

Comparison of Mean Red Cell Distribution Width in Ischemic Heart Disease Patients with and Without Heart Failure

Muhammad Uzair Ijaz Malik, Tariq Bashir Tareen*, Mehar Rehman

Department of Medicine, PAC Hospital Kamra/National University of Medical Sciences (NUMS) Pakistan,

*Department of Medicine, Combined Military Hospital/National University of Medical Sciences (NUMS), Rawalpindi Pakistan

ABSTRACT

Objective: To compare mean red cell distribution width in ischemic heart disease patients with and without heart failure.

Study Design: Cross Sectional study.

Place and Duration of Study: General Medicine Department, Pakistan Aeronautical Complex Hospital, Kamra Pakistan, from Sep 2021 to Apr 2022.

Methodology: Patients presenting to outpatient department or admitted in general medical ward with diagnosed Ischemic heart disease were included in the study as per the inclusion criteria. Basic demographics (age, gender, height, weight on weighing machine, BMI) were noted. 12 lead ECGs and 2D ECHO were performed on all patients. Presence of heart failure with reduced ejection fraction (<45%) was documented and patients were categorized into heart failure and non-heart failure groups. Mean RDW-CV was noted in all patients for comparison.

Results: In this study a total of One Hundred and fifteen patients were recruited with a mean age of 63.13 ± 10.13 years (normal distribution $p > 0.05$). The mean RDW in ischemic heart disease patients was found to be $15.23 \pm 1.04\%$. The mean RDW was significantly higher among patients with heart failure than those without heart failure i.e., $15.51 \pm 1.09\%$ and $14.85 \pm 0.83\%$ respectively (p -value 0.005). Similarly, significantly higher mean RDW was noted among advanced heart failure cases when stratified based on ejection fraction (p -value 0.001).

Conclusion A significant difference of mean red cell distribution width was observed in between heart failure patients and non-heart failure patients.

Keywords: Heart Failure, Ischemic Heart Disease (IHD), Mean Red Cell Distribution Width (RDW).

How to Cite This Article: Malik MUI, Tareen TB, Rehman M. Comparison of Mean Red Cell Distribution Width in Ischemic Heart Disease Patients with and Without Heart Failure. Pak Armed Forces Med J 2026; 76(Suppl-9): S1539-S1543. DOI: <https://doi.org/10.51253/pafmj.v76iSUPPL-9.10539>

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Ischemic heart disease is a medical condition ensuing from a deficient blood supply to a portion of the myocardium, which occurs secondary to atherosclerotic narrowing of the lumens of coronary arteries, hence impeding oxygen delivery to the heart. It is a major cause of deaths and disability and supersedes many other illnesses in the developed world. Over time the progression of ischemic heart disease can deteriorate the strength of the heart muscle, leading to heart failure, which is described as a clinical entity resulting from any structural or functional impairment of ventricular filling or ejection of blood, culminating in the symptoms of shortness of breath, fatigue and retention of fluid. Ischemic coronary artery disease has become the predominant cause of heart failure and is responsible for 60-75% cases. Hypertension, valvular heart diseases, Diabetes mellitus and cardiomyopathies are also major

contributors in disease etiology.¹ Heart failure is a deleterious, resource draining syndrome requiring polypharmacy and resulting in enhanced morbidity, early mortality and impaired quality of life. It is a rapidly increasing ailment worldwide with more than 64.3 million people affected from it. In developed countries, the prevalence of heart failure in adult population is approximately 1-2%. Heart failure incidence rises with age, affecting approximately 11.8% individuals of age greater than 65 years.² In South Asia in general, and Pakistan in particular, the prevalence of heart failure is also increasing with approximately 2.8 million Pakistani population suffering from it.³ Many factors namely high prevalence of non-communicable diseases (IHD, HTN and Diabetes), deskbound lifestyle, smoking, abdominal obesity, polluted atmosphere, rheumatic heart disease and impoverished health care systems contribute the rising prevalence in these areas. The commonest cause in Pakistan was also found to be ischemic heart disease with hypertension, valvular heart disease and cardiomyopathy being the other notable causes.⁴

Correspondence: Dr Muhammad Uzair Ijaz Malik, Department of Medicine, PAC Hospital, Kamra Pakistan

Received: 23 Jun 2023; revision received: 09 Jan 2024; accepted: 10 Jan 2024

Recent studies have demonstrated the role of inflammation in the pathogenesis and progression of heart failure as suggested by the elevation of pro-inflammatory biomarkers.⁵ Increased levels of C reactive protein, Inflammatory cytokines (Tumor necrosis factor-Alpha, IL-1, IL-6,) and procalcitonin are found to be independently related to the incidence and progression of heart failure.⁶ Red cell distribution width (RDW) is a parameter in blood complete count that measures the variation of red blood cell size or volume. RDW is elevated when marked variation in red cell size i.e. anisocytosis is present. It has also been studied as a marker for inflammation, as inflammation is frequently associated with bone marrow dysfunction and increased premature erythrocytes in circulation resulting in anisocytosis. Elevated RDW values may indicate inflammatory stress and compromised iron mobilization leading to impaired erythropoiesis. In chronic heart failure, RDW has been studied as an independent predictor of adverse outcomes.⁷⁻⁹

Although multiple studies regarding association of RDW with heart failure have been performed globally, but local data is scarce. Currently, the Red Cell Distribution width is not routinely monitored in patients with Heart failure. However is inexpensive and widely available as compared to other markers such as N-terminal pro-BNP and 2D ECHO. So, this study was designed with an aim of studying association of mean red cell distribution width with progression in heart disease.

METHODOLOGY

This cross-sectional study was performed in the Department of General medicine, Pakistan Aeronautical Complex Hospital Kamra Pakistan from September 2021 to April 2022. For this study, the sample size was calculated to be 111 using a 95% confidence interval and 7 % margin of error, with the expected local frequency of Ischemic heart disease as 17%.¹⁰ We obtained ethical approval from the hospital ethical committee before commencing the research (Certificate no. 9/2021 dated 10.7.2021). A total of One hundred and fifteen ischemic heart disease patients were included in the study who satisfied the mentioned inclusion criteria. Volunteer participation was encouraged throughout the study.

Inclusion Criteria: Patients of either gender, with ages ranging from 30-85 years presenting to the outpatient department with diagnosed ischemic heart disease with heart failure (Ejection Fraction <45%) and without heart failure, were included. Patients having

past history of myocardial infarction, percutaneous transluminal coronary angioplasty/coronary artery bypass grafting, angiographically documented disease or positive exercise tolerance test were diagnosed as patients of ischemic heart disease. Heart failure was defined by reduced ejection fraction (<45%) on 2D ECHO with concurrent presence of either 2 major criteria or 1 major and 2 minor criteria according to Framingham study.¹¹

Exclusion Criteria: All the patients having nutritional deficiencies (Iron, Vitamin B12, Folate), having medical conditions and/ or consuming drugs known to affect RBC morphology i.e. Hemolysis, recent transfusion (<6 months), chronic diseases (CLD, CKD, Malignancies) and malabsorption states were excluded. Pregnant or lactating women were also not entertained.

Written consent was acquired from patients to ensure discretion and patient well-being. Basic demographics (age, gender, height, weight on weighing machine, BMI) were noted. 5ml of venous blood was drawn for routine biochemical tests like complete blood count, including RDW. Of the 5 ml of blood drawn, 3ml sample was collected in an Ethylene diamine tetra acetic acid (EDTA) vial for CBC. Using SYSMEX XP-100 Automated hematology analyzer, RDW was noted. 12 lead ECGs and 2D ECHO were also performed on all patients. All the information was recorded in a specially designed proforma. Patients lost to follow-up were replaced by new candidates.

Statistical package for social sciences (SPSS) version 23 was utilized for analyzing the collected data. Both qualitative and quantitative variables were measured by using descriptive statistics. Mean and standard deviations were used for quantitative variables like age, weight, height, BMI, RDW, and Ejection Fraction. For qualitative variables like gender, age groups and Heart failure, frequency and percentages were calculated. Data were presented in tables. Independent sample t-test was applied for comparing the means of variables. One way ANOVA was used for comparison of mean RDW amongst heart failure groups stratified according to severity (low ejection fraction) i.e. Group 1 (Ejection fraction 46-60%), Group 2 (Ejection fraction 31-45%), and Group 3 (Ejection fraction 15-30%). The *p*-value of ≤ 0.05 was considered significant.

RESULTS

For this study One hundred and fifteen patients were enrolled with a mean age of 63.13±10.13 years

(normal distribution $p>0.05$). Almost half of the patients ($n=57$, 49.5%) presented with >65 years of age. Males were predominantly higher ($n=76$, 66.1%) than females ($n=39$, 33.9%). The mean weight, height, and BMI of the patients were 74.54 ± 11.65 kg, 1.70 ± 0.09 m, and 25.71 ± 3.73 kg/m², respectively. We found that 53% of the patients had >25 kg/m² BMI. The mean ejection fraction was noted as $44.38\pm13.08\%$ while the mean RDW was observed as $15.23\pm1.04\%$ (Table-I). A total of 82(71.3%) patients reported red blood cell width $>14.5\%$, while 33(28.7%) had $\leq 14.5\%$ RDW. Heart failure (Ejection fraction $<45\%$) was found in 66(57.4%) patients. The mean RDW was significantly higher among patients with heart failure than those without i.e., $15.51\pm1.09\%$ and $14.85\pm0.83\%$ respectively (p -value 0.005) (Table-II). Similarly, significantly higher mean RDW (p -value 0.001) was noted among advanced heart failure cases when stratified based on ejection fraction (Table-III).

Table-I: Demographic Characteristics of Patients (n=115)

Variables	Mean $\pm$ SD	Range
Age (years)	63.13 $\pm$ 10.13	37 - 82
Weight (Kg)	74.54 $\pm$ 11.65	54 - 98
Height (m)	1.70 $\pm$ 0.09	1.45 - 1.92
Body Mass Index (Kg/m ²)	25.71 $\pm$ 3.73	18.5 - 34.5
Ejection fraction (%)	44.38 $\pm$ 13.08	20-60
Mean Red Blood Cell Distribution Width (%)	15.23 $\pm$ 1.04	12.6-17.2

Table-II: Mean Red Blood Cell Distribution Width of Heart Failure and Non-Heart Failure Patients (n=115)

Heart failure	Number of patients (n)	Mean Red Blood Cell Distribution Width $\pm$ SD (%)	p -value
YES	66	15.51 $\pm$ 1.09	0.005
NO	49	14.85 $\pm$ 0.83	

Table-III: Mean Red Blood Cell Distribution Width of Ischemic Heart Disease Patients stratified according to Ejection Fraction (n=115)

Heart Failure Group	Number of patients (n)	Mean Red Blood Cell Distribution Width (Mean $\pm$ SD)	p -value
Ejection Fraction 46-60%	49	14.85 $\pm$ 0.83	0.001
Ejection Fraction 31-45%	35	15.39 $\pm$ 1.23	
Ejection Fraction 15-30%	31	15.65 $\pm$ 0.90	

DISCUSSION

Red blood cell distribution width is a parameter in complete blood count that measures the variability of red blood cell size or volume. RDW is elevated when marked variation in red cell size i.e. anisocytosis is present. It is also a marker for inflammation. RDW is reported statistically as standard deviations (RDW-SD = 42.5 ± 3.5 fL) or coefficient of variation (RDW-CV $12.8\pm1.2\%$).¹² It is a low-priced, widely accessible test which is routinely generated by the contemporary

hematology analyzers as a part of complete blood picture. Studies have shown that it has diagnostic as well prognostic value in patients with IHD. High RDW values ($>14\%$) were significantly related to lessened red blood cell deformability, with subsequent impairment of blood flow through the micro-circulation. Ultimately the outcome is reduced oxygen supply at tissue level, hence clarifying the increased adverse cardiac events in patients with raised RDW.¹³

In the current study, the mean RDW in ischemic heart disease patients was found to be 15.23 ± 1.04 , which is higher than mean RDW for general population without IHD. The association of IHD with RDW was studied by Nagula *et al.*,¹⁴ where RDW was established as an independent predictor of angiographic coronary artery disease, and a RDW value of 14.3% was identified as the cutoff point in diagnosing IHD (sensitivity 58.9%, specificity 84.8%). In a recent meta-analysis including 13 trials and involving 10410 patients, a lower RDW value was associated with a reduced mortality (all cause and cardiovascular) in acute coronary syndrome patients (RR 0.35, (95% CI 0.30 to 0.40), $p<0.00001$)¹⁵ indicating its prognostic significance.

In addition to the demonstration of mean RDW in IHD patients, the aim of our study was to compare the mean RDW between IHD patients having diagnosed heart failure and with normal cardiac systolic function. In our study, a significant higher mean RDW was observed among heart failure cases than that of patients without heart failure, i.e. 15.51 ± 1.09 and 14.85 ± 0.83 respectively (p -value 0.0005). Similarly, significantly higher mean RDW (p -value 0.001) was noted among advanced heart failure cases when stratified based on ejection fraction. When compared amongst ejection fraction groups, RDW was significantly high when Group 3 (EF 15-30%) and Group 2 (EF 31-45%) were each compared independently with Group 1 (EF 46-60%) (p -values 0.002 and 0.04 respectively). However no significant difference was noted in the comparison between Group 2 and Group 3 patients (p -value 0.52). Comparing these results with International literature, we found that multiple authors are in agreement to the debate that RDW has a significant role in this regard, either alone or in combination with other authenticated biomarkers such as the natriuretic peptides. In a study by Liu *et al.*,¹⁶ baseline value of RDW was studied as a predictor for advanced heart failure and its comparison with NT-pro BNP. The RDW significantly

increased in the NYHA stage III and IV heart failure patients and predictive value of RDW was comparable to NT-ProBNP in Stage IV patients.

The clinical utility of RDW as a forecaster in patients with heart failure was studied by Kim M *et al.*, 6599 chronic heart failure patients were followed up for 887 days with serialized RDW measurements. A higher all-cause mortality (primary endpoint) was noted amongst the high RDW group patients. In patients with heart failure, a 1% increase in RDW value was associated with a 7% increase in the primary endpoint after adjustment.¹⁷ Comparative results were shown by multiple meta analysis in the recent past which have shown that for each 1% increase in RDW over time, there is a significant increase in all cause mortality and major adverse cardiac events including heart failure (Hou *et al.*,¹⁸ Hazard Ratio 1.11 (95% CI:1.05-1.17). Study of Felker *et al.*,¹⁹ reported 2679 heart failure patients and revealed that the highest RDW values were significantly associated with mortality and morbidity (HR 1.17 per 1-SD increase in RDW $p<0.001$). The mid term prognostic role of RDW in patients admitted with acute heart failure was studied by Melchio *et al.*,²⁰ 451 patients admitted with acute heart failure were followed for a 18 moths duration with RDW measured at inclusion (Low RDW <14.8%, High RDW >14.8%). Mortality was found to be higher amongst the High RDW group (165 patients vs 70 patients), and was noted as a major predictor ($p=0.003$, HR 1.73, 95% CI 1.2-2.48) of a lower survival rate on long term follow up.

In light of the studies, it can be emphasized that in patients with IHD and heart failure, the RDW can serve two important purposes. Firstly it serves as a prognostic marker for major adverse events in both acute and chronic heart failure (Cardiovascular as well as all-cause mortality). Secondly it has importance as a significant and independent prognosticator of developing heart failure, in patients free of this ailment at the time of evaluation.

The findings of this study could be highlighted in the light of the limitation that it was a single centre based study with a limited sample size. Longitudinal assessment of the RDW values over time and long term follow up of the patients was not done to highlight the prognostic value. We suggest that further studies should be conducted to assess the predictive value of RDW to estimate the disease prognosis. We also propose that serial measurements of RDW; especially the combination of admission value with

future changes during in-hospital stay or monitoring at home; may be an affordable and efficient future marker to help assess the prognosis of patients with HF and to reliably predict the risk of adverse events.

CONCLUSION

The mean RDW in ischemic heart disease patients was found to be 15.23 ± 1.04 with a significantly higher RDW among patients with heart failure than of patients without heart failure. Recent and past data suggests that both heart failure and anisocytosis may have several shared pathogenic mechanisms, elucidating as to why both the clinicopathological processes may arise and progress simultaneously, thus stressing the significance of RDW as a well-grounded marker of heart failure. This study also offers new avenues like consideration of anti-inflammatory treatment for management of heart failure in the years to come.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MUIM & TBT: Data acquisition, data analysis, critical review, approval of the final version to be published.

MR: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Mann DL, Chakinala M. Disorders of the heart. In: Kasper DL, Hauser SL, Jameson J, Fauci A, Longo D, Loscalzo J, editors. *Harrisons principles of internal medicine*. 20th ed. New York: McGraw-Hill; 2018.
2. Groenewegen A, Rutten FH, Mosterd A, Hoes AW. Epidemiology of heart failure. *Eur. J. Heart Fail*. 2020; 22(8): 1342-1356.
<https://doi.org/10.1002/ehf.1858>
3. Martinez-Amezcu P, Haque W, Khera R, Kanaya AM, Sattar N, Lam CS, et al. The upcoming epidemic of heart failure in South Asia. *Circ Heart Fail* 2020; 13(10): e007218.
<https://doi.org/10.1161/CIRCHEARTFAILURE.120.007218>
4. Khan Z, Khan B, Hiader I, Khan I, ud Din J, Khan H, et al. Etiology of congestive heart failure at a tertiary care hospital. *Rawal Med J* 2010; 35(2): 141-144.
5. Murphy SP, Kakkar R, McCarthy CP, Januzzi Jr JL. Inflammation in heart failure: JACC state-of-the-art review. *J Am Coll Cardiol* 2020; 75(11): 1324-1340.
<https://doi.org/10.1016/j.jacc.2020.01.014>
6. Sarhene M, Wang Y, Wei J, Huang Y, Li M, Li L, et al. Biomarkers in heart failure: the past, current and future. *Heart Fail Rev* 2019; 24: 867-903.
<https://doi.org/10.1007/s10741-019-09807-z>

7. Parizadeh SM, Esfehiani RJ, Bahreyni A, Ghandehari M, Shafiee M, Rahmani F, et al. The diagnostic and prognostic value of red cell distribution width in cardiovascular disease; current status and prospective. *Biofactors* 2019; 45(4): 507-516. <https://doi.org/10.1002/biof.1518>
8. Lippi G, Turcato G, Cervellin G, Sanchis-Gomar F. Red blood cell distribution width in heart failure: a narrative review. *World J Cardiol* 2018; 10(2): 6-14. <https://doi.org/10.4330/wjc.v10.i2.6>
9. Rahamim E, Zwas DR, Keren A, Elbaz-Greener G, Ibrahimli M, Amir O, et al. The ratio of hemoglobin to red cell distribution width: A strong predictor of clinical outcome in patients with heart failure. *J Clin Med* 2022; 11(3): 886. <https://doi.org/10.3390/jcm11030886>
10. Kazmi T, Nagi ML, Razzaq S, Hussnain S, Shahid N, Athar U. Burden of noncommunicable diseases in Pakistan. *East Mediterr Health J* 2022; 28(11): 798-804. <https://doi.org/10.26719/emhj.22.083>
11. Löfström U, Hage C, Savarese G, Donal E, Daubert JC, Lund LH, et al. Prognostic impact of Framingham heart failure criteria in heart failure with preserved ejection fraction. *ESC Heart Fail* 2019; 6(4): 830-839. <https://doi.org/10.1102/ehf2.12458>
12. Briggs C, Bain BJ. Basic Hematological Techniques. In: Bain BJ, Bates I, Laffan MA, Lewis SM, editors. *Dacie and Lewis practical hematology*. 12th ed. Philadelphia, PA: Elsevier; 2017.
13. Patel KV, Mohanty JG, Kanapuru B, Hesdorffer C, Ershler WB, Rifkind JM. Association of the red cell distribution width with red blood cell deformability. *Adv Exp Med Biol* 2013; 765: 211-216. https://doi.org/10.1007/978-1-4614-4989-8_29
14. Nagula P, Karumuri S, Otikunta AN, Yerrabandi SR. Correlation of red blood cell distribution width with the severity of coronary artery disease—A single center study. *Indian Heart J* 2017; 69(6): 757-761. <https://doi.org/10.1016/j.ihj.2017.04.007>
15. Abraham IV LL, Ramos JD, Cunanan EL, Tiongson MD, Punzalan FE. Red cell distribution width and mortality in patients with acute coronary syndrome: a meta-analysis on prognosis. *Cardiol Res* 2018; 9(3): 144-152. <https://doi.org/10.14740/cr732w>
16. Liu S, Wang P, Shen PP, Zhou JH. Predictive values of red blood cell distribution width in assessing severity of chronic heart failure. *Med Sci Monit* 2016; 22: 2119-2125. <https://doi.org/10.12659/msm.898103>
17. Kim M, Lee CJ, Kang HJ, Son NH, Bae S, Seo J, et al. Red cell distribution width as a prognosticator in patients with heart failure. *ESC Heart Fail* 2023; 10(2): 834-845. <https://doi.org/10.1002/ehf2.14231>
18. Hou H, Sun T, Li C, Li Y, Guo Z, Wang W, et al. An overall and dose-response meta-analysis of red blood cell distribution width and CVD outcomes. *Sci Rep* 2017; 7: 43420. <https://doi.org/10.1038/srep43420>
19. Felker GM, Allen LA, Pocock SJ, Shaw LK, McMurray JJ, Pfeffer MA et al. Red cell distribution width as a novel prognostic marker in heart failure: data from the CHARM program and the Duke databank. *J Am Coll Cardiol* 2007; 50(1): 40-47. <https://doi.org/10.1016/j.jacc.2007.02.067>
20. Melchior R, Rinaldi G, Testa E, Giraudo A, Serraino C, Bracco C, et al. Red cell distribution width predicts mid-term prognosis in patients hospitalized with acute heart failure: the RDW in Acute Heart Failure (RE-AHF) study. *Intern Emerg Med* 2019; 14: 239-247. <https://doi.org/10.1007/s11739-018-1958-z>