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Original Article

Assessment of relationship between red blood cell distribution width and renal function in patients with acute heart failure

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Abstract

Objectives: To investigate the association between Red Blood Cell Distribution Width (RDW) and renal function in patients experiencing acute decompensated heart failure (ADHF).

Methods: A retrospective analysis was conducted on the medical records of 254 patients admitted to Seyyed Al-Shohada Hospital in Urmia, Iran, between July 2021 and July 2023. Patients' RDW values and Glomerular Filtration Rate (GFR) were analyzed using statistical methods.

Results: The study revealed a significant inverse relationship between RDW and GFR. Patients with elevated RDW levels (greater than 14.5%) demonstrated reduced GFR values compared to those with lower RDW levels. The mean GFR in patients with RDW ≤14.5% was 59.31 ml/min, while in patients with RDW >14.5% it was 49.71 ml/min ($p < 0.001$).

Conclusions: RDW is an important biomarker for evaluating renal function and predicting outcomes in ADHF patients. RDW inclusion in evaluating ADHF patients could improve risk stratification and facilitate early intervention. Additional studies are necessary to validate these findings and examine the underlying mechanisms. RDW Integration into routine clinical practice may enhance the identification of patients at higher risk for renal complications, enabling timely therapeutic interventions and potentially improving overall patient management and outcomes.

Keywords: Red Blood Cell Distribution Width (RDW), Acute Decompensated Heart Failure, Renal Function

Introduction

Heart failure (HF) is a prevalent cardiovascular disorder marked by progressive and debilitating symptoms. The incidence of this disease is on the rise, attributed to an aging demographic, improvements in the treatment of myocardial infarction, and lower mortality rates. In the United States, approximately five million individuals are affected by HF, with around 550,000 new cases diagnosed each year (1). In Iran, the prevalence of heart failure varies from 0.47 to 9.05 per 100 people (2). The incidence and spread of HF is increasing in developed countries. Although contemporary therapies for HF exist, the outlook for patients with HF continues to be unfavorable, characterized by elevated rates of mortality and hospitalization. Ongoing symptoms of cardiac congestion and renal impairment are critical prognostic indicators (3).

Renal function plays an essential role in patients with HF, as enhancements in renal status frequently result in improved outcomes and diminished symptoms. Worsening Renal Function (WRF), characterized by increasing serum creatinine levels of 0.3 mg/dL or more from baseline, is an independent prognostic indicator (4). Hemodynamic abnormalities in HF diminish cardiac output, elevate venous congestion, and lead to a decrease in renal perfusion pressure and Glomerular Filtration Rate (GFR). The rise in renal venous pressure may induce interstitial renal hypertension, tubular hypertrophy, fibrosis, and tubular injury, thereby establishing a connection between cardiac dysfunction and renal impairment. Individuals with a decreased GFR encounter more than twice the mortality risk compared to those who do not experience renal failure (5). Moreover, worsening renal function (WRF) is associated with an increased risk of mortality and hospitalization among chronic heart failure patients, regardless of whether they have reduced or preserved ejection fraction (6). In cases of acute HF, where worsening renal function is present in 20-30% of patients, there is a notable rise in the risk of mortality (5). Elevated serum creatinine levels, which tend to stabilize with extended hospital stays, indicate the mean alteration in renal function during hospitalization at the population level. This observation highlights considerable variability in renal changes across different patients (7).

Red Blood Cell Distribution Width (RDW) significantly predicts overall cardiovascular and cancer-related mortality within the general population. This measurement, included in a complete blood count, refers to the variation in the size of circulating red blood cells and is instrumental in classifying various types of anemia, including thalassemia, iron deficiency anemia, and anemia linked to chronic diseases. Elevated RDW levels correlate with unfavorable clinical outcomes across a range of conditions, such as acute coronary syndrome, pancreatitis, and rheumatoid arthritis (10, 11). Elevated RDW demonstrates a significant negative predictive value (NPV) for the diagnosis of multiple conditions and may serve as a valuable tool for both short-term and long-term prognostic evaluation in cardiovascular and thrombotic diseases. (12,13). Numerous studies have indicated a correlation between RDW and HF, suggesting that elevated RDW levels during hospitalization are associated with a higher mortality rate in HF patients(14,15). Individuals suffering from acute HF and exhibiting elevated RDW levels may have a worse prognosis than those with lower RDW values. However, additional studies are necessary to investigate the underlying mechanisms that drive this relationship (16). The third National Health and Nutrition Examination Survey (NHANES), accomplished from 1988 to 1994, indicated that RDW is linked to a higher risk of mortality, extending beyond cardiovascular disease (CVD) alone(17).Furthermore, elevated RDW levels in these individuals have been associated with more advanced disease stages and a less favorable prognosis (18). Given that RDW is regularly provided by clinical laboratories, comprehending its prognostic importance can be desirable for risk stratification in clinical decision-making. This research seeks to evaluate the correlation between RDW and renal function in patients admitted with acute decompensated heart failure (ADHF), with the potential to identify a valuable marker to assess risks and make clinical decisions. This study explores the association between RDW and renal function in individuals experiencing ADHF, aiming to identify a significant indicator for risk assessment and clinical decision-making.

Literature Review

Uemura et al. (2016) evaluated the association between RDW during hospitalization and mortality rates in patients with ADHF in Japan. They found that elevated RDW during hospitalization was linked to an increased risk of cardiac mortality (19). In another study, Cheng et al. (2016) studied RDW and mortality risk in ADHF patients with or without Cardiorenal Anemia Syndrome (CRAS) in Taiwan. The study found that elevated RDW levels were independently associated with an increased mortality risk in ADHF patients, irrespective of their CRAS status (20).Yamada et al. (2020) conducted a systematic review examining the relationship between deteriorating renal function and increased mortality in patients suffering from ADHF.They found that individuals with compromised renal function faced an increased risk of mortality; however, those who effectively achieved decongestion enjoyed more favorable prognoses (21). Patel et al. (2021) evaluated renal function and outcomes in hospitalized patients suffering from HF.Their findings indicated that diminished renal function correlated with increased

rates of mortality and hospitalization (22). Beldhuis et al. (2019) conducted a study examining alterations in kidney function among patients with ADHF in the Netherlands. Their findings revealed a correlation between elevated RDW levels and deteriorating renal function, as well as a rise in in-hospital mortality rates (23). Xanthopoulos et al. conducted a meta-analysis systematic review on RDW in hospitalized patients with acute decompensated heart failure. They found that RDW measured at admission, and discharge, and the variations observed during hospitalization contribute significant prognostic implications. Specifically, they noted that a 1% rise in baseline RDW correlates with a 10% rise in the mortality risk (24). Givertz et al. (2014) evaluated the patterns of renal function and clinical outcomes in ADHF.Their findings indicated that initial renal function and variations in creatinine levels significantly predict both mortality and the likelihood of rehospitalization (7). Damman et al. (2014) performed a meta-analysis examining renal failure, the decline in kidney function, and its effects on patients with HF. Their findings indicated that chronic kidney disease and WRF were both linked to unfavorable outcomes (5).

Materials and Methods

This retrospective study was conducted on the medical records of 254 patients diagnosed with ADHF at Seyyed Al-Shohada Hospital in Urmia, Iran, from July 2021 to July 2023. The researchers used patient records to extract data regarding demographic characteristics, clinical features, and laboratory data. The study protocol was approved by the institutional ethics committee (IR.UMSU.REC.1402.301).The criteria for inclusion are individuals aged between 18 and 80 who have a confirmed diagnosis of acute decompensated heart failure (ADHF). This diagnosis was made based on clinical symptoms such as dyspnea, orthopnea, fatigue, peripheral edema, and findings from a physical examination. Furthermore, a reduced left ventricular ejection fraction (LVEF) $\leq$ 45%, determined by the echocardiography was considered. Exclusion criteria included patients with incomplete medical records, coagulation disorders, coagulopathies including abnormal PT, PTT, and INR, Abnormal platelet count, acute myocardial infarction, primary valvular diseases, chronic kidney disease, diabetic nephropathy, a history of dialysis, or organ transplantation, pregnancy, active malignancy, and severe liver disease The researchers categorized RDW values according to the laboratory reference range of 9-15% and divided the patients into two groups based on the median cut-off value of 14.5%. Renal function was evaluated through GFR, with diminished renal function indicated by an eGFR of less than 60 mL/min per 1.73 m^2 or a serum creatinine level of 1.5 mg/dL or higher for men and 1.4 mg/dL or higher for women. Statistical analysis was conducted using SPSS 26 software.The statistical analysis involved descriptive statistics, the Mann-Whitney U test, and Spearman's correlation. $p < 0.05$ was considered statistically significant.

Results

This study aimed to investigate the relationship between RDW and renal function in patients with ADHF at Seyyed Al-Shohada Hospital.The participants included 254 patients.The mean (standard deviation) age of the patients studied was 65.66 years(8.83 years), with an age range of 38 to 79.Of the 254 patients examined, examined, 165 (65%) were male and 89 were female (35%) Figure 4.1. Patient's' mean(standard deviation) weight was 78.4 (14.96) kg and their weight range was 45 to 128 kg.

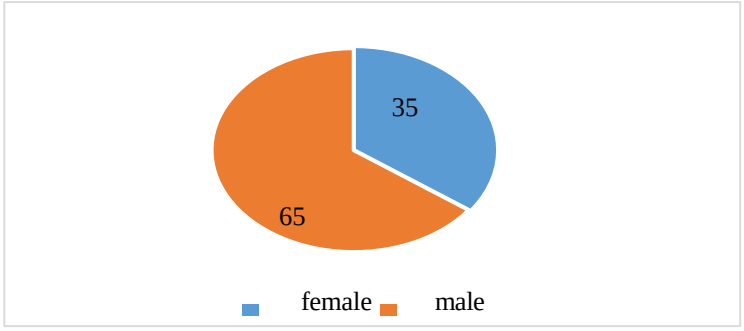

Figure 4-1. Gender frequency distribution of the patients

Table 4.1 shows the distribution of laboratory findings of the participants. The mean (standard deviation) serum BUN level in the patients was 69.88 mg/dL, and the range of reported values was 5 to 660 mg/dL. The mean (standard deviation) serum Cr level was 1.73 (1.23) mg/dL and the range of reported values was 0.65 to 11.92 mg/dL. The mean (standard deviation) RDW was 15.25 (2.17) percent and the range of reported values was 7.9 to 23.9 percent.

Table4-1. The distribution of laboratory findings of the patients studied

VARIABLE	MEAN	SD	MINIMUM	MAXIMUM
(mg/dl)BUN	69.88	58.18	5	193
(mg/dl) Creatinine	1.73	1.23	0.65	11.92
(%)RDW	15.25	2.17	7.9	23.9

Table 4.2 shows the distribution of the clinical findings. The mean (standard deviation) EF was 26.81(10.12) percent and the range of reported values was 5 to 45 percent. The mean (standard deviation) GFR was 53.97(24.06) ml/min and the range of reported values was 7.09 to 152.78 ml/min.

Table4-2. The distribution of clinical findings

VARIABLE	MEAN	SD	MINIMUM	*MAXIMUM*
(%)EF	26.81	10.12	5	45
(ml/min) GFR	53.97	24.06	7.09	152.78

There is a significant reverse correlation between RDW and GFR values. Figure 4.2 shows that high RDW levels are associated with low patient GFR (and vice versa). This correlation is also statistically significant ($P < 0.001$, Spearman's rho $r = -0.23$).

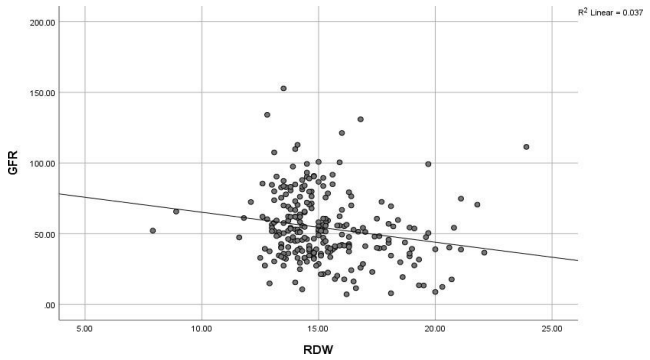

Figure4-2. The scatter plot of GFR values based on RDW values

Figure 4-3 shows the frequency distribution of RDW in the patients studied. In 114 patients (44.9%), it was less than or equal to 14.5 percent and in 140 patients it was higher than 14.5 percent (55.1%).

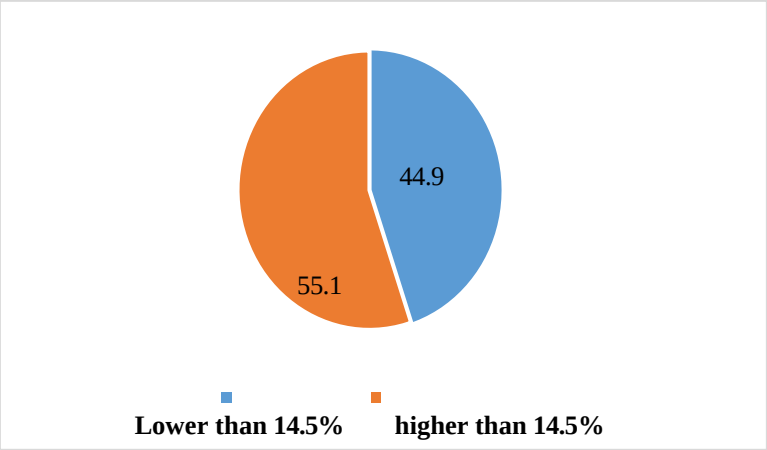

Figure4-3. The frequency distribution of RDW

Table 4.3 compares the mean and median GFR based on RDW in the patients studied. The mean GFR in patients with RDW≤14.5% was 59.31 ml/min. It was 49.71 ml/min in patients with RDW>14.5% ml/min. The median GFR in patients with RDW≤14.5% was also higher than in patients with RDW>14.5%, and the observed difference in GFR between the two groups was statistically significant (P <0.001).

Table 4-3. The comparison of mean and median GFR based on RDW

RDW	RDW>14.5%	RDW≤14.5%	P value*
mean GFR	49.71	59.31	
SD	23.30	24.04	0.001
median GFR	46.08	55.95	

*Mann-Whitney

Discussion

Our research demonstrates a notable inverse correlation between RDW and renal function in individuals experiencing ADHF. These results add to the growing evidence that RDW may serve as a significant prognostic indicator in cardiovascular conditions, particularly in addressing heart failure and renal performance. The identified relationship between increased RDW and reduced GFR is consistent with earlier studies in this area. For example, Mucsi et al. (2017) found that elevated RDW levels lower estimated GFR in patients suffering from chronic kidney disease (25). Our findings broaden this association to the ADHF demographic, implying a possible connection between hematological irregularities and cardio-renal interactions in AHF. Several mechanisms explain the relationship between RDW and renal function in patients with ADHF. An increased RDW indicates more variability in red blood cell characteristics, originating from many factors such as inflammation, oxidative stress, and nutritional deficiencies (26). These elements are involved in the processes underlying both heart failure and renal impairment. Recent research has provided valuable insights into the possible mechanisms that connect RDW to cardiovascular and renal outcomes. Lippi et al. (2021) suggested that RDW could serve as an indicator of overall health, representing the ability of the body to maintain homeostasis in the face of various stressors (27). This notion is consistent with our results, indicating that patients with elevated RDW demonstrated poorer renal function. Additionally, research conducted by Hu Y et al. (2017) revealed a correlation between increased RDW and a heightened risk of acute kidney injury and mortality in patients in the coronary care unit (CCU), suggesting that RDW could act as a valuable predictor of renal complications within

this population (28). Our findings in patients with ADHF align with and build upon previous observations, as we demonstrated significantly lower GFR values in patients with higher RDW. This consistency across different cardiac patient groups enhances the potential use of RDW as a predictor of renal impairment. Deterioration of renal function can result in anemia and changes in erythropoiesis, which may ultimately elevate RDW levels. On the other hand, an elevated RDW may suggest systemic inflammation and oxidative stress, which can negatively impact renal function. This intricate relationship necessitates further studies to clarify the specific mechanisms involved. The findings of our study have important clinical implications. RDW is a commonly assessed parameter in complete blood counts, rendering it an easily accessible and economical marker. Integrating RDW into clinical practice could improve prognostic assessments and guide management strategies in ADHF. For example, patients exhibiting elevated RDW levels may require more rigorous monitoring of renal function and the prompt initiation of Renoprotective interventions. This strategy is corroborated by the research conducted by Churpek et al. (2017), indicating that adding RDW to current risk prediction models improved their accuracy in predicting adverse outcomes for critically ill patients. Furthermore, our findings suggest that RDW may be a useful marker for identifying a specific subgroup of ADHF patients who could gain from more intensive fluid management or the earlier commencement of renal replacement therapy.This is particularly relevant given the frequent decline in renal function in patients with ADHF and its association with poor outcomes, as emphasized by Damman et al. (2014) in their meta-analysis (5). This study also offers new insights by expanding research findings to encompass the Iranian population, presenting accurate clinical threshold values, and illustrating its significance in settings with limited resources. However, it is crucial to note the limitations of our study. Since the study is a retrospective, single-center investigation, the results are not generalizable to all populations affected by ADHF. Furthermore, we did not evaluate longitudinal variations in RDW or renal function, which could provide more insights into how these factors are evolving about one another. Future prospective, multi-center research is necessary to confirm these findings and investigate the potential clinical implications of RDW in treating ADHF. Gaining a deeper understanding of the mechanisms that connect RDW and renal function may also create opportunities for new therapeutic strategies designed to improve patient outcomes. In conclusion, our study demonstrates a significant inverse relationship between RDW and renal function in patients with ADHF. These findings add to the growing evidence supporting the use of RDW as a prognostic marker in cardiovascular diseases and underscore its potential role in evaluating the interactions between cardiac and renal health. The findings are particularly relevant for the Iranian healthcare system, highlighting RDW's potential as a prognostic tool in cardiovascular conditions. Additional studies are required to clarify the mechanisms involved and to assess whether interventions targeting factors influencing RDW could enhance the prognosis for AHF patients with compromised renal function.

Ethical Statements

This research was carried out according to the Declaration of Helsinki and received approval from the Ethics Committee of Urmia University of Medical Sciences (Approval code: IR.UMSU.REC.1402.301).Due to the retrospective design utilizing pre-existing medical records, the ethics committee waived the necessity for individual patient consent. All patient information was anonymized and managed confidentially, adhering to institutional and national data protection laws.

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Author Contributions

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Validation: Dr. Venus Shahabi

Writing - original draft: Dr. Nesa Naji
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All authors have reviewed and approved the final version of the manuscript.

Conflicts of Interest
The authors report no conflicts of interest.

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