

## Evaluation of red cell distribution width as a prognostic marker in coronary artery disease patients

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**Abstract**

**Background & Objectives:** Red cell distribution width (RDW) is measure of erythrocyte size variability and heterogeneity. RDW is a newly identified risk marker that has been reported in various studies to be a predictor for morbidity and mortality in many diseases affecting the cardiovascular system. The aim of this study is to determine the values of red cell distribution width in patients admitted with acute cardiovascular events and to prove its co relation with echocardiographic findings of systolic and diastolic functions in coronary artery disease patients. **Methodology:** This study was a descriptive study including 70 patients who satisfy the inclusion and exclusion criteria. Informed consent was taken from all the patients. The patients were assessed by clinical and laboratory methods. The patients were evaluated using echocardiogram and hematological investigations. Statistical evaluation was performed using suitable statistical methods like Sperman's rank correlation method and Karl Pearson correlation method. **Results:** High values of RDW is seen in people with less ejection fraction. Red Cell Distribution Width (RDW) levels are in a higher levels in patients who was admitted with myocardial infarction. Patients with low LV ejection fraction have elevated RDW levels compared with normal LV ejection fraction, thus RDW levels correlated with severity of LV dysfunction. Patients with high RDW have more severe grade of left ventricular dysfunction, thus it's a poor prognostic indicator in them. **Conclusion and interpretation:** Thus the study proved its objectives in a well disciplined manner. Instead of using more expensive studies as a screening for prediction of adverse cardiovascular outcome, a meagre testing of complete hemogram will help you to identify the high risk in a population to develop any illness pertaining to the cardiovascular system. Various other studies have proven as mentioned in the below sections that RDW is a predictor of morbidity and mortality in many of heart diseases. This study proved the use of RDW as a prognostic marker in one of the major debilitating cause of present era morbidity that is Myocardial Infarction.

**Keywords:** RDW; Myocardial infarction; Coronary artery disease.

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**Introduction**

Myocardial infarction (MI) is a syndrome arising from injury to the myocardial tissues due to mismatch in the demand and myocardial perfusion with the coronary atherosclerosis with a superimposed thrombus being the major cause. MI is defined as death of myocardial cells caused by prolonged ischemia[1]. When an injury occurs to myocardium, various enzymes are released in to the blood after two hours and they are detectable by various biochemical assays. The important biomarkers of myocardial injury are Cardiac troponin T, troponin I, creatine kinase MB(CK-MB) and when these are elevated, they signify myocardial damage with good sensitivity and specificity[2,3]. MI can be classified based on its transmural, etiology, age, and also with its relation to reperfusion.

Red blood cell distribution width (RDW) is a parameter of circulating erythrocytes measured by haematological analyzer. It can be calculated automatically or manually by formulas and expressed in percentage. Recent studies have shown that RDW played a significant role in evaluating cardiovascular disease progression by various physiological and pathological manifestations[4,5,6]. Increased attention has been focused on the prognostic and predictive value of RDW in patients with coronary artery disease, atrial fibrillation, heart failure, aortic valve replacement surgery, pulmonary embolism and cerebrovascular accidents especially infarction. A high RDW is associated with cardiovascular morbidity and mortality in patients following myocardial infarction[7].

RDW thus was recognized as a marker of adverse outcomes in cardiovascular disease other than the haematological diseases for which it was intended. This was shown to have similar role in the acute setting of heart failure[8], coronary artery disease, acute myocardial infarction(AMI), and many other diseases. Multiple studies showed an association of RDW with the ultrasound parameters of both systolic dysfunction and diastolic dysfunction of heart in different cardiovascular diseases. RDW is described as a measure of RBC size variability[9]. It is represented in 2 different forms- RDW- CV (coefficient of variation) and RDW-SD (standard deviation). It is easily available as most of the hematology instruments measure RBC volume and give RDW. An elevated value of RDW can predict mortality and morbidity in heart failure and various other heart diseases. There are many postulates and theories which have been put forth by many researchers as a reason for elevated RDW in the context of heart disease.

**Demography**

India is under the phase of a rapid health transition with increasing burden of coronary heart disease (CHD)[10]. Among adults over 20 years of age, the estimated prevalence of CHD measures around 3-4 per cent in rural areas and almost 8-10 per cent in urban areas. There was no sex differentiation for the risk of heart attacks imposed by these risk factors, among all the population groups studied at all ages in almost all regions emphasizing the role of environmental origin of cardiovascular risk factors for all the ethnicities of the present world. The only difference which was observed in the study was the earlier occurrence of AMI in South Asian population[11]. But this was attributed to the higher level of risk factors mainly smoking and diabetes among Asians. abnormal lipids, hypertension, diabetes, smoking, abdominal obesity, psychosocial stress, decreased amounts of fruits and vegetable consumption, moderate consumption of alcohol, and physical activity accounted for most of the risk of myocardial

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infarction worldwide. Together all these nine risk factors accounted for 90 per cent of the population attributable risk (PAR) in men and 94 per cent of that in women. There was no sex differentiation for the risk of heart attacks imposed by these risk factors, among all the population groups studied at all ages in almost all regions emphasizing the role of environmental origin of cardiovascular risk factors for all the ethnicities of the present world. The only difference which was observed in the study was the earlier occurrence of AMI in South Asian population[11]. But this was attributed to the higher level of risk factors mainly smoking and diabetes among Asians.

#### Materials and methods

##### Source of the data

Data was collected from patients fulfilling the inclusion and exclusion criteria, attending either outpatient department or inpatient of Chigateri General Hospital and Bapuji Hospital attached to J.J.M. Medical College, Davangere.

#### Method

##### Inclusion criteria

1. Patients aged between 16 and 80 of both gender.
2. Newly detected patients of myocardial infarction.
3. Old cases of ischemic heart disease presented with new onset features of infarction.

##### Exclusion criteria

1. Anemia with haemoglobin < 11 g/dl.
2. Blood transfusion within past 3 months.
3. Haematological malignancy.

##### Type of study

Descriptive study

##### Sample Size and design

This is a descriptive study including 70 patients who satisfy the inclusion and exclusion criteria. Informed consent was taken from all

the patients. The patients were assessed by clinical and laboratory methods. The investigations mainly concentrated were:-

1. Complete Hemogram
2. Vitamin B12 and Folic Acid Assay
3. Electrocardiogram
4. Echocardiograph
5. Cardiac biomarkers – CKMB and Troponin-I.

All the patients were evaluated properly by clinical examination and with the above mentioned investigations confirmed to have MI. And for all patients Vitamin B12 and Folic Acid assays were done to rule out megaloblastic anemia which may affect the RDW values.

M-mode echocardiography was used to assess left ventricle dimensions.

Following parameters were checked

- LVESD
- LVEDD
- Ejection fraction (Simpson's method).
- Left ventricle end diastole and Left ventricle end systole volumes are estimated.

Blood samples were collected from antecubital vein using 2cc syringe, transferred to an EDTA test tube and analysed in an automated cell counter Sysmex KX21. Hemoglobin, MCV, Hematocrit and RDW were determined as part of complete blood count

##### Statistical analysis

SPSS software ver.21.0 was used for calculations using the following statistical methods:

- Independent samples 't' test-unpaired
- Independent samples 't' test-paired
- ANOVA
- Pearson correlation coefficient Spearman's rank correlation method

#### Results

**Table 1: Age distribution of the study data**

Age	Frequency	Percentage
≤60	38	54.3
>60	32	45.7
<b>Total</b>	<b>70</b>	<b>100.0</b>

From Table 1, one can infer that 54.3 percent of the people in the study are less than or equal to age 60 and 45.7 percent are above age 60. Out of 70

**Table 2: Sex distribution of the study data**

Sex	Frequency	Percentage
Male	42	60.0
Female	28	40.0
<b>Total</b>	<b>70</b>	<b>100.0</b>

In this study, there are 28 female patients and 42 male patients. Out of 70 cases 40 percent of the were female patients and 60 percent are male patients. There is an increased incidence of MI in male patients compared to the female patients.

**Table 3: MI distribution of the study data**

MI	Frequency	Percentage
NSTEMI	38	54.3
STEMI	32	45.7
<b>Total</b>	<b>70</b>	<b>100.0</b>

Out of 70 people in this study, 38 members have NSTEMI and 32 have STEMI i.e., 54.3 percent comprises of NSTEMI and 46 percent comprises of STEMI.

**Table 4: LVDD distribution of the study data**

LVDD	Frequency	Percentage
Normal	6	8.6
Grade I	20	28.6
Grade II	24	34.3
Grade III	20	28.6
<b>Total</b>	<b>70</b>	<b>100.0</b>

Table 4 describes the frequency of LVDD. Here, 8.6 percent has normal level, 28.6 percent has Grade I, 34.3 percent has Grade II and 28.6 percent has Grade III i.e., 6 out of 70 people has normal level, 20 out of 70 patients has Grade I, 24 out of 70 has Grade II and the remaining has Grade

III left ventricular diastolic dysfunction.

**Table 5: Pearson Correlation between the variables RDW-CV and EF**

Variable	EF		
	N	Pearson Correlation	p Value
RDW-CV	70	-0.707	<0.001

From the Table, we can see that the variables RDW-CV and EF are negatively correlated. Also the p-value obtained in Table 5 is <0.001 and that is statistically significant. High values of RDW is seen in people with less

**Table 6: Pearson Correlation between the variables RDW-CV and LVDD**

Variable	LVDD		
	N	Pearson Correlation	p Value
RDW-CV	70	0.858	<0.001

From the Figure 6, we can see that the variables RDW-CV and LVDD are positively correlated. Also the p-value obtained in Table 6 is statistically significant. The Pearson correlation coefficient is 0.858.

**Table 7: Chi-Square association of the variables AGE with MI**

Age	MI				p Value
	NSTEMI		STEMI		
	n	%	n	%	
≤60 (38)	16	42.1	22	57.9	0.026
>60 (32)	22	68.8	10	31.2	

In our study of 38 patients in the age group less than or equal to 60, 16 patients have NSTEMI (42.1 %) and 22 patients have STEMI (57.9%) whereas out of 32 patients in the age group of greater than 60, 22 patients have NSTEMI (68.8%) and 10 patients have STEMI (31.2%). From the p-value (0.026) obtained in Table 7, the test is statistically significant..

**Table 8: Chi-Square association of the variables Sex with MI**

Sex	MI				p Value
	NSTEMI		STEMI		
	n	%	n	%	
Male (42)	18	42.9	24	57.1	0.019
Female (28)	20	71.4	8	28.6	

In our study out of 42 patients in the male group, 18 patients have NSTEMI (42.9 %) and 24 patients have STEMI (57.11 %) where as in female group, 20 patients have NSTEMI (71.4 %) and 8 patients have STEMI (28.6 %). From the p-value (0.019) obtained in Table 8, the test is statistically significant.

## Discussion

Out of 70 people studied in the present study 54.3 % were below or equal to 60 years of age 45.7 % were above 60 years of age. Out of them 38 had NSTEMI and 32 had STEMI. If we come to sex distribution male were 60% and females were 40%. Since this was a descriptive study with a large age limit and small sample size this results are also random. But this also showed the male preponderance of MI. The age distribution of MI showed elderly individuals are prone for NSTEMI since 68.8% of above 60 age group had NSTEMI. And in opposite manner age below or equal to 60 has more incidence of STEMI with 57.9%. The p-value of the association of MI with Age is 0.026 which is statistically significant. In the sex distribution majority of females, 71.4% has NSTEMI and males 57.1% were prone for STEMI within a statistically significant p-value of 0.019. In another observation it was found that out of 70 people studied 34.3% were having grade II diastolic dysfunction.

The correlation of RDW-CV with EF was calculated using Pearson correlation and was found to be negatively correlated with a correlation coefficient of -0.707 and the test was proved statistically significant with a P value of <0.001. That is as the values of RDW-CV was on the increasing trend the ejection fraction was found to be decreasing indicating RDW-CV as a marker of poor prognosis in a patient with MI.

The correlation with RDW-CV and LVDD was also measured with Pearson correlation coefficient and was proved to be positively correlated with a coefficient of 0.858 and with a p- value of <0.001 proving the test to be statistically significant. In the present study as the value of RDW-CV increased the patients was deteriorating indicated by a severe grade of diastolic dysfunction in the echocardiography. This also proves the value of RDW-CV as a marker of poor prognosis in an individual with a history of MI.

The predictive and prognostic value of RDW for adverse outcomes

has also been demonstrated in patients with various diseases. Subsequent studies have confirmed the significance of RDW level as an independent predictor for future cardiovascular events in ACS patients[12].

Ghaffari et al reported that an elevated baseline RDW could predict adverse outcomes in patients with STEMI undergoing thrombolytic therapy, during a follow-up period of (7.7 ± 3.2) months[13].

Isik et al studied the effects of RDW level on long-term prognosis in 96STEMI patients who underwent primary PCI, and finally found that admission RDW level was an independent predictor of long term Mace[14].

The prognostic value of RDW for short-term or long-term cardiovascular events have been demonstrated in STEMI patients[15].

In a meta-analysis involving 80216 patients from 22 studies, RDW was a remarkably strong predictor of all-cause mortality (HR = 1.80, 95% CI:1.35–2.41, P<0.001) and non-fatal adverse events (HR = 1.86, 95% CI:1.50–2.31, P < 0.001), although there was significant heterogeneity in the different studies[16].

Exact physiological mechanisms between RDW and cardiovascular outcomes are not clearly understood. Several previous studies suggest that the level of RDW may reflect the extent of oxidative stress, chronic subclinical inflammation, and lipid abnormalities which in turn can be the reason for relation between RDW and MI[17].

At the moment, particular mechanism by which RDW is directly related to ventricular dysfunction is unknown, but many possible indirect associations exist. Other studies has also observed that RDW was significantly associated with some of the classic CV risk factors, such as haemolytic anemia and hyperlipoproteinemia, but it was also somewhat surprisingly associated with patients who were non-smokers. It could be that both smoking and RDW reflect a high risk for the development of a CV incident, and patients who did not smoke were otherwise burdened with CV risk (manifested with high RDW

alone) and developed MI despite positive lifestyle habits. HbA1C also had an impact on the severity of coronary disease, as seen with RDW, and a potential linking mechanism between these two parameters could therefore exist [18]. However, a significant and graded correlation between RDW and a high sensitive CRP (hs-CRP) exists independently from numerous confounding factors as proved in a large cohort of unselected patients [19]. Jasmina C. Atic et al [20], proved that elevated RDW is significantly associated with the parameters of both systolic and diastolic dysfunction even after its being adjusted for several confounding factors in the setting of STEMI and subsequent percutaneous coronary intervention (PCI). RDW seems to be better at discriminating patients with diastolic dysfunction rather than systolic dysfunction. Therefore, RDW is considered to represent subclinical inflammation and is accepted as an inflammatory biomarker, which potentially explains its strong prognostic properties in different benign and malignant diseases.

### Conclusion

Through this study its aimed to use RDW as a prognostic indicator in one of the major forms of coronary artery disease, that is myocardial infarction. Cost effectiveness is the major advantage when this parameter is used for predicting the prognosis. More over the easy availability and affordability of complete hemogram helps this parameter to be useful as a prognostic indicator. Elevated RDW, even after adjusting for several confounding factors, remained significantly associated with the parameters of systolic and diastolic dysfunction after MI and subsequent treatment. This relationship is especially interesting when considering RDW and the combination of the parameters of diastolic dysfunction, where it has good potential as a screening test for predicting non development of this complication. Compared with other inflammatory biomarkers, RDW performs best in predicting systolic and diastolic dysfunction in a patient suffered from myocardial infarction. So by measuring this value the candidates can be considered as high risk group and monitored closely for the development of morbidities involving cardiovascular system. Also they can be given extra care for decreasing the rate of progression to severe heart failure by adopting proper prophylactic measures.

RDW is the investigation which is available in almost all the smallest health care centres even. It can be accumulated in the NCD clinics which is conducted under various national programmes and this variable can be used as a warning call to avoid dreaded complications of myocardial infarction. This variable satisfies the qualities to be used as a screening tool to predict the prognosis of a dreaded disease.

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