



A STUDY ON THE CORRELATION OF RED BLOOD CELL DISTRIBUTION WIDTH (RDW) IN PATIENTS ADMITTED AS NON-ST ELEVATION ACUTE CORONARY SYNDROME (NSTE-ACS) IN A TERTIARY HOSPITAL

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ABSTRACT

Introduction: Cardiovascular diseases (CVD) are the main cause of death in both the developed and developing countries. Each year, 6 million people are affected by acute myocardial infarction (AMI), and 25% die of the diseases. Recent studies show Red blood cell Distribution Width (RDW) was significantly related to major cardiac adverse event and independently related to long term mortality in patients with acute coronary syndrome. Acute Coronary Syndrome (ACS) is group of clinical symptoms compatible with Acute Myocardial Ischemia (AMI), unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI). This study will focus mainly on Unstable Angina and NSTEMI which is collectively called Non-ST elevation Acute Coronary Syndrome (NSTE ACS). **General Objective:** To determine the clinical correlation of RDW in patients admitted as Non-ST Elevation Acute Coronary Syndrome mainly the Unstable Angina and NSTEMI. **Methodology:** This is cross sectional retrospective study based on one hundred thirty-six (136) admitted patients in our institution from January, 2017 to March, 2018 as Acute Coronary Syndrome (UA and NSTEMI) who were diagnosed clinically. Demographic characteristics, laboratory studies including cTnI, lipid profile, complete blood counts (CBC), ECG and 2D echo results were retrieved and documented. Patients with low RDW (<14.0) and high RDW (≥ 14.0) were categorized according to the median of the baseline RDW values. Clinical information was obtained regarding the patient's history of systemic hypertension (HTN), diabetes mellitus (DM), dyslipidemia and smoking. **Results And Conclusions:** Our study showed that there was a significant correlation between high Red blood cell Distribution Width (RDW) and Acute Coronary Syndrome (ACS) ($p .007 < .05$). The higher the Red blood cell Distribution Width the higher their risk of having Acute Coronary Syndrome particularly the Unstable Angina and NSTEMI.

KEYWORDS: Acute Coronary Syndrome, Red blood cell Distribution Width, Cardiac Biomarker, Complete Blood Counts.

INTRODUCTION

Cardiovascular diseases (CVD) are the main cause of death in both the developed and developing countries.^[2] In the beginning of the 20th century, every 10th individual die from CVD, whereas in the beginning of the 21st century, that percentage rose to 30%. Each year, 6 million people are affected by acute myocardial infarction (AMI), and 25% of them die of the disease. It is thought that by 2020, the diseases affecting the heart and blood vessels will have become the leading cause of

death in all countries, especially in undeveloped ones.^[1] During 2010, 7.4 million people died of ischemic heart disease which was 13.2% of the total mortality rate.^[2] Acute coronary syndrome was found to be more common among patients who were in the advanced age. Males also dominated the highest number of cases of acute coronary syndrome and those who were classified to have NSTEMI. Acute Coronary Syndrome (ACS) is group of clinical symptoms compatible with acute myocardial ischemia, unstable angina (UA), non-ST-

segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI). This study focuses only on UA and NSTEMI.

Red blood cell distribution width (RDW) is a numerical value measure of the variability in size of circulating erythrocytes. RDW is part of routine hematology laboratory tests and has been a useful diagnostic tool for differentiation and classification of anemia. RDW is defined as the quotient of standard deviation of red blood cell volume and its mean volume and is expressed as a percentage according to the following formula: $RDW = (\text{standard deviation of red blood cell volume} / \text{mean cell volume}) \times 100$. Higher RDW values reflect greater variations in red blood cell volume indicating that high RDW values are an independent predictor of prognosis in patients with cardiovascular diseases such as acute coronary syndromes (ACS).^[1,3]

Cardiac troponin I (cTnI) is the preferred cardiac enzymes that are sensitive and specific indicators of damage to the myocardium. Elevated troponin levels are associated with increased risk and are additive to other risk factors, such as electrocardiography (ECG) changes and markers of inflammatory activity. The identification of patients with elevated troponin levels is especially useful for selecting the appropriate treatment in patients with acute coronary syndrome, especially the NSTEMI and STEMI. However, in UA, cardiac troponin is negative. In this retrospective study, our aim is to investigate the relationship between the RDW and acute coronary syndrome (ACS), particularly UA and NSTEMI.

GENERAL OBJECTIVES

To determine the clinical correlation of RDW in patient admitted as Non-ST Elevation Acute Coronary Syndrome (UA and NSTEMI).

SPECIFIC OBJECTIVES

1) To determine demographic profile of NSTEMI ACS cases (NSTEMI & UA)

2) To correlate RDW of patients with acute coronary syndrome with the following risk factors:

- ◆ Sex
- ◆ Age
- ◆ Comorbidities (Hypertension, Diabetes Mellitus)
- ◆ Lipid profile particularly LDL
- ◆ Smoking
- ◆ Left Ventricular Ejection Fraction

3) To correlate blood parameters such as Hemoglobin, WBC, NLR, MCV, Platelet with NSTEMI ACS cases

SIGNIFICANCE / PURPOSE OF STUDY

Recently, many studies have revealed that the baseline RDW value has been shown to be associated with long term adverse cardiac events like acute myocardial infarctions (MI), heart failures, stable and unstable angina, stroke, and peripheral artery disease, also it has been proposed as an independent predictor of

mortality.^[3] RDW is inexpensive index that is routinely reported as a part of the complete blood count, hence it can be convenient and inexpensive risk predictor tool for ACS patients.

It would provide the local data and can compare to international data regarding the correlation between RDW in ACS cases those with comorbidities such as hypertension, diabetes, smoking, high LDL, which will be beneficial for management and counselling of the ACS patients.

DEFINITION OF TERMS

Acute Coronary Syndrome (ACS): group of clinical symptoms compatible with acute myocardial ischemia, unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI).

Red Blood Cell Distribution Width (RDW): is a measure of the range of variation of red blood cell (RBC) volume that is reported as part of a standard complete blood count.

Troponin I (cTnI): cardiac enzymes that are sensitive and specific indicators of damage to the myocardium.

Hypertension (HTN): a systolic blood pressure (SBP) of 140 mm Hg or more, or a diastolic blood pressure (DBP) of 90 mm Hg or more, or taking antihypertensive medication.

Diabetes Mellitus (DM): a metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both.

Coronary Artery Diseases (CAD): Impedance or blockage of one or more arteries that supply blood to the heart.

REVIEW OF RELATED LITERATURE

Felker et al. were one of the first who made study to assess the role of RDW in cardiovascular disease. The authors noted the usefulness of RDW as a prognostic marker among patients with heart failure.^[4] Subsequent studies have confirmed the significance of RDW as a predictor of mortality both in the general population^[5] and in patients with various diseases, including peripheral artery disease (PAD), chronic obstructive pulmonary disease (COPD)^[6], and kidney failure.

In the study of Azab et al., it showed that RDW is an independent predictor of all-cause long-term mortality in NSTEMI patients. It has also been reported that high levels of RDW are associated with the presence, severity and complexity of coronary artery disease in patients with stable angina pectoris and ST elevation myocardial infarction (STEMI).^[3]

G. Ertaş, C. Aydın, O. Sönmez et al conducted a prospective study in 132 patients undergoing nonemergency CABG, they retrospectively analyzed 132 consecutive patients with mean age of 60.55 ± 9.5 years, composing of 99 male and 33 female. The RDW level was determined preoperatively and on postoperative day 1. Preoperative RDW levels were significantly higher in patients who developed AF than in those who did not (13.9 ± 1.4 vs. 13.3 ± 1.2 , $p=0.03$). There was no noted correlation between postoperative RDW levels and AF. Using a cut point of 13.45, the preoperative level correlated with the incidence of AF with a sensitivity of 61% and specificity of 60%.^[7]

In an abstract of the study of Y. Borné, et al, RDW was measured in 26 820 subjects (aged 45 to 73 years, 61.6% women), without history of myocardial infarction or stroke, during a mean follow-up of 14 years, 1995 subjects had a first coronary events, of which 415 subjects died on the same day as the coronary events (fatal on day 1), another 86 died within 28 days (fatal in 28 days) and 1494 were non-fatal (survived >28 days), for risk factors, baseline RDW was significantly associated with incidence of fatal coronary events but not with non-fatal coronary events. They concluded that high RDW was associated with increased incidence of fatal coronary events. No relationship was observed for incidence of non-fatal coronary events.^[8]

In a study of Lippi et al.^[9], researchers investigated the role of the RDW in patients with chest pain suggestive of ACS. These researchers reported that the combined measurement of cardiac troponin and the RDW at admission increased the already impressive sensitivity of cardiac troponin from 94% to 99% in diagnosing ACS. In the study of Tonelli M et al,^[10] post hoc analysis of data from the Cholesterol and Recurrent Events study was performed with baseline RDW in 4111 participants who were randomized to receive pravastatin 40 mg daily or placebo and followed for a median of 59.7 months, 376 participants died. A significant association was noted between baseline RDW level and the adjusted risk of all-cause mortality (hazard ratio per percent increase in RDW, 1.14; 95% confidence interval, 1.05 to 1.24). Participants with RDW in the highest quartile had an adjusted hazard ratio for death of 1.78 (95% confidence interval, 1.28 to 2.47) compared with those in the lowest quartile. Higher levels of RDW were also associated with increased risk of coronary death/nonfatal myocardial infarction, new symptomatic heart failure, and stroke.

In the study of Cavusoglu E et al,^[11] investigated the long-term prognostic significance of baseline RDW in a well-characterized cohort of 389 male patients who were referred to coronary angiography for a variety of indications. All patients were followed prospectively for all-cause mortality. After controlling for a variety of baseline variables (including hemoglobin and heart failure), RDW analyzed as a categorical variable comparing the upper tertile of baseline values to the

lower two levels combined) was a strong and independent predictor of all-cause mortality using a Cox proportional hazards model [hazard ratio (HR) 2.69, 95% confidence interval (CI) 1.50-4.84, $p=0.0008$]. Baseline RDW was also an independent predictor of all-cause mortality in the non-anemic (HR 4.73, 95% CI 2.06-10.86, $p=0.0003$) and ACS (HR 2.90, 95% CI 1.32-6.38, $p=0.0082$) subpopulations of patients.

In the study of Patel KV et al^[12], Red blood cell distribution width was measured in a national sample of 8175 community-dwelling adults 45 years or older, followed respectively for all cause mortality. Compared with the lowest quintile of RDW, the following were adjusted hazard ratios (HRs) for all-cause mortality (and 95% confidence intervals [CIs]): second quintile, HR, 1.1 (95% CI, 0.9-1.3); third quintile, HR, 1.2 (95% CI, 1.0-1.4); fourth quintile, HR, 1.4 (95% CI, 1.2-1.8); and fifth quintile, HR, 2.1 (95% CI, 1.7-2.6). For every 1% increment in RDW, all-cause mortality risk increased by 22% (HR, 1.22; 95% CI, 1.15-1.30; $P < .001$). Even for nonanemic participants or to those in the reference range of RDW (11%-15%) without iron, folate, or vitamin B (12) deficiency, RDW remained strongly associated with mortality. The prognostic effect of RDW was observed in both middle-aged and older adults for multiple causes of death.

H.-M. Yao, T.-W. Sun, X.-J. Zhang et al,^[13] conducted a study in total of 2169 non-anemic patients (1468 men, mean age 60.2 ± 10.9 years) with CAD who had undergone successful PCI and had at least one drug-eluting stent were included, patients were grouped according to their baseline RDW: Quartile 1 ($RDW < 12.27\%$), Quartile 2 ($12.27\% \leq RDW < 13\%$), Quartile 3 ($13\% \leq RDW < 13.5\%$), and Quartile 4 ($RDW \geq 13.5\%$). The incidence of in-hospital mortality and death or myocardial infarction was significantly higher in Quartiles 3 and 4 compared with Quartile 1 ($P < 0.05$). After a follow-up of 29 months, the incidence of all-cause death and stent thrombosis in Quartile 4 was higher than in Quartiles 1, 2, and 3 ($P < 0.05$). The incidence of death/myocardial infarction/stroke and cardiac death in Quartile 4 was higher than in Quartiles 1 and 2 ($P < 0.05$). Multivariate Cox regression analysis showed that RDW was an independent predictor of all-cause death (hazard ratio (HR)=1.37, 95% confidence interval (CI)=1.15–1.62, $P < 0.001$) and outcomes of death/myocardial infarction/stroke (HR=1.21, 95% CI=1.04–1.39, $P=0.013$).

In study of Yaron Arbe et al,^[14] a cohort of 535 STEMI patients undergoing PPCI were divided into two groups ($RDW > 14\%$, $RDW \leq 14\%$) using CHAID and CART methods. The association between RDW and 5-year all-cause mortality was assessed using Cox's proportional hazards analysis. A total of 37 patients died during follow up of 5 years (mean: 1059, median: 1013, range 2–2130 days). $RDW > 14\%$ was associated with increased risk of all-cause mortality (HR = 5, CI 95%

2.7– 9.9, $p < 0.001$). In multivariate analysis, $RDW > 14$ remained significantly associated with increased risk for all-cause mortality (HR = 3.8, CI 95% 1.8– 7.99, $p < 0.001$). Patients with RDW above 14% did not have lower ejection fraction, higher CPK or more conventional risk factors.

S. Tsuboi, K. Miyauchi, T. Kasai et al.^[15] subjects comprised 560 consecutive diabetic patients (mean age, 66.6 years; male, 80%) with stable CAD who had undergone elective percutaneous coronary intervention (PCI), divided into 2 groups according to median RDW at baseline (13.1%): a high RDW group (mean RDW, 14.0%; interquartile range, 13.3–14.2%); and a low RDW group (mean RDW, 12.6%; interquartile range, 12.4–12.9%). All-cause mortality rates were compared in duration of follow up was 3.9 years. Patients with high RDW were more likely to be older, with dyslipidemia and have a lower ejection fraction and decreased hemoglobin level. Twenty-nine patients (5.2%) died during follow up. The cumulative incidence of all-cause death was significantly higher in the high RDW group than in the low RDW group (log-rank $P=0.0015$). Multivariate analysis identified high RDW as being associated with all-cause mortality (hazard ratio, 2.56; 95% confidence interval, 1.12–6.62; $P=0.025$).

In this study, Şahin, A. Karabulut, A. Kaya et al.^[16] compared red cell distribution width (RDW), neutrophil lymphocyte ratio (NLR) and mean platelet volume (MPV) measurements among patients with poor coronary collateral circulation (CCC) and well-developed CCC. A total of 326 patients with stable coronary artery disease (CAD) were evaluated retrospectively. CCC was graded by using the Rentrop classification. The poor CCC group included patients with Rentrop 0-1 CCC, and the good CCC group included Rentrop 2-3 CCC. There were 171 subjects (84% male; mean age 56.6 ± 10.4 years) in the poor CCC group, and 155 subjects (89% male; mean age 57.6 ± 9.7 years) in the good CCC group. The total number of vessels with $>95\%$ stenosis (1.1 ± 0.5 vs. 1.0 ± 0.4 ; $p=0.64$) and Gensini scores (84.4 ± 38.8 vs. 83.3 ± 37.4 ; $p=0.83$) was not higher in the poor CCC group compared to the good CCC group. RDW was significantly higher in the poor CCC group compared to the good CCC group ($14.19 \pm 1.36\%$ vs. $13.89 \pm 1.19\%$; $p=0.04$). Poor CCC was found to be independently correlated with RDW, but not with any other hematological parameters in patients with stable CAD.

In study of Marianela Sánchez-Martínez et al.^[17] Red cell distribution width was measured at admission in 293 patients with non-ST-segment elevation acute coronary syndrome. All patients were clinically followed up and major bleeding events were recorded (Bleeding Academic Research Consortium Definition criteria). During a follow-up of 782 days [interquartile range, 510–1112 days], events occurred in 30 (10.2%) patients. Quartile analyses showed an abrupt increase in major

bleedings at the fourth red cell distribution width quartile ($> 14.9\%$; $P = .001$). After multivariate adjustment, red cell distribution width $> 14.9\%$ was associated with higher risk of events (hazard ratio = 2.67; 95% confidence interval, 1.17–6.10; $P = .02$). Patients with values $\leq 14.9\%$ and a CRUSADE score ≤ 40 had the lowest events rate, while patients with values $> 14.9\%$ and a CRUSADE score > 40 points (high and very high risk) had the highest rate of bleeding (log rank test, $P < .001$).

STUDY DESIGN

This is a retrospective study conducted from January, 2017 to March, 2018 of in-patients admitted at Mariano Marcos Memorial Hospital and Medical Center. Baseline demographics such as age, gender, final diagnosis, CBC, 2D echo results, ECG, lipid profile was collected.

SAMPLE SIZE ESTIMATION

Patients diagnosed with Non-ST Elevation acute coronary syndrome (NSTEMI & UA) admitted at the Mariano Marcos Memorial Hospital and Medical Center from January, 2017 to March, 2018 were reviewed and eligibility criteria were applied. Since the total population of ACS cases within 15 months duration is unknown, taking target population of 140, error margin 5% & confidence level 95%, using Slovin's formula minimum required sample size is 103 cases.

INCLUSION CRITERIA

- 1) Age 40 years old and above
- 2) All the NSTEMI diagnosed cases
- 3) Unstable Angina diagnosed cases

EXCLUSION CRITERIA

1. Patients with a history of trauma, surgery, neoplasm, infection in last 30 days prior to hospitalization
2. Patients with evidence of anemia, active or chronic inflammatory or autoimmune diseases
3. Pregnancy, recent blood transfusion and patient on immunosuppressant therapy (including corticosteroids) and current intake of aspirin.

MATERIALS AND METHODS

This cross-sectional retrospective study is based on patients admitted at Mariano Marcos Memorial hospital and Medical Center from January, 2017 to March, 2018 with diagnosis of acute coronary syndrome (NSTEMI, UA). Applying the inclusion and exclusion criteria a total of 136 patients were enrolled in this study. Diagnosis was based on standard diagnostic flowchart that include clinical presentations with symptoms, ischemic ECG changes (ST segment deviation, T-wave inversion and new Q-waves) as well as biochemical measurements of markers of myocardial necrosis such as cardiac troponin I. All patients age 40 years old and above who were diagnosed with non-ST elevation myocardial infarction (NSTEMI) or unstable angina (UA) clinically, ischemic ECG changes and according to cTnI value were included in this study. Demographic characteristics, laboratory

studies including RDW in complete blood counts (CBC), peripheral differential counts, lipid profile, cardiac troponin I, ECG, 2D echo, clinical information regarding the patient's history of systemic hypertension (HTN), diabetes mellitus (DM), dyslipidemia, and smoking were retrieved and documented from medical records section, heart station, department of laboratory section respectively. Upon admission venous blood sample were collected in tube containing K3-EDTA and sent to laboratory within 30 minutes for measurement of hematological indices and for baseline determination of cTnI levels in all patients. Hemoglobin (Hb), mean corpuscular volume (MCV), red blood cell distribution width (RDW), white blood cell (WBC), neutrophil, lymphocytes, platelet count were all measured as part of automated complete blood count using a Sysmex Automated Hematology Analyser XN-2000 (Sysmex Corporation, Kobe, Japan). The normal reference range for RDW in our laboratory is 12 to 16%, in this study patients were categorized low RDW (<14.0%) and high RDW ($\geq$ 14.0%) according to the median of the baseline RDW values. It's known that association between anemia and cardiovascular events are high so we selected the patients who are not anemic using WHO criteria of anemia (<12.0 g/dl in women, <13.0 g/dl in men). Fasting lipid profile were assessed by Roche cobas C 311 automated analyzer (Hitachi Technologies, Tokyo, Japan). In this study cut-off range of patients LDL cholesterol were based on ACC/AHA guideline on treatment of blood cholesterol 2013. Patients with a history of trauma, surgery, neoplasm, infection in last 30 days prior to hospitalization, evidence of anemia, hematological proliferative diseases, active or chronic inflammatory or autoimmune diseases, pregnancy, recent blood transfusion and patient on immunosuppressant therapy (including corticosteroids), current intake of aspirin were excluded. cTnI levels were assessed using the electrochemiluminescence immunoassay (ECLIA) by

Elecsys 2010 and cobas e 411 immunoassay analyzers (Hitachi Technologies, Tokyo, Japan). A level of cTnI >0.3 ng/ml were considered positive. To confirm the presence of NSTEMI, cTnI measurement were repeated after 6 hours. Transthoracic echocardiography was performed on each patient during admission, results were retrieved from record section and heart station. The Simpson's method was used in the 2-dimensional echocardiographic apical 4-chamber view to assess the left ventricular ejection fraction (LVEF) using the commercially available machine (EKO 7, Samsung Madison, Seoul, Korea). ECG were performed by Kenz ECG 108 (Japan).

STATISTICAL ANALYSIS

Continuous variables were expressed as the mean $\pm$ SD. Categorical variables were expressed as percentages. T-test were used to compare parametric continuous variables. To compare categorical variables, the χ^2 -test was used. Relationships between variables were examined using chi square with power of eta.

ETHICS STATEMENT

This study was reviewed by the Research Ethics Review Committee (RERC) of Mariano Marcos Memorial Hospital and Medical Center. Necessary application letters were submitted to the medical record section and Office of the Medical Center Chief (OMCC) for proper retrieval of records in accordance to the Data Privacy Law (appendix).

RESULTS

Three hundred ten (310) patient's records were retrieved and a total of 136 patients were included in this study after elimination using the exclusion criteria, among which 77 patients are diagnosed as NSTEMI and 59 patients are diagnosed as Unstable Angina.

Table 1: Baseline Demographics of the Study Population according to the Final Diagnosis.

Demographics	Acute Coronary Syndrome		Total	p
	Unstable Angina	NSTEMI		
Age (years)				.718^s
Mean $\pm$ SD	66.23 $\pm$ 11.94	65.62 $\pm$ 11.75	-	
Sex, n(%)				.008[‡]
Male	28(20.6)	47(34.6)	75(55.1)	
Female	31(22.8)	30(22.1)	61(44.9)	
Hypertension, n(%)				.380[‡]
Absent	20(14.7)	32(23.5)	52(38.2)	
Present	39(28.7)	45(33.1)	84(61.8)	
DM, n(%)				.096[‡]
Absent	50(36.8)	57(41.9)	107(78.7)	
Present	9(6.6)	20(14.7)	29(21.3)	
LDL, n(%)				.054[‡]
Normal	21(15.4)	31(22.8)	52(38.2)	
High	38(27.9)	46(33.8)	84(61.8)	
Smoking, n(%)				.069[‡]
No	39(28.7)	40(29.4)	79(58.1)	
Yes	20(14.7)	37(27.2)	57(41.9)	

LVEF, n(%)				.003 [‡]
Normal function	41(30.1)	32(23.5)	73(53.7)	
Mild dysfunction	9(6.6)	20(14.7)	29(21.3)	
Moderate dysfunction	5(3.7)	22(16.2)	27(19.9)	
Severe dysfunction	4(2.9)	3(2.2)	7(5.1)	
Ischemic ECG Findings, n(%)				.001 [‡]
None	22(16.2)	10(7.4)	32(23.5)	
Present	37(27.2)	67(49.3)	104(76.5)	

Legend: LDL Low Density Lipoprotein; LVEF Left Ventricular Ejection Fraction; ECG Electrocardiogram;

NSTEMI Non-ST Elevation Myocardial Infarction; DM Diabetes Mellitus;

Note: Results are expressed as Mean±SD, unless otherwise stated.

Significance is at $\leq .05$ [‡]Chi Square Test [§]t-test for Independent Samples

[†] No statistical analysis was conducted due to internal consistency of data

The baseline demographics of study population are shown in Table 1. The mean age of patients with unstable angina was 66.23 with SD of 11.94 and NSTEMI patients was 65.62 with SD of 11.75 ($p = .718 > .05$). Males dominated the highest number of cases admitted as acute coronary syndrome (75; 55.1%) with 47 (34.6%) patients diagnosed as NSTEMI. There were only 61 (44.9%) females, 31 (22.8%) had unstable angina and 30 (22.1%) had NSTEMI ($p = .008 < .05$). Hypertension was found to be very common among the admitted acute coronary syndrome patients (84; 61.8%) where 45 (33.1%) had NSTEMI, the rest was non-hypertensive before admission and no elevation of BP noted during hospital stay ($p = .380 > .05$).

Diabetes Mellitus was found to be not common on most subjects (107; 78.7%) and in this, only 29 (78.7%) had DM, among them 20 (14.7%) were diagnosed as NSTEMI and 9 (6.6%) were unstable angina ($p = .096 > .05$). High LDL was found to be common in most of subjects (84; 61.8%), 46 (33.8%) with NSTEMI group and 38 (27.9%) with unstable angina group. There were 52 cases with normal LDL, 31(22.8%) from NSTEMI

group and 21(15.4%) from unstable angina group ($p = .054 > .05$).

Also, smoking was found to be not common among the subject population (79; 58.1%). However, the rest found to be smoking are noted more in the NSTEMI group (37; 27.2%) than in the UA group (20; 14.7%) ($p = .069 > .05$). Two-dimensional echocardiography was done in all subject population. It was noted that a total of 73 (53.7%) subjects had normal LVEF, 32 (23.5%) from NSTEMI group and 41 (30.1%) from the UA group. Using the ESC classification guideline on LV EF, we categorized the LVEF as mild dysfunction (45 - 54%), moderate dysfunction (30 - 44%), and severe dysfunction ($<30\%$). From this, 29 (21.3%) had mild LV dysfunction, mostly (20 cases) from the NSTEMI group. Twenty-seven subjects had moderate LV dysfunction, still mostly (22 cases) from the NSTEMI group ($p = .003 < .05$). Ischemic ECG findings was found to be present in most subjects (104; 76.5%), 67 (49.3%) patients from NSTEMI and 37 (27.2%) from UA ($p = .001 < .05$). The rest had normal ECG finding (NSTEMI 10; 7.4% and UA 22; 16.2%).

Table 2: Correlation of Acute Coronary Syndrome with CBC parameters.

Demographics	Acute Coronary Syndrome		P
	Unstable Angina	NSTEMI	
Blood Hemoglobin (g/dl)			.873[§]
Mean±SD	13.42±1.09	13.78±1.04	
WBC (10⁹/L)			.051[§]
Mean±SD	17.89±65.47	10.61±3.09	
Neutrophils (%)			.365[§]
Mean±SD	64.66±13.10	71.45±11.82	
Lymphocytes (%)			.495[§]
Mean±SD	22.84±9.61	17.15±9.61	
NLR			.003[§]
Mean±SD	3.83±2.90	6.37±5.25	
Platelets (10⁹/L)			.612[§]
Mean±SD	259.0±81.54	258.7±72.7	
MCV (fl)			.338[§]
Mean±SD	81.01±14.24	96.12±94.14	
RDW (%)			.048[§]
Mean±SD	14.10±1.46	14.29±1.58	

Legend: WBC White Blood Cell; NLR Neutrophil to Lymphocyte Ratio; MCV Mean Corpuscular Value; NSTEMI Non-ST Elevation Myocardial Infarction

Note: Results are expressed as Mean±SD, unless otherwise stated.

Significance is at $\leq .05$ [‡]Chi Square Test with power of Eta [§]t-test for Independent Samples

[†] No statistical analysis was conducted due to internal consistency of data

Table 2 Shows correlation of Acute Coronary Syndrome with CBC of the study population. In this table it was noted that Neutrophil to Lymphocytes Ratio (NLR) and RDW was significantly correlated with acute coronary syndrome respectively ($p .003 < .05$), ($p .048 < .05$). In those with NSTEMI, mean of neutrophil and MCV are higher compared to unstable angina patients.

WBC was found to be higher among unstable angina patients compared to those with NSTEMI (17.89 ± 65.47 vs. 10.61 ± 3.09 $p .051 = .05$) and the mean of lymphocytes and platelet was higher among patients of unstable angina compared to NSTEMI patients.

Table 3: Correlation of RDW with baseline Demographics of the study population.

Demographics	Red Cell Distribution Width		Total	p
	Low (RDW<14.0)	High (RDW≥14.0)		
Age (years)				.718[§]
Mean±SD	64.69±11.57	66.80±11.95	-	
Sex, n(%)				.864[‡]
Male	32(23.5)	43(31.6)	75(55.1)	
Female	27(19.9)	34(25)	61(44.9)	
ACS, n(%)				.007[‡]
Unstable Angina	27(19.9)	32(23.5)	59(43.4)	
NSTEMI	32(23.5)	45(33.1)	77(56.6)	
Hypertension, n(%)				.492[‡]
Absent	22(16.2)	30(22.1)	52(38.2)	
Present	37(27.2)	47(34.6)	84(61.8)	
DM, n(%)				.326[‡]
Absent	48(35.3)	59(43.4)	107(78.7)	
Present	11(8.1)	18(13.2)	29(21.3)	
LDL, n(%)				.050[‡]
Normal	20(14.7)	32(23.5)	52(38.2)	
High	39(28.7)	45(33.1)	84(61.8)	
Smoking, n(%)				.334[‡]
No	36(26.5)	43(31.6)	79(58.1)	
Yes	23(16.9)	34(25)	84(61.8)	
LVEF, n(%)				.099[‡]
Normal function	32(23.5)	41(30.1)	73(53.7)	
Mild dysfunction	17(12.5)	12(8.8)	29(21.3)	
Moderate dysfunction	9(6.6)	18(13.2)	27(19.9)	
Severe dysfunction	1(.7)	6(4.4)	7(5.1)	
Ischemic ECG Findings, n(%)				.560[‡]
None	14(10.3)	18(13.2)	32(23.5)	
Present	45(33.1)	59(43.4)	104(76.5)	

Legend: LDL Low Density Lipoprotein; LVEF Left Ventricular Ejection Fraction; ECG Electrocardiogram;

NSTEMI Non-ST Elevation Myocardial Infarction; DM Diabetes Mellitus;

Note: Results are expressed as Mean±SD, unless otherwise stated.

Significance is at $\leq .05$ [‡]Chi Square Test with power of Eta [§]t-test for Independent Samples

[†] No statistical analysis was conducted due to internal consistency of data

Table 3. Shows the correlation of RDW with baseline demographics of the study population. It was noted that the acute coronary syndrome (ACS) and Low-Density Lipoprotein (LDL) is significantly correlated with high RDW levels. In those with high RDW, the mean age is higher at 66 years old, with higher LDL levels and more than half of the study population. Most of patients are hypertensive but non-diabetic and mostly non-smoker. LV dysfunction show no significant correlation with

higher levels of RDW; however, it was still noted that those with moderate to severe LV dysfunction is seen in those with higher RDW levels. ECG with ischemic changes though not significant with RDW levels but were present in most of the study population.

Table 4: Independent Predictors of ACS in a Binary Logistic Regression Analysis.

Variables	95% CI		p
	Lower	Upper	
LDL	.635	1.58	.001 [‡]
LVEF	1.030	.993	.113 [‡]
Blood Hemoglobin	.874	2.20	.165 [‡]
WBC	.831	1.106	.566 [‡]
Neutrophils	.983	1.106	.006 [‡]
Ischemic ECG Findings	1.852	14.67	.002 [‡]
Lymphocytes	.928	1.096	.846 [‡]
NLR	.907	1.338	.009 [‡]
Platelets	.995	1.007	.732 [‡]
MCV	1.014	1.131	.014 [‡]
RDW	.832	1.514	.004 [‡]

Legend: LDL Low Density Lipoprotein; LVEF Left Ventricular Ejection Fraction; ECG Electrocardiogram; NSTEMI Non-ST Elevation Myocardial Infarction; WBC White Blood Cell; NLR Neutrophil to Lymphocyte Ratio; MCV Mean Corpuscular Value; RDW Red Blood Cell distribution width;
 Note: Results are expressed as Mean±SD, unless otherwise stated.

Significance is at $\leq .05$ [‡]Binary Logistic Regression

[†] No statistical analysis was conducted due to internal consistency of data

Table 4 shows the predictors for ACS that could potentially lead to NSTEMI. It was found that LDL ($p .001 < .05$); Neutrophils ($p .006 < .05$); Ischemic ECG findings ($p .002 < .05$); Neutrophil Lymphocyte Ratio ($p .014 < .05$); Mean Corpuscular Volume ($p .014 < .05$); and RDW ($p .004 < .05$) were independently correlated with NSTEMI in subject population.

DISCUSSION

Acute coronary syndrome was found to be more common among patients who were in the advanced age. Males also dominated the highest number of cases with acute coronary syndrome and classified to have NSTEMI. Most of them have pre-existing condition such as hypertension and ischemic ECG findings. The data obtained in this research paper is supported by several authors where they found that acute coronary syndrome was observed generally among the older group and mostly male patients, particular with 65 to 70 years old.^[18] This suggests that males were more likely to have this condition over female.

The results of this particular investigation were in line with the data obtained in study of Lerner DJ, Kannel WB et al, where patients with hypertension were found to have an increase in prevalence of having acute coronary syndrome, because we all know that chronic uncontrolled hypertension could further decrease the integrity of the blood vessels, giving a long-term effect on the cardiovascular system of the individual.^[19]

In this study, correlation existed between WBC, neutrophils and lymphocyte ratio and cases of acute coronary syndrome (UA & NSTEMI), because its known that inflammatory response plays an important role in the progression and destabilization of atherosclerosis and cardiovascular diseases.^[20-21] Among the various inflammatory markers, the white blood cell count and its subtypes are associated with increased cardiovascular

risk factors.^[22-23] Recently, the neutrophil to lymphocyte ratio (NLR), which is inexpensive, routinely used, reproducible, and widely available in most hospitals, has been proven to be an important inflammatory marker and potential predictor of cardiovascular risk.^[24] Further, high LDL together with ischemic ECG findings correlated well with high RDW in our NSTEMI population.

Today, neutrophil and lymphocyte ratio (NLR) are accepted as a parameter that shows the adverse effects of both high neutrophil levels, which reflect acute inflammation, and low lymphocyte levels, which reflect physiological stress.^[25] The inflammatory reaction does not only show a response to tissue damage in ACS, but also leads to a poor clinical course.^[26-27]

LIMITATIONS

Main limitations were the small number of study populations and single center design; hence the result cannot be generalized.

CONCLUSION

Based on our results, it shows that higher RDW is seen in patients admitted as unstable angina and NSTEMI and most of them has moderate to severe LV dysfunction. Majority of those with high RDW are older male, hypertensive with ischemic ECG changes and elevated LDL level. Correlation of RDW with higher white blood counts and neutrophils to lymphocytes ratio are significantly noted.

RECOMMENDATIONS

Patients who have LVEF dysfunction, high LDL cholesterol level, hypertension and other laboratory parameters should be strictly monitored, and if possible, such must be controlled in order to prevent any unwanted complications. Patients found to be at risk for possible NSTEMI with high Neutrophil to Lymphocyte ratio, Red

blood cell Distribution width should be taken in full consideration as this could lead to potential issues.

For the study population to follow them up 1 to 5 years after their ACS admission as to their current condition.

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