW and severity of heart failure. Several studies have suggested that elevated RDW values are associated with high inflammatory (hs-crp) and neurohumoral markers (such as B type natriuretic peptide)[5]. Inflammation probably contributes to an increase in RDW by impairing iron metabolism, inhibiting the production of or response to erythropoietin and shortening red cell survival. Moreover, inflammatory cytokines suppress the maturation of RBCs, and immature RBCs enter circulation[12].Study by KontostantinosSotiropoulous et al [6]on heart failure patients also showed that IL-6 was increased in patients with symptoms of heart failure. Oxidative stress was proposed as another mechanism for elevated RDW in HF. Red blood cells are prone to oxidative damage and reduce its survival and enhance release of immature RBCs[13].

VII. LIMITATIONS:

Sample size of the study was not large. Follow up of the cases was not done. We did not measure Vitamin B12 and folate levels which are potential causes of raised RDW.

VIII. CONCLUSION:

Ischemic heart disease and Hypertensive heart disease are the commonest causes leading to heart failure.

RDW values increase with severity of heart failure. Hence can be used as a prognostic marker at

admission. However, follow up studies should be done in the future to further support the data.

RDW values can be used in both HFrEF and HFpEF as a prognostic marker at admission, however more significant with HFrEF.

It can be used as an additional marker for heart failure.

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