

# Impact of Elevated Red Cell Distribution Width on Patients with Acute Myocardial Infarction

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## Abstract

**Background:** Red cell distribution width (RDW) is an important parameter that has a critical impact on the severity of coronary artery disease, especially on that of acute myocardial infarction (AMI). **Objective:** This study was aimed to determine the effect of elevated RDW on the outcome of AMI. **Materials and Methods:** This is a retrospective, case-control study conducted on two groups of participants; the first group (cases) comprised 87 patients suffering from AMI, while the second one (controls) comprised an equal number of patients having stable angina. Matching of controls to patients was done according to age (within 5 years) and gender. The study extended from the beginning of October 2017 to the end of March 2018. Participants in both groups were collected from Al-Sadr Teaching Hospital and Merjan Medical City at Iraqi Najaf and Babylon Governorates, respectively. RDW values were determined by the use of hematological auto-analyzer. **Results:** Statistically significant differences found between the study groups regarding RDW ( $P = 0.0001$ , odds ratio [OR] = 9.481, 95% confidence interval [CI] = 5.127–17.535) and cardiac troponin I (cTnI) ( $P = 0.0001$ , OR = 1.325, 95% CI = 1.109–1.584). Strong positive correlation was found between RDW and cTnI ( $r = 0.272$ ,  $P = 0.0001$ ). Other measured parameters which are age, gender, history of hypertension, diabetes and smoking, body mass index, hemoglobin (Hb), packed cell volume, mean cell volume, and mean cell Hb concentration all showed no significant differences between the study groups regarding them. **Conclusion:** RDW owns substantial diagnostic and prognostic value that can aid in the management of AMI patients.

**Keywords:** Acute myocardial infarction, red cell distribution width, troponin I

## INTRODUCTION

Acute myocardial infarction (AMI) is a disease condition that can be manifested by clinical characteristics, including electrocardiographic changes, elevated levels of biochemical indicators of myocardial necrosis, also by imaging, or may be defined by pathological changes. It is a major cause of decease and disability around the world. Myocardial infarction may be the first feature of coronary artery disease (CAD), or it may have repeated occurrence, in patients with the well-known disease.<sup>[1]</sup>

Elevated red cell distribution width (RDW) values are independent predictors of prognosis in patients with different MI types; it has also been noted that elevated levels of RDW are associated with the presence and severity of AMI.<sup>[2]</sup>

The correlation between RDW and AMI, heart failure, and stroke had been mentioned in some studies. High RDW

values are linked to the unfavorable outcomes in patients with MI and heart failure.<sup>[3]</sup> The relation between RDW and adverse outcomes in those patients is not fully understood. Inflammation, neurohormonal, and adrenergic system activation may lead to changes in red cell maturation by distressing the red blood cell (RBC) membrane, and hence leading to increased RDW values. An association between RDW and inflammatory markers had also been stated.<sup>[4]</sup>

The aim of this study was to determine the effect of elevated RDW on the outcome of AMI in a sample of the Iraqi population.

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## MATERIALS AND METHODS

This is a retrospective, case–control study conducted on two groups of participants; the first group (cases) comprised 87 patients suffering from AMI, while the second one (controls) comprised an equal number of patients having stable angina. Matching of controls to patients was done according to age (within 5 years) and gender. The study extended from the beginning of October 2017 to the end of March 2018. Participants in both groups were collected from Al-Sadr Teaching Hospital and Merjan Medical City at Iraqi Najaf and Babylon Governorates, respectively. The cases were selected according to the inclusion and exclusion criteria listed below in addition to the decision of their attendant physician. Accordingly, 17 cases were excluded. All the cases were incident, and some of them had a prior attack of MI. All the controls agreed to participate in the study, and there were no nonrespondents [Figure 1]. A clear and valid, written and verbal informed consent from each participant in the study was achieved before their inclusion.

### Inclusion and exclusion criteria

#### Inclusion criteria

The definition of AMI is established by occurrence of typical chest pain (more than 20 min in duration, new onset, continuous, diffuse one that is not localized or positional and it may be associated with sweating, nausea, or fainting) in addition to elevated cardiac enzymes (above the 99<sup>th</sup> percentile upper reference limit) with or without electrocardiographic changes suggestive of myocardial ischemia (ST elevation, T inversion, and pathological Q wave). Angina is an indication of myocardial ischemia that is recognized in clinical practice by its character and site. Angina is referred to as stable if it is not a new symptom and when there is no worsening in its frequency of occurrence, severity or duration of the attacks of the chest pain.<sup>[1]</sup>

#### Exclusion criteria

- Renal disease
- Clinical evidence of active infection
- Active cancer
- Pregnancy
- History of chronic obstructive pulmonary disease and
- Hyperlipidemia.

Short history notes were obtained from each participant in the study, including the name, age, gender, clinical history of hypertension (HT), diabetes and smoking, and finally, the weight and height were addressed to determine body mass index (BMI) as follows:

$$\text{BMI} = \text{Weight (kg)} / \text{height (m}^2\text{)}$$

### Blood collection and serum preparation

Three milliliter of fresh blood were drawn at 9:00 am from both groups of participants. Two types of labeled tubes were used; the first one contains ethylenediaminetetraacetic acid as an anticoagulant to prevent clotting of blood to be used for molecular studies; the second type of tubes was without anticoagulant as gel tubes, for preparing sera by putting

blood in the tubes and allowing it to clot for 15–30 min, then separating it by centrifugation for 10 min at 3000 round per minute to be used in the subsequent biochemical tests.<sup>[5]</sup> Each sample was labeled and given a serial number together with the participant's name. Blood and serum samples were kept frozen at –20°C for subsequent molecular and biochemical analyses.

### Hematological parameters

RDW, hemoglobin (Hb), packed cell volume (PCV), mean cell volume (MCV), and mean cell Hb concentration (MCHC) were all done by the use of an automated auto-analyzer (Orphée, Switzerland).

### Biochemical parameters

Cardiac TnI was measured by the use of human cardiac troponin I (cTnI) ELISA kit and was done according to the company (Abcam, UK) instructions.

### Statistical analysis

Continuous variables were reported as mean  $\pm$  standard deviation (SD), while the other categorical variables were reported as percentages (no. [%]). The two groups of participants were compared using independent-samples *t*-test for the continuous variables and Chi-square test for the categorical variables. The strength of association between the exposure and the outcome in respect to each variable was estimated by the calculation of odds ratio (OR) with 95% confidence interval (95% CI). OR was calculated by the use of Chi-square test for categorical variables and multinomial logistic regression analysis for continuous variables. In addition to that, correlation analyses were done between all the continuous variables to report the strength of the relationship between them. All analyses were done by the use of a Statistical Package of Social Science (SPSS) version 18.0 software (SPSS Inc., Chicago, IL, USA).  $P < 0.05$  was considered statistically significant.<sup>[6]</sup>

## RESULTS

Table 1 demonstrates the age distribution for patients and control groups of the study (AMI and stable angina patients). The ages of patients range between 45 and 85 years and the range for controls were 47–85 years. No statistically significant difference was present between the two groups of participants regarding age ( $P = 0.136$ , OR = 1.027; 95% CI = 0.992–1.063).

Table 2 shows the gender distribution for the study groups. Fifty-two males and 35 females were present in the patients' group, while in the control group, there were 50 males and 37 females. No significant difference present between the two groups regarding gender distribution ( $P = 0.758$ , OR = 1.099, 95% CI = 0.601–2.010).

The distributions of clinical history parameters (HT, diabetes mellitus [DM], and smoking) are shown in Tables 3–5, respectively. For all of them, there were no statistically significant differences between the two groups of the study ( $P$  values are: 0.875 for HT, 0.756 for DM and 0.497 for smoking. ORs are: 0.951 for HT, 0.908 for DM, and 1.259 for

smoking. 95% CIs are: 0.513–1.955 for HT, 0.494–1.670 for DM and 0.647–2.453 for smoking).

Table 6 presents the values of BMI for the patients and control group. No statistically significant difference was

there between the two groups ( $P = 0.074$ , OR = 1.046, 95% CI = 0.995–1.100).

Values of RDW, Hb, PCV, MCV and MCHC are presented in Table 7. A statistically significant difference was found between

**Table 1: Age distribution for patients and control groups**

Age	Groups		P	OR	95% CI
	Patients (AMI) (n=87)	Controls (SA) (n=87)			
Age (years), mean±SD	62.40±9.237	60.44±8.051	0.136	1.027	0.992-1.063

AMI: Acute myocardial infarction, SA: Stable angina, SD: Standard deviation, OR: Odds ratio, CI: Confidence interval

**Table 2: Gender distribution for patients and control groups**

Gender	Groups		Total, n (%)	P	OR	95% CI
	Patients (AMI) (n=87)	Controls (SA) (n=87)				
Males, n (%)	52 (59.8)	50 (57.5)	102 (58.6)	0.758	1.099	0.601-2.010
Females, n (%)	35 (40.2)	37 (42.5)	72 (41.4)			
Total, n (%)	87 (50)	87 (50)	174 (100)			

AMI: Acute myocardial infarction, SA: Stable angina, OR: Odds ratio, CI: Confidence interval

**Table 3: Distribution of hypertensive history between patients and control groups**

HT	Groups		Total, n (%)	P	OR	95% CI
	Patients (AMI) (n=87)	Controls (SA) (n=87)				
Present, n (%)	55 (63.2)	56 (64.4)	111 (63.8)	0.875	0.951	0.513-1.955
Absent, n (%)	32 (36.8)	31 (35.6)	63 (36.2)			
Total, n (%)	87 (50)	87 (50)	174 (100)			

AMI: Acute myocardial infarction, SA: Stable angina, HT: Hypertension, OR: Odds ratio, CI: Confidence interval

**Table 4: Distribution of diabetic history between patients and control groups**

DM	Groups		Total, n (%)	P	OR	95% CI
	Patients (AMI) (n=87)	Controls (SA) (n=87)				
Present, n (%)	33 (37.9)	35 (40.2)	68 (39.1)	0.756	0.908	0.494-1.670
Absent, n (%)	54 (62.1)	52 (59.8)	106 (60.9)			
Total, n (%)	87 (50)	87 (50)	174 (100)			

AMI: Acute myocardial infarction, SA: Stable angina, DM: Diabetes mellitus, OR: Odds ratio, CI: Confidence interval

**Table 5: Distribution of smoking history between patients and control groups**

Smoking	Groups		Total, n (%)	P	OR	95% CI
	Patients (AMI) (n=87)	Controls (SA) (n=87)				
Smoker, n (%)	26 (29.9)	22 (25.3)	48 (27.6)	0.497	1.259	0.647-2.453
Nonsmoker, n (%)	61 (70.1)	65 (74.7)	126 (72.4)			
Total, n (%)	87 (50)	87 (50)	174 (100)			

AMI: Acute myocardial infarction, SA: Stable angina, OR: Odds ratio, CI: Confidence interval

**Table 6: Body mass index for patients and control groups**

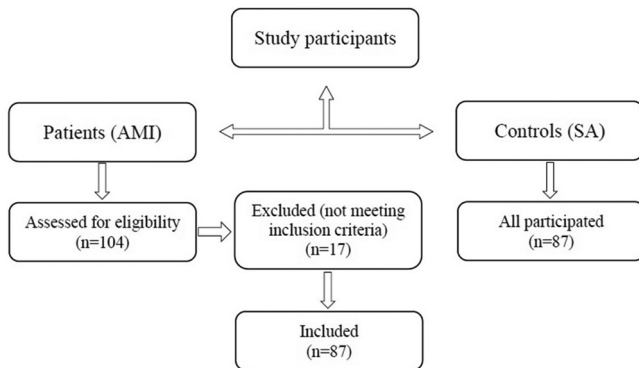
BMI	Groups		P	OR	95% CI
	Patients (AMI) (n=87)	Controls (SA) (n=87)			
BMI (kg/m <sup>2</sup> ), mean±SD	34.741±5.666	33.089±6.451	0.074	1.046	0.995-1.100

AMI: Acute myocardial infarction, SA: Stable angina, BMI: Body mass index, SD: Standard deviation, OR: Odds ratio, CI: Confidence interval

**Table 7: Hematological parameters for patients and control groups**

Parameters	Groups		P	OR	95% CI
	Patients (AMI) (n=87)	Controls (SA) (n=87)			
RDW (%), mean±SD	15.070±1.012	13.195±0.737	0.0001	9.481	5.127-17.535
Hb (g/dl), mean±SD	13.513±1.425	13.818±1.272	0.137	1.021	0.637-1.638
PCV (%), mean±SD	40.657±4.469	41.711±4.221	0.112	0.898	0.773-1.043
MCV (fl), mean±SD	86.660±4.671	87.991±4.376	0.054	0.937	0.876-1.002
MCHC (%), mean±SD	33.130±1.284	33.146±1.019	0.927	1.033	0.712-1.499

AMI: Acute myocardial infarction, SA: Stable angina, RDW: Red cell distribution width, Hb: Hemoglobin, PCV: Packed cell volume, MCV: Mean cell volume, MCHC: Mean cell hemoglobin concentration, SD: Standard deviation, OR: Odds ratio, CI: Confidence interval



**Figure 1:** Scheme of the study design

patients and controls regarding RDW only ( $P = 0.0001$ ,  $OR = 9.481$ ,  $95\% CI = 5.127-17.535$ ). On the other hand, no significant differences were present in respect to Hb, PCV, MCV, and MCHC ( $P$  values are 0.137, 0.112, 0.327, and 0.927, respectively. ORs are 1.021, 0.898, 0.966, and 1.033, respectively. 95% CIs are 0.637–1.638, 0.773–1.043, 0.879–1.062, and 0.712–1.499, respectively).

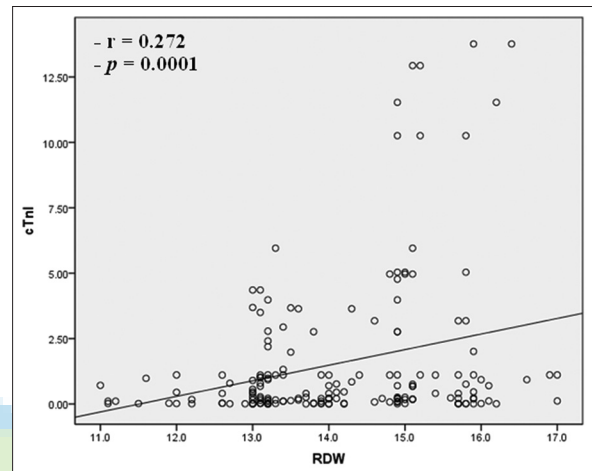
Figure 2 shows the relationship between RDW and cTnI, demonstrating a positive correlation between them regarding the group of patients ( $r = 0.272$ ,  $P = 0.0001$ ).

## DISCUSSION

As represented in Table 1, age distribution showed no significant difference between patients and controls, their mean ages were close, and both of them were lying in the sixth decade of life, reflecting the fact that the participants in both groups were old. Moreover, controls, when selected, were matched by age and gender with cases, so logically, no significant difference will be seen between them.

CAD is strongly associated with age and is the leading cause of death in the US. Unprecedented growth in the 65 years of age and older population is expected over the coming decades. This growth will result in a substantial increase in CAD incidence, prevalence, mortality, and cost.<sup>[7]</sup>

The distribution of males and females of the study was demonstrated in Table 2 with no obvious significant difference between patients and controls in this respect. This may be attributed to the fact that in this study, there is no



**Figure 2:** Relationship between red cell distribution width and cardiac troponin I in the group of patients

gender-specific affection by atherosclerosis and CAD and that these conditions affect both males and females almost evenly, which is probably linked to the difference in the distribution of risk factors among men and women between different societies. Added to the effect of matching mentioned in the previous section.

In the US, for example, evidence that gender-related variables may help in explaining health-related sex differences includes the higher prevalence of CAD in men than in women. The reason why men are at an increased risk may partly be explained by their gender-based propensity to engage in risk-taking behaviors such as smoking or excessive alcohol consumption.<sup>[8]</sup>

The clinical history parameters (HT, diabetes, and smoking) and BMI listed in Tables 3-6 showed nonsignificant differences between the study members. These findings may be attributed to the fact that all of them are risk factors and comorbidities for atherosclerosis and CAD that affect most of the study participants up to a certain extent.

Atherosclerosis is a multifactorial disease. The impact of traditional risk factors such as age, sex, elevated blood pressure, and smoking on CAD risk has long been demonstrated beyond any doubt. In addition, epidemiological studies have shown that patients with DM and glucose intolerance are at increased

risk for CAD. Atherosclerosis accounts for 80% of all diabetic mortality rates.<sup>[9]</sup>

Obesity is related to multiple risk factors of CAD such as HT, Type 2 DM and increased level of inflammation, while also likely to be an independent risk factor for CAD and is associated with reduced overall survival.<sup>[10]</sup>

The values of RDW for patients and controls were presented in Table 7, revealing an extremely significant difference between them. This finding exhibits the role of RDW as an important and essential factor that is associated with a more severe form of CAD which is AMI.

RDW is a novel and universal predictor for cardiovascular disease and mortality and reflects multiple physiological impairments related to atherosclerosis and CAD. It is an important marker for both diagnostic and prognostic purposes in various clinical cardiovascular settings.<sup>[11]</sup>

Sharma *et al.*<sup>[12]</sup> conducted a research that aimed to assess the correlation between RDW and left ventricular ejection fraction in patients presenting with AMI. They came out with a finding that increased RDW and decreased left ventricular ejection fraction were linked together with a statistically significant relation between them, so RDW can be used to assess severity and outcome in patients of acute myocardial infarction, especially at peripheral health center on their initial presentation, where echocardiography is not available routinely.

Bekler *et al.*<sup>[13]</sup> hypothesized in their investigation that RDW level on admission would be predictive of adverse outcomes in non-ST elevation acute coronary syndrome (NST-ACS), and concluded that high RDW level on admission is associated with increased long-term mortality and major adverse cardiac events in patients with NST-ACS. RDW levels are available through routine applications using simple and inexpensive methods for evaluating patients with ACS. In addition, elevated RDW levels may be helpful in identifying high-risk patients and determining appropriate treatment strategies.

Earlier studies in the general population identified the existence of an interesting association between RDW and carotid atherosclerosis. Cemin *et al.*<sup>[14]</sup> found in their study that RDW was a significant predictor of AMI. Zalawadiya *et al.*<sup>[15]</sup> studied 7556 participants of the National Health and Nutrition Examination Surveys 1999–2006, and observed that an increased RDW value was a powerful and independent risk factor for CAD.

Hb, PCV, MCV, and MCHC values that were listed in Table 7, all showed no significant difference between the two groups of the study, reflecting the fact that those parameters probably had no notable impact on CAD and AMI.

These results were consistent with the findings that came out from some studies. Khode *et al.*<sup>[16]</sup> tested the hypothesis that hematocrit and other RBC indices are associated with CAD;

and, after they completed their work, concluded that there was no association between hematocrit and other RBC indices with AMI and stable CAD.

Madjid and Fatemi<sup>[17]</sup> demonstrated in their review that several factors related to RBCs are associated with CAD, including Hb levels and the hematocrit; however, there are not enough data to suggest an association between the RBC-related factors and cardiovascular disease. Several studies have shown a relationship between the hematocrit and incident cardiovascular events in patients who have had an MI. However, results of some studies do not show a significant relationship between hematocrit and CAD risk. In fact, while most studies of different patient populations do show an association between increased hematocrit and increased risk of CAD, the observed risk ratios are generally low; and therefore, the clinical usefulness of hematocrit is unclear.

As shown in Figure 2, a positive correlation was present between RDW and cTnI. cTnI is the preferred biomarker for predicting not only short-term (30 days) but also long-term (1 year and beyond) outcomes with respect to MI and death. Elevated troponin levels are associated with increased risk and are additive to other risk factors, such as markers of inflammatory activity.<sup>[18]</sup>

Tenekecioglu *et al.*<sup>[19]</sup> conducted a study to assess the relationship between RDW values and cTnI levels in patients admitted with NST-ACS. A positive correlation was present between them, and as a result, they concluded that a greater baseline RDW value was associated with myocardial injury and elevated cTnI levels in NST-ACS. Therefore, RDW could be considered as a significant predictor of increased cTnI levels and can be also used for risk stratification of ACS patients admitted to emergency departments.

In a study by Lippi *et al.*,<sup>[20]</sup> researchers investigated the role of the RDW in patients with chest pain suggestive of ACS. These researchers reported that the combined measurement of cTnI and the RDW at admission increased the already impressive sensitivity of cTnI from 94% to 99% in diagnosing ACS.

## CONCLUSION

RDW is a simple and available test in routine laboratory work that has relatively good diagnostic accuracy. High RDW level on admission can predict more severe outcome in patients with CAD.

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## Conflicts of interest

There are no conflicts of interest.

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