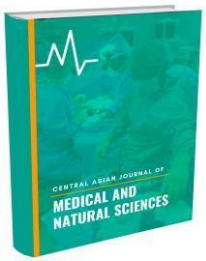

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Article

Correlation Between Red Blood Cell Distribution Width and Acute Coronary Syndrome in Mosul City

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Abstract: Red cell distribution width (RDW) is a quantitative assessment of anisocytosis, reflecting variability in the size of red blood cells. This measurement is typically included in the complete blood count reported by haematology laboratories. Emerging research indicates that RDW may offer significant prognostic insights regarding clinical outcomes in acute coronary syndrome**.** To evaluate the relationship between elevated red cell distribution width (RDW) in patients experiencing acute coronary syndrome (ACS) and findings from electrocardiography (ECG), troponin I levels, white blood cell count (WBC), and ejection fraction (EF). The study involved 100 patients admitted to the Intensive Cardiac Care Unit (ICCU) at Ibn-Sina Teaching Hospital in Mosul, Iraq, between October 2018 and March 2019. Of the participants, 77 were male and 23 were female. Demographic information was collected, and informed consent was obtained from the patients or their relatives. Patients with haemoglobinopathy, enzymopathy, membrane defects, leukaemia, pulmonary hypertension, chronic obstructive pulmonary disease, renal diseases, iron deficiency, and chronic inflammatory conditions were excluded from the study. All patients were tested for haemoglobin (Hb), packed cell volume (PCV), white blood cell (WBC) count, and red cell distribution width (RDW) using a haematological analyzer from Nihon Corporation. The troponin I assay was also conducted using the Monoclonal Antibody Technique and an Enzyme-Linked Immunofluorescent Assay. Echocardiography was also performed, all within 24 hours of admission. Results**:** The study identified 19 patients with elevated levels of Red Cell Distribution Width (RDW), comprising 16 males and 3 females. Among these patients, one was younger than 50 years old, 15 were between 50 and 60 years old, and 3 were over 60 years old. A significant correlation was observed between elevated RDW levels and an ejection fraction (EF) of less than 50% ($p < 0.05$). In contrast, RDW levels were normal in the remaining 81 patients. Of these, 43 had an EF greater than 50%, while 38 had an EF below 50%. Elevated levels of cardiac troponin I, high white blood cell (WBC) counts and the use of thrombolytic drugs were significantly associated with increased red cell distribution width (RDW) levels ($p < 0.05$). There was a notable relationship between elevated RDW, increased troponin I levels, leukocytosis, and decreased ejection fraction (EF) in patients diagnosed with non-ST elevation myocardial infarction (NSTEMI). Additionally, a significant association was found between increased RDW, elevated troponin I level, leukocytosis, and decreased EF in patients with non-ST elevation myocardial infarction (NSTEMI). In patients diagnosed with acute coronary syndrome (ACS), a significant association was found between increased red cell distribution width (RDW), elevated troponin I levels, leukocytosis, and reduced ejection fraction (EF) in cases of non-ST elevation myocardial infarction (NSTEMI). These factors may serve as predictors for the severity and outcomes of acute myocardial infarction (MI).

Keywords: Red Blood Cell Distribution Width, Leukocytosis, NSTEMI, Troponin I Level, Ejection Fraction

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1. Introduction

The term acute coronary syndrome (ACS) refers to any group of clinical symptoms due to acute myocardial ischemia, which covers a range of clinical conditions, including unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI)[1]. The pathogenesis of ACS involves an intricate interplay among the endothelium, the inflammatory cells, and the thrombogenicity of the blood.

The lipid and tissue factor content of the plaque, the severity of the plaque rupture, the degree of inflammation at the site, the blood flow in the area, and the patient's antithrombotic and prothrombotic balance are among the factors important in controlling the degree of thrombus formation and determining whether a given plaque rupture will result in ACS[2].

Leukocytosis plays a key role in the pathogenesis of ACS, given its effect on the instability of atherosclerotic plaques[3]. Red blood cell distribution width (RDW) measures the variability in the size of circulating erythrocytes[4]. It is used to analyze the type of anaemia and assist in the differential diagnosis of different leukemic conditions[5].

Clinical studies recently have suggested that RDW has a prognostic value in patients with heart failure and coronary heart disease [6]. However, the exact relationship between RDW and AMI remains ill-defined. Still, the resultant diminution of oxygen supply at the tissue may help to explain the increased risk of cardiovascular events associated with elevated RDW [7]. Cardiac troponins are the preferred biomarkers for diagnosing acute MI because elevated levels correlate with a more accurate diagnosis[8]. Electrocardiographic findings reflective of unstable angina or NSTEMI include ST-segment depression and inverted T waves. ST depression will not always resolve when the ischemia or pain has resolved, although T-wave inversion may persist[9].

This study aimed to assess the RDW in patients with acute coronary syndrome and the association between increased RDW, reduced ejection fraction, leukocytosis, and raised troponin I levels in patients with AMI.

2. Materials and Methods

The study focused on patients diagnosed with acute coronary syndrome (ACS) who were admitted to the Intensive Coronary Care Unit (ICCU) at Ibn-Sina Teaching Hospital in Mosul between October 2018 and March 2019. A prospective case series design was employed to fulfill the study's objectives. Demographic information was gathered, and written informed consent was obtained from either the patients or their relatives. Ultimately, 100 patients with acute coronary syndrome were included in the study, consisting of 77 males and 23 females aged 40 to 85 years (median age: 54 years). Patients with conditions such as hemoglobinopathy, enzymopathy, membrane defects, leukemia, pulmonary hypertension, chronic obstructive airway disease, renal disease, iron deficiency, or chronic inflammation were excluded from the study. The study examined patients diagnosed with acute coronary syndrome (ACS) who were admitted to the Intensive Coronary Care Unit (ICCU) at Ibn-Sina Teaching Hospital in Mosul between October 2018 and March 2019. A prospective case series design was employed to fulfill the study's objectives. Demographic information was gathered, and written informed consent was obtained from the patients or their relatives. In total, 100 patients with acute coronary syndrome participated in the study, including 77 males and 23 females aged 40 to 85 years (median age: 54 years).

Patients with hemoglobinopathy, enzymopathy, membrane defects, leukemia, pulmonary hypertension, chronic obstructive airway disease, renal disease, iron deficiency, or chronic inflammation were excluded from the study. A 5 ml venous blood sample was collected from all patients within the first 24 hours following the onset of chest pain. Blood samples were obtained in two types of tubes: 2 ml EDTA tubes for assessing

levels of hemoglobin (Hb), packed cell volume (PCV), red cell distribution width (RDW), and white blood cell (WBC) count, using a hematological analyzer from Nihon Corporation. The remaining 3 ml was collected in plain tubes, which were subsequently centrifuged to measure cardiac Troponin I levels utilizing the Monoclonal Antibody Technique and enzyme-linked immunofluorescent assay with the VIDAS Troponin Ultra kit (REF 30 448, Bio Merieux - France).

RDW measurement is typically represented by RDW-CV (red blood cell distribution width-coefficient of variation) and RDW-SD (red blood cell distribution width-standard deviation). RDW-CV was calculated from the erythrocyte volume distribution histogram, with values exceeding 14.5% considered elevated. Echocardiography was conducted for all patients within 24 hours of their admission.

Statistical Analysis

Performed by SPSS 21. The p-value calculated by the Chi-square test, P value (≤ 0.05), was considered significant.

3. Results and Discussion

A study revealed that 60% of the 100 patients were between 50 and 60 years old. Additionally, 15% of these patients had a prior history of ischemic heart disease. The demographic characteristics of the study group are detailed in Table 1.

Table 1. Socio-demographic characteristics of the study sampled population.

Variable	No. [n = 100]	%
Gender		
Male	77	77.0
Female	23	23.0
Age(years)		
< 50	18	18.0
50 – 60	60	60.0
> 60	22	22.0
R**esidence**		
Urban	66	66.0
Rural area	34	34.0
Previous IHD		
Yes	15	15.0
No	85	85.0
Smoking		
Yes	33	33.0
No	67	67.0

In 19 patients, RDW levels are high, consisting of sixteen males and three females. One patient is under 50 years old, fifteen patients are between 50 and 60 years old, and three patients are over 60 years old.

Three patients experienced ST-Elevation Myocardial Infarction (STEMI), while sixteen patients had Non-ST-Elevation Myocardial Infarction (NSTEMI).

The Troponin test yielded positive results for all 19 patients. None of the patients with a high Red Cell Distribution Width (RDW) received thrombolytic drugs, including the

three patients with STEMI, because the time between the onset of chest pain and their presentation exceeded 12 hours, see Tables 2 and 3.

Table 2. Complete blood count in the studied group.

Variable	Ranges	Results	No.=100	Mean ± SD
HB	Male (14-17) g/dl Female (12-16) g/dl	Normal	99	13.59 ± 1.80
		High	1	
PCV	Male (0.40-0.54) Female 0.37-0.47)	Normal	99	40.86 ± 4.59
		High	1	
WBC	(4.0-10.0) 10^3/ML	Normal	68	9.76 ± 2.87
		High	32	
RDWCV **RDWSD**	RDWCV (11.6-14.0) % RDWSD (39.0-46.0) Fl	Normal	81	42.90 ± 2.43
		High	19	13.14 ± 2.15

Table 3. Patients characteristic according to high RDW.

Variables		No. [n = 19]	%
Age in years	<50	1	5.3
	50-60	15	78.9
	> 60	3	15.8
Sex	Male	16	84.2
	Female	3	15.8
ECG	ST elevation	3	15.8
	Non-ST elevation	16	84.2
ECHO	< 50 %	19	100.0
	> 50 %	0	0.0
Troponin	Positive	19	100.0
	Negative	0	0.0
WBC	Normal	0	0.0
	> (10)10^3/mL	19	100
Thrombolytic Drugs	Yes	0	0.0
	No	19	100.0
Smoking	Yes	6	31.6
	No	13	68.4

Table 3 presents the characteristics of patients with high red cell distribution width (RDW), including sixteen males and three females. Among these patients, one was under 50 years old, fifteen were between 50 and 60 years old, and three were above 60 years old.

Regarding ECG findings, three patients had ST-Elevation Myocardial Infarction (STEMI), while sixteen had Non-ST-Elevation Myocardial Infarction (NSTEMI). The troponin test returned positive results for all 19 patients. Despite three cases of STEMI, none of the patients with high RDW received thrombolytic drugs due to the elapsed time for administering these treatments.

The correlation between RDW and EF < 50% was significant ($p < 0.05$). The remaining 81 patients had normal RDW, with 43 patients having their EF>50% and 38 patients < 50% EF, see Table 4.

Table 4. Relationship between RDW, ECG, ECHO finding, troponin.

Variables		RDW		Total [n=100]	P value
		Normal [n=81] No. (%)	More than 46Fl [n=19] No. (%)		
ECG	ST elevation	61(75.3)	3 (15.8)	**64 (64.0)**	0.000
	Non-ST elevation	20 (24.7)	16 (84.2)	**36 (36.0)**	
ECHO (ejection)	< 50%	38 (46.9)	19 (100.0)	**57 (57.0)**	0.000
	> 50 %	43 (53.1)	0 (0.0)	**43 (43.0)**	
Troponin	Positive	61 (75.3)	19 (100.0)	**80 (80.0)**	0.015

Table 5. Relationship between RDW, age, sex, previous IHD, and smoking.

Variables		RDW		Total [n=100]	P value
		Normal [n=81] No. (%)	More than 46Fl [n=19] No. (%)		
Age	<50	17(21.0)	1(5.3)	18(18.0)	0.140
	50--60	45(55.6)	15(78.9)	60(60.0)	
	> 60	19(23.5)	3(15.8)	22(22.0)	
Sex	Male	61(75.3)	16(84.2)	77(77.0)	0.407
	Female	20(24.7)	3(15.8)	23(23.0)	
Previous IHD	Yes	9(11.1)	4(21.o)	13(13.0)	0.246
	No	72(88.9)	13(68.4)	87(87.0)	
Smoking	Yes	27(33.3)	6(31.6)	33(33.0)	0.884

There is no correlation between RDW, age, gender, previous IHD, and smoking history ($p>0.05$), see Table 5.

4. Discussion

The Red Cell Distribution Width (RDW) is calculated from the distribution curves of red blood cell sizes. This measurement can serve as an indicator of morbidity and mortality in various cardiovascular diseases, including acute myocardial infarction (MI). Additionally, it is suggested that RDW may act as an independent predictor of mortality in cases of non-ST elevation myocardial infarction (NSTEMI). [10]. The link between RDW and ACS was initially established by Felker et al.[11] in 2007.

In this study, factors such as the patient's age, sex, smoking habits, and history of ischemic heart disease (IHD) did not show a significant relationship with elevated RDW levels (Table 5). This finding aligns with the studies conducted by Wang et al.[12] and Biase et al. [13].

The research findings indicated a significant positive correlation between Non-ST-Elevation Myocardial Infarction (NSTEMI) and elevated Red Cell Distribution Width (RDW) levels. Specifically, the study observed that patients diagnosed with NSTEMI tended to exhibit higher RDW values, suggesting that increased RDW may serve as a

potential biomarker for this type of myocardial infarction. These results are consistent with previous work by Bekler et al., which also reported similar associations between RDW levels and NSTEMI cases. This relationship highlights the importance of monitoring RDW in patients at risk for myocardial infarction, as it may aid in early diagnosis and intervention strategies. This aligns with the findings of Bekler et al. in 2014[14] and a 2015 study by Tenekecinoglu et al.[15], which noted that patients with NSTEMI had higher baseline RDW values linked to myocardial injury and increased levels of cardiac Troponin I. These results further bolster the conclusions drawn in this research paper.

Cardiac Troponin I is widely recognized as the most reliable biomarker for assessing the risk of adverse outcomes following a myocardial infarction. It plays a crucial role in both short-term and long-term patient management. For short-term outcomes, typically within 30 days of the event, elevated levels of Cardiac Troponin I can indicate the severity of heart damage and help in predicting complications. For long-term outcomes, particularly those extending to one year or beyond, its levels can provide valuable insights into the patient's risk of mortality and the potential for recurrent cardiovascular events. As such, measuring Cardiac Troponin I is essential for informing clinical decisions and guiding treatment strategies in patients with suspected or confirmed heart issues[16]. A decreased ejection fraction (EF) is a critical indicator of compromised heart function and can result from reduced cardiac perfusion in patients suffering from acute coronary syndrome (ACS). This condition can arise from various factors, such as blockages in the coronary arteries, which hinder blood flow and, consequently, oxygen to the heart muscle.

Moreover, a high red cell distribution width (RDW) level can also correlate with a decreased EF. Elevated RDW indicates significant variability in the size of red blood cells, which can affect their overall functionality. Larger variations in cell size may suggest underlying issues with erythropoiesis, leading to the production of red blood cells that are less stable and more susceptible to hemolysis

When red blood cells (RBCs) are prone to destruction, they exhibit a reduced ability to transport oxygen effectively throughout the body. This diminished oxygen-carrying capacity can result in inadequate oxygen supply to the cardiac muscle, further impairing perfusion. Consequently, both reduced cardiac perfusion and abnormally high RDW levels can profoundly impact heart health and overall patient outcomes[17].

This study found a significant positive relationship between low ejection fraction (EF) and high red cell distribution width (RDW) in patients with acute coronary syndrome (ACS). This finding aligns with research by Biase et al[13], who determined that EF was higher in patients with normal RDW compared to those with high RDW in ACS cases.

Our study revealed a significant correlation between leukocytosis and elevated red cell distribution width (RDW) levels in patients diagnosed with acute coronary syndrome (ACS). This finding suggests that higher white blood cell counts may indicate more severe underlying conditions or stress on the body related to ACS. Additionally, Sabatine et al.[18] highlighted that leukocytosis is an important risk factor for increased mortality within the first 30 days following an ACS event and a continued heightened risk for up to six months. This is particularly relevant for patients experiencing unstable angina or non-ST-elevation myocardial infarction (NSTEMI), emphasizing the need for careful monitoring and management of these patients during their critical recovery periods.

5. Conclusion

In conclusion, our study identified a significant relationship among patients with acute coronary syndrome (ACS), where higher levels of red cell distribution width (RDW) were correlated with increased serum troponin I levels, elevated white blood cell counts (leukocytosis), and a reduced ejection fraction (EF) specifically in those diagnosed with non-ST-elevation myocardial infarction (NSTEMI).

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