

Study Of The Relationship Of Red Cell Distribution Width And Mean Platelet Volume With Severity Of Heart Failure

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Abstract:

Background: Heart failure is a chronic, progressive condition where in there is a diminished capacity of the heart to circulate blood, affecting all organ systems. This study aims to study the relationship between RDW and MPV levels with the severity of HF in patients diagnosed clinically and their comparison with echocardiography findings. **Material & Methods:** This hospital based observational study was conducted among 132 patients in the department of internal medicine in Government Multispeciality Hospital, Sector 16, Chandigarh over a period of 18 months. All the eligible participants were evaluated thoroughly by complete history. Measurement of RDW and MPV were done by taking venous sample. The statistical analysis was carried out using IBM SPSS (Statistical Package for Social Sciences) statistical version 20. **Results:** Results showed that there was a weak positive correlation between RDW and LVEF ($r=0.0285$). However, this was found to be statistically non significant ($p\text{-value} > 0.05$). There was a weak negative correlation between MPV and LVEF ($r=-0.1163$). However, this was also found to be non significant ($p\text{-value} > 0.05$). **Conclusion:** The study concluded that RDW was increased in heart failure patients, however we couldn't elicit any proportional rise in its value with a proportional decrease in the LVEF i.e the severity of heart failure.

Keywords: Heart failure, Red Cell Distribution width and mean platelet volume.

Introduction:

Heart failure (HF) is defined as “a complex clinical syndrome resulting from functional or structural impairment of ventricular filling or ejection of the blood, causing the inability of the heart to maintain sufficient output, inadequate to meet the metabolic demands of the body.” It is a chronic, progressive condition where in there is a diminished capacity of the heart to circulate blood, affecting all organ systems[1]. Patients with heart failure can be categorized as those with low or reduced ejection fraction, preserved ejection fraction, and mid-range ejection fraction[2-4]. According to the Indian College of Cardiology, coronary artery disease and rheumatic heart disease are the major causes of heart failure in India[5]. Several prognostic markers are

employed for HF management. Some of the most commonly used are brain natriuretic peptide (BNP), Troponins, and echocardiography[6]. Due to the increasing economic burden of the disease, alongside the need for routine monitoring and follow-up, cost-effective prognostic indicators for HF are needed. One such parameter is the measurement of blood parameters. Studies have found that parameters such as red cell distribution (RDW) and platelet parameters such as mean platelet volume (MPV) can be used as prognostic markers of HF[7]. The RDW quantitatively measures anisocytosis, the erythrocyte variability in the systemic circulation. Among normal adults, this ranges between 11.5 to 14.5%. Higher levels are said to be associated with poorer prognosis in patients with HF. RDW is usually reported along side complete blood counts and carried out using automated hematology analyser[8]. Similarly, MPV is another

marker reported in complete blood counts. It measures the platelet size and reflects increased platelet activation or an increase in the quantity of large, hyper aggregable platelets[9]. Similar to RDW, MPV is linked to HF due to inflammation and endothelial dysfunction, which is seen in cases of HF. These lead to increased platelet activation and aggregation, leading to increased MPV[7]. Thus, MPV and RDW serve as pragmatic and user-friendly tools for prognostic assessment in heart failure. However, very few studies have been conducted to understand the implications of these parameters in our country. Therefore, this study aims to study the relationship between RDW and MPV levels with the severity of HF in patients diagnosed clinically and their comparison with echocardiography findings.

Material & Methods:

This hospital based observational study was conducted in the department of internal medicine in Government Multispeciality Hospital, Sector 16, Chandigarh over a period of 18 months. 120+12 patients were recruited from medicine (OPD) and medical wards of GMSH-16 hospital fulfilling inclusion and exclusion criteria. A written and informed consent was taken from all the patients. The defined guidelines of central ethics committee for biomedical research on human subjects by ICMR and guidelines as per Helsinki Declaration were strictly adhered to in the project.

A total of 130 Patients of age group 18 and above, follow up cases of heart failure coming in compensated/ decompensated state of HF, newly diagnosed cases of heart failure as per the NYHA criteria, Classical symptoms of heart failure with ischemic heart disease, hypertensive heart disease, valvular heart disease and non-ischemic cardiomyopathy were included in the study. Patients who refused of give consent, congenital heart disease, chronic obstructive pulmonary disease, severe anemia, neoplastic metastasis to bone marrow, pregnancy, severe arthritis, inflammatory bowel disease, hypothyroidism, liver disease were excluded from the study. All the eligible participants were

evaluated thoroughly by complete history which includes onset of symptoms, precipitating factors, use of diuretics etc. In subjects with previously diagnosed heart failure and newly diagnosed patients who were graded according to the classification NYHA in grades I to IV. Also echocardiography of the patients were done to assess the LVEF, and were divided into patients with preserved ejection fraction and reduced ejection fraction. They were classified as HFREF- “having LVEF $\leq$ 40%”, HF with mildly reduced EF- “having LVEF 41%-49%”, HFPEF – “having LVEF $\geq$ 50%”, (with evidence of spontaneous or provokable increased LV filling pressures). In subjects of previously diagnosed heart failure, details from their previous diagnosis and management were noted. Detailed physical examination were recorded including JVP, chest auscultation, presence of peripheral edema, dyspnea etc. All participants were subjected to relevant investigations including complete blood count, renal function tests, liver function tests, serum electrolyte according to presenting symptoms. Other necessary special investigations like chest x-ray pa view, ECG, 2d echo, were done. Measurement of RDW and MPV were done by taking venous sample collected in k2 EDTA (Ethylene Diamine Tetra acetic Acid) vial of 2ml capacity, blood filled to the labeled mark, rotated 6-8 times so that blood mixes with the EDTA anticoagulant, to prevent the micro clot formation in the sample which can affect the platelet count, and processed on fully automated five part hematology analyzer, Elite 580 and XL 1000 installed in emergency and pathology lab. Daily quality controls are being run on both the fully automated hematology analyser to ensure the accuracy of the results. The RDW in predicting heart failure according to atac celic et al study is set to be $\geq$ 13.6 and for MPV a value of $\geq$ 11.6 may represent a higher risk for infarction. Stay duration was defined as the number of days of admission in the hospital till the discharge of the patient. The statistical analysis was carried out using IBM SPSS (Statistical Package for Social Sciences) statistical version 20. The analysis includes frequency table, bar, pie chart, association of variables based on Chi-square test and if any cell frequency was <5 , then

Yates corrections was used for 2x2 contingency table or method pooling and Fisher exact test was used (for higher order than 2x2 table).

Results:

Of the 130 participants, 49 (37.69%) were aged <60 years, and the remaining 62.31% were found to be of age ≥ 60 years, thus the participants' mean ($\pm$ SD) age was 61.23($\pm$ 10.9) years. There was nearly an equal distribution of genders among the participants, with 53.85% females and 46.15% males. Among the participants, 43.9% presented with NYHA grade 4 dyspnea, 36.9% with grade 3, and 16.9% with grade 2 dyspnea. The remaining 2.3% did not present with any form of dyspnea. Among the participants, 75.3% had presented to the OPD with cough, more than half (70.7%) had edema on presentation and 10.8% of the participants presented with fever. Among the participants, 58.4% had complaints of orthopnea, and 49.3% had complaints of PND. 0.8% of the participants presented with decreased appetite, flank pain or anasarca, whereas 99.2% had no such issues.

Among the participants, 5.3% presented with other symptoms such as palpitations, chest pain, dizziness, and headache. The majority of the study participants (92.3%) had a concurrent co-morbidity, whereas 7.7% did not have any history of co-morbidities. Most of the participants had multimorbidity, i.e., the presence of 2 or more comorbid conditions. Among the 130 participants, more than half (66.9%) were known cases of hypertension. Similarly, 53.1% were known cases of Diabetes mellitus. Coronary artery disease and Chronic kidney disease were present in 22.3% and 4.6% of the participants, respectively. Moreover, 0.8% of the participants were known cases of bronchial asthma.[Table 1].

Distribution of participants according to each general physical examination finding-Among the study participants, 29.3% had pallor. Similarly, more than 3/4th of the patients had signs of edema. Also, among the participants, 27.7% had visible neck veins. Among the participants, more than half (58.4%) had features of orthopnea. A raised jugular venous pressure was found in 43.1% of the participants.

Table 1: Distribution Of Participants According To The Each Co-morbidity

Co-morbidity	Present/Absent	Frequency(n)	Percentage
Hypertension	No	43	33.1
	Yes	87	66.9
Diabetes mellitus	No	61	46.9
	Yes	69	53.1
Coronary artery disease	No	101	77.7
	Yes	29	22.3

Chronic kidney disease	No	124	95.4
	Yes	6	4.6
Bronchial asthma	No	129	99.2
	Yes	1	0.8

The RDW-CV was categorized as normal if the values were between 11.5 and 14.5. In our study, the RDW values ranged from 11.2 to 26.2, with a mean ($\pm$ SD) of 15.7 ($\pm$ 2.4). Among the study participants, more than half (70%) had a high RDW-CV, whereas the remaining 30% had a value falling in the reference range. In our study, MPV values ranged from 8.3 to 14.9, with a sample mean ($\pm$ SD) of 11.9

($\pm$ 1.2). Among the study participants, the majority (82.3%) fell within the normal range, whereas 16.9% and 0.8% had a high and low MPV value, respectively [Table 2]. In our study, half the participants had HFrEF, whereas the remaining 33.1% and 16.1% had HFmrEF and HFpEF, respectively. In our study, the LVEF was ranged between 18 and 55%, with a mean ($\pm$ SD) of 37.34 ($\pm$ 10.36). [Table 3]

Table 2: Distribution Of Participants According To MPV&RDW-CV

MPV values	Frequency(n)	Percentage (%)
Low	1	0.8
Normal	107	82.3
High	22	16.9
RDW-CV		
Normal	39	30
High	91	70

Table 3: Distribution Of Participants According To LVEF

Categories of HF	Frequency(n)	Percentage (%)
HFrEF	66	50.8
HFmrEF	43	33.1
HFpEF	21	16.1

There was a weak positive correlation between RDW and LVEF ($r=0.0285$). However, this was found to be not significant ($p\text{-value} > 0.05$) [Table 4]. There was a weak negative correlation between MPV and LVEF ($r=-0.1163$). However, this was found to be not significant ($p\text{-value} > 0.05$) [Table 5]. Univariate linear regression found that as the value of RDW increases by 1 unit, the value of

LVEF also increases by 0.123. However, this was found to be non significant [Table 6]

Similarly, our analysis revealed that as the value of MPV increases by 1 unit, the value of LVEF decreases by 1. While this correlation was not found to be statistically significant, it adds to our understanding of the complex dynamics of cardiovascular health.

Table 4: Pearson's Correlation On RDW vs LVEF

RDW vs LVEF	n	130
	Pearson's correlation coefficient	0.0285
	P-value	0.7472

Table 5: Pearson's Correlation On MPV vs LVEF

MPV vs LVEF	n	130
	Pearson's correlation coefficient	-0.1163
	P-value	0.1877

Table 6: Univariate Regression:

Variable	β coefficient	p-value
RDW	0.123	0.747
MPV	-1.00	0.188

Discussion:

Very few studies have assessed the association between these blood markers and HF in India. To our knowledge, those studies compared the mean RDW among HF patients and the same among controls[10]. In our study, the participants' mean ($\pm$ SD) age was 61.23 ($\pm$ 10.9) years. In the Trivandrum HF registry, the mean age was 61.2 years, which is in line with the findings of our study[11].

In our study, 53.8% of the participants were females, which was more than the males (46.15%), similar to few studies conducted in the country[10,12]. In our study, most patients presented with Grade 4 dyspnea according to the NYHA classification, possibly due to the preponderance of HFrEF among the study participants[13]. Majority of the patient also presented with cough, which was without expectoration in most of the cases. Similarly, we also found other common symptoms of heart failure, such as pedal edema, orthopnea and PND among the study participants. In our study, the most common comorbidity was found to be hypertension, followed by diabetes mellitus, CAD, and CKD. These factors are implicated as risk factors for HF. Similarly, in the Trivandrum HF registry, the most commonly associated comorbidities were hypertension (58%), followed by diabetes (55%), chronic kidney disease (18%), and COPD (15%)[14,15]. The most common signs on general physical examination of participants in our study were

the presence of pedal edema, followed by orthopnea and raised JVP, which is similar to other studies[16]. The reference range for RDW CV ranges from 11.5 to 14.5 fl. The mean ($\pm$ SD) RDW was 15.7 ($\pm$ 2.4). This is similar to the study by Rudresh MG et al, wherein the mean ($\pm$ SD) RDW was found to be 15.7 ($\pm$ 2.6). This is similar to a few other studies wherein the mean ranged between 14-15[17]. Similarly, the reference range for MPV ranges from 9 to 13. The mean ($\pm$ SD) RDW in our study was 11.9 ($\pm$ 1.2). Even though this falls in the reference range, few other studies that had controls with no HF found that even though the MPV fell in the reference range, it was significantly higher than that of controls[18]. Further, MPV was comparatively higher in patients with decompensated HF than those with stable HF; however, both the mean values fell in the reference range[19]. Similarly, it has been found that mean MPV values differed significantly between HFrEF and HFpEF, wherein higher values have been found in those with HFrEF, falling in the reference range[20]. In our study, half (50%) of the participants had HFrEF, whereas the remaining 33.1% and 16.1% had HFmrEF and HFpEF, respectively. Similarly, according to the Trivandrum HF study, the percentage of patients with HFrEF (then defined as HF with EF<35%) was 45%, and the percentage of patients with HFpEF(then defined as HF with EF>45%) was 26%[11]. Our study was one of the few studies that tried to find an independent correlation between RDW, MPV, and

severity of HF. We also tried to find evidence that whether these blood markers could be used to assess the severity of HF. In our study, there was a weak positive correlation between RDW and LVEF($r=0.0285$); however, this was not significant ($p\text{-value}>0.05$). Also, there was a weak negative correlation between MPV and LVEF ($r=-0.1163$). However, this was found to be not significant ($p\text{-value}>0.05$) Similarly, on univariate linear regression, it was found that as the value of RDW increases by 1 unit, the value of LVEF also increases by 0.123. However, this was not found to be significant. Similarly, as the value of MPV increases by 1 unit, the value of LVEF decreases by 1, which is also insignificant. Similarly, we could not elicit any statistically significant findings on multiple linear regression,

Conclusion:

In our study, we found that RDW is increased in heart failure patients, however we couldn't elicit any proportional rise in its value with a proportional decrease in the LVEF i.e the severity of heart failure. However, this study was one of few studies which have researched on this to completely dismiss the idea that such an association may exist in the Indian population. Hence, further studies are required to assess the true relationship between the blood markers and heart failure in India.

Limitations Of The Study:

We could not find any significant correlation between the variables. A few of the limitations of our study include the study design, small sample size, and the use of a convenient sampling method. Also, using data from patients visiting the hospital could have led to bias. As a significant number of patients of heart failure were already on medications to reduce the symptoms, this could be a confounding factor for RDW and MPV values. Therefore, it is crucial to conduct further studies to uncover the true relationship between these blood markers and HF. Such research could significantly reduce the cost burden and

increase the coverage in low-resource settings, making it a matter of utmost importance.

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