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NON-ST ELEVATION MYOCARDIAL INFARCTION: CORRELATION OF RED BLOOD CELL DISTRIBUTION WIDTH WITH SYNTAX SCORE

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Contribution
MA conceived the idea and designed the study. Data collection and manuscript writing was done by MA, MA, SA, MY, RR, and AE. All the authors contributed equally to the submitted manuscript.

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ABSTRACT

Objective: To determine the correlation between mean RDW values and mean SYNTAX scores in patients of non ST elevation myocardial infarction.

Methodology: This descriptive study was conducted at adult Angiography Department of Faisalabad Institute of Cardiology, Faisalabad from September, 2017 to October, 2018. A total of 130 patients were enrolled in this study. Patients were divided into high (n=89) and low (n=41) SYNTAX groups. The high SYNTAX group was defined as patients with value in the third tertile (SYNTAX score, SX score ≥ 33) while the group with low SNTAX score was defined as patients with values in the lower 2 tertiles (SYNTAX score, SX score < 33). The high RDW group was defined as patients with RDW value > 16 % and the low RDW group as those with RDW value < 16 %.

Results: The mean RDW value was correlated with mean SYNTAX score in both groups. The RDW levels were significantly high in patients with high SNTAX score than those with low SYNTAX score (16.2 ± 1.8 vs. 14.2 ± 1.2, p <0.001). Pearson's coefficient was used to determine the correlation between RDW levels and SYNTAX scores. There was a significant positive correlation between mean RDW value and mean SYNTAX score value (r=0.831, p <0.001).

Conclusion: We found a positive and significant correlation between mean RDW values and mean SYNTAX scores in patients of non-ST elevation myocardial infarction. This reflects the utility of RDW being a non-invasive and readily available laboratory test to determine the severity and complexity of coronary disease in these patients.

Keywords: Red blood cell distribution width, Non-ST elevation myocardial infarction, SYNTAX score

INTRODUCTION

Ischemic heart disease (IHD) is the main cause of demise worldwide.[1] Almost half of such cases occur in Asia.[2] IHD includes stable coronary artery disease, unstable angina and ST segment related myocardial infarction. By definition both ST segment elevation and non ST segment elevation acute coronary syndrome (ACS) is a constellation of symptoms and signs resulting from acute myocardial ischemia from plaque rupture or erosion leading to partial or complete coronary artery occlusion. ACS remains a major health problem in the world being responsible for greater number of deaths due to cardiovascular diseases.[3] Coronary artery disease can be diagnosed using tests like exercise tolerance test, stress thallium scan, stress echocardiography, CT coronary angiography and invasive coronary arteriography (CA). However invasive CA is considered the diagnostic test of choice to diagnose ischemic heart disease by making it possible to directly visualize the anatomy of coronary vessels.[4]

IHD is the sequel of atherosclerosis. Besides traditional risk factors for atherosclerosis there are some novel risk factors such as inflammation being implicated in its pathogenesis[5].Inflammation has a role in the formation and rupture of athermanous plaques as well as thrombosis. Red cell distribution width (RDW) is considered an indicator for inflammation plus a biomarker of worsening atherosclerosis.[5-7] RDW is an integral part of automated complete blood picture that represents variation in volume and size of circulating red blood cells.[8] RDW is obtained by dividing the standard deviation of variation in the size of circulating red blood cells to mean red cell volume that is multiplied by 100 and expressing the result as percentage. The normal RDW value ranges between 11-16%.[9] RDW is a valuable diagnostic and prognostic biomarker in patients of cardiovascular disorders.[10] RDW has also been shown to have a good relation for prognosis in patients of acute coronary syndrome patients.[11]

In patients of IHD, the severity and complexity of the disease can be assessed using different scoring models. The SYNTAX score[12] angiography based scoring system that can assess the severity with complexity of disease in coronary vessels. Every lesion in a coronary vessel with diameter narrowing of equal or greater than 50% in vessels of 1.5 mm must be scored. The number of the diseased vessels is scored from 1 to 3 or more and cumulative number is presented as low (SS < 22), intermediate (SS= 23-32) or high (SS ≥33) SYNTAX score respectively. RDW has been shown to have good relation with different CAD parameters.[7-11] RDW has been correlated with severity of IHD in patients with ST elevation and non ST elevation ACS and in stable IHD patients.[13-16] In a study by Sahin et al.[8] a strong and positive association (r=0.460, p <0.001) was found between RDW and SYNTAX scores in non ST elevation myocardial infarction (NSTEMI) patients.

After robust literature search no data was found in Pakistani population regarding correlation between RDW levels and SYNTAX scores regarding severity and complexity of ischemic heart disease in patients of NSTEMI. The aim of this study was to determine the correlation between mean RDW values and mean SYNTAX scores in patients of NSTEMI.

METHODOLOGY

This descriptive study was conducted in adult Cardiac Catheterization Department, Faisalabad Institute of Cardiology, Faisalabad, from September 2017 to October 2018. A sample size of 130 patients was required to achieve the objective calculated with the help of WHO sample size calculator using r=0.460[8] with 95% confidence interval, with type –I error of 5 % and type- II error of 10% respectively. Consecutive patients of either gender between 25-75 years of age with the diagnosis of non-STEMI undergoing invasive coronary angiography were included in the study. Patients with history of past MI, coronary angioplasty with stenting, and coronary artery bypass graft surgery, patients with anemia (Hb <13gm% in males and <12 gm% in females), history of blood transfusion within last 3 months, chronic kidney disease (serum creatinine level >1.5mg/dl), history of Thalassemia and other hematological disorders, active infection (TLC > 11,000 /cu.mm), severe chronic liver disease (INR >1.5) and those having thyroid disorders were excluded from the study. Study protocol was approved by the institute ethical board and written consent was taken from all patients. A comprehensive clinical history along with detailed history for major risk factors for IHD was taken from all patients followed by detailed clinical examination. A 10ml venous blood sample was taken from

antecubital vein for baseline chemistry (urea, creatinine, serum electrolytes, random blood sugar, cardiac troponin, lipid profile) and complete blood count with estimation of red cell distribution width (RDW) using (Roche Diagnostic Modular Systems, Tokyo, Japan) and (Sysmex K-1000) auto analyzers respectively. RDW was obtained as percentage in all the study patients. All patients underwent for coronary angiography using Siemens' machine (Siemens Axiom Artis, Germany) by senior interventional cardiologist and all angiogram were evaluated for syntax score using online software by two study blinded interventional cardiologists. Coronary artery lesion with a diameter narrowing of ≥ 50% in an artery ≥ 1.5 mm size was scored separately and added to provide cumulative SYNTAX score. On the basis of SYNTAX score the patients were sub-classified into low SYNTAX score (SS <22), intermediate SYNTAX score (SS 22-32) and high SYNTAX score (SS ≥33) groups. All information was collected in a prescribed Performa. Non ST Segment Elevated Myocardial Infarction was labeled as when patients presented with typical chest pain of > 20 minutes duration associated with horizontal or down sloping ST depression > 1mm or deep inverted T waves (> 2mm) and with rise in cardiac tropnin T > 0.01 ng/ml. Red Blood Cell Distribution Width was labeled on the basis of ratio of red blood cells volume standard deviation of variation to mean corpuscular volume and multiplied by 100 expressing as a percent (Normal value = 11% - 16%).

For SYNTAX Score every lesion in a coronary vessel with diameter narrowing of equal or greater than 50% in vessels of 1.5 mm was scored using online software (http://www.SYNTAXscore.com).

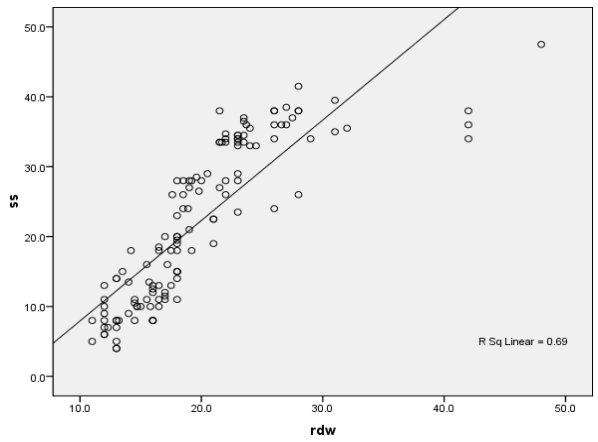
All data was analyzed using SPSS version 16 software. Quantitative data was expressed as mean and standard deviations while quantitative data was expressed in frequencies and percentages. Mean RDW and mean SYNTAX score correlation was determined using Pearson correlation coefficient. A p value of ≤ 0.05 was set as significant. Receiver operator characteristic curve (ROC) was utilized to find the RDW cut off for separating the low SS patients from intermediate and high SS scores patients respectively.

RESULTS

Present study was composed of 130 subjects, out of which 108 (83.1%) were male and 22 (16.9%) female patients. Over all patients mean age was 53.25±11.19) years. There was no statistical significant difference in In low versus intermediate and high syntax group patients (p 0.092), likewise for smoking difference in low, intermediate and high syntax scores was also not statistically significant (p, 0.733). Regarding hypertension (p, 0.004), diabetes mellitus (p, 0.000) and dyslipidemia (p, 0.005) we noted statistical important difference among low, intermediate and high syntax groups. Coronary stenting was the main treatment strategy opted in the low syntax group and bypass coronary graft surgery was the main treatment strategy in intermediate and high syntax groups (p value < 0.0001). Over all a greater proportion of patients had multi vessel disease in the high and intermediate syntax groups (Table 1).

The RDW values were significantly higher in intermediate and high Syntax groups versus low Syntax group (20.5 ± 2.6, 26.84± 6.3 vs. 15.2 ± 1.1, p < 0.0001 (Table 2). Similarly random blood sugar (p, 0.018), serum creatinine (p, 0.0001) were found higher in intermediate and high syntax groups than low Syntax group. RDW levels revealed positive strong correlation with Syntax scores (r=0.831, p < 0.0001) as shown in Figure 1.

Figure 1: Pearson's correlation between SYNTAX score and RDW (r=0.831, p= <0.000)



Using multivariate linear regression analysis, the RDW (F = 21.318, p value < 0.0001) and blood sugar (F=1.792, p 0.010) remained independent predictors of Syntax scores (Table 3). The ROC curve demonstrated a cut off value for RDW > 17.25 to differentiate intermediate and high Syntax groups from low Syntax group with a sensitivity of 78% and a specificity of 62% and with AUC of 0.76% respectively.

Table 1: Baseline demographic and clinical characteristics according to SYNTAX severity score

Characteristics	Overall	Low	Intermediate	High	p-value
N	130	65	25	40	-
Age	53.25±11.193	51.4±10.93	53.16±11.09	56.3±11.29	0.092
Gender					
Male	108 (83.1%)	56 (86.2%)	20 (80%)	32 (80%)	0.646
Female	22 (16.9%)	9 (13.8%)	5 (20%)	8 (20%)	
Syntax Score	22.08±11.21	13.54±6.1	25.77±3.48	35.54±3.37	0.0001
CAD Risk Factors					
Diabetes	43 (33.1%)	11 (16.9%)	10 (40%)	22 (55%)	0.0001
Hypertension	89 (68.5%)	36 (55.4%)	22 (88%)	31 (77.5%)	0.004
Smoking	86 (66.2%)	43 (66.2%)	18 (72%)	25 (62.5%)	0.733
Dyslipidemia	32 (24.6%)	5 (15.6%)	11 (34.3%)	16 (50%)	0.005
Treatment					
Medical	21 (16.2%)	19 (29.2%)	2 (8%)	0	0.0001
PCI	56 (43.1%)	42 (64.6%)	14 (56%)	0	
CABG surgery	53 (40.8%)	4 (6.2%)	9 (36%)	40 (100%)	

CAD=coronary artery disease, PCI=percutaneous coronary intervention, CABG=coronary artery bypass graft

Table 2: Laboratory parameters of patients according to syntax severity score

Characteristics	Overall	Low	Intermediate	High	p-value
N	130	65	25	40	-
Hemoglobin	13.93±1.7	14.18±1.7	14.23±1.22	13.33±1.84	0.026
WBC	10896.13±2840	10895.92±2850	11277.28±2733	10658.25±2932	0.697
Platelet	272194±81226	256250±76104	281000 ± 90900	292600±79579	0.069
RDW	22.08±11.21	15.27±10.93	20.5±2.64	26.84±6.32	0.0001
Trop-I	1.21±1.36	1.14±1.66	1.16±1.1	1.37±0.9	0.684
CK	74.8±59.8	70.57±5.56	88±61.45	73.41±65.4	0.46
RBS	170.15±62.63	158.57±59.32	163.48±53.44	193.15±68.18	0.018
CRT	1.033±1.08	0.98±0.18	1.03±0.15	1.13±0.17	0.0001

WBC=white blood cells, Trop-I= Troponin-I, RBS=random blood sugar CRT=serum creatinine CK=creatinine kinase, LDL- C= low density lipoprotein cholesterol

Table 3: Effects of various variables on syntax scores

Variable	Low	Intermediate	High	Test Value	p-value
N	65	25	40	-	-
Age	51.4±10.93	53.16±11.09	56.3±11.29	F= 1.209	0.228
RBS	158.57±59.32	163.48±53.44	193.15±68.18	F=1.793	0.010
CRT	0.98±0.18	1.03±0.15	1.13±0.17	F=1.430	0.078
RDW	15.27±10.93	20.5±2.64	26.84±6.32	F=21.318	0.000
Trop-I	1.14±1.66	1.16±1.1	1.37±0.9	F=0.782	0.820

DISCUSSION

Coronary artery disease (CAD) and other vascular disorders are mainly the result of atherosclerosis. The important risk factors causing atherosclerotic coronary artery disease are smoking, hypertension, diabetes mellitus and hyperlipidemia. Today modern research has shown some novel risk factors such as inflammation being implicated in pathogenesis of atherosclerosis.[17] Inflammation has been linked to different cardiovascular and cerebrovascular disorders.[17-18] Inflammation has been linked to the process of initiation and continuation of athermanous plaque including its rupture and related thrombosis.[5] Bone marrow responds to inflammation by releasing premature cells like neutrophils and red blood cells. There is also small rise in inflammatory biomarkers like hs-CRP, neutrophils and red blood cells.[18] These biomarkers can help in risk stratification of patients with cardiac failure and acute coronary syndrome patients. Due to this reason these biomarkers are being studied for their diagnostic and prognostic role in above conditions.

Studies have shown the role of various hematological indices in prognosis of acute coronary syndromes but red cell distribution width (RDW) appears to be more promising in some studies.[10-11] This is an inexpensive, readily available laboratory test as a part of routine complete blood count by modern hematology auto analyzers with no additional cost. RDW represent variation in the size of circulating RBCs and its value rises in response to variation in red cell size and volume. RDW is an inflammatory biomarkers and increases in atherosclerotic CAD as a result of the release of immature RBCs in peripheral circulation related to interference with maturation of RBCs in the bone marrow. This fact is supported by Lippie et al.[19] study showing a strong association between inflammation and RDW represented by concomitant rise in hs-CRP. This view is further supported by elevated inflammatory cytokines seen in patients with acute myocardial infarction.[20]

There is close association between elevated RDW and coronary lesions severity. We found a strong and positive correlation ($r=0.831$, $p < 0.001$) between mean RDW and coronary artery disease severity in terms of SYNTAX scores in patients of non-ST elevation MI (NSTEMI) who underwent coronary angiography during hospitalization in our study. This finding coincide with the findings of the study by Sahin O et al.[8] who also reported positive and significant association ($r=0.463$, p value <0.001) of RDW with SYNTAX score in terms of CAD severity in NSTEMI patients. In another study of NSTEMI involving 251 patients by Bekler et al.[21] also reported positive correlation ($r=0.190$; $P=0.002$) between RDW and CAD severity that also supports the result of our study. Similarly in a study by Siregar A et al.[15] involving 97 patients of ACS undergoing coronary angiography showed good relation of RDW with coronary artery lesions severity.

RDW has also been shown to have good relation with CAD severity in patients of ST elevation Myocardial infarction and stable CAD. Akin F et al.[1] demonstrated positive correlation ($r = .252$, $P < .001$) between high RDW and coronary artery lesion presence, severity and complexity in terms of SYNTAX score. Study by Siregar et al also demonstrated similar relationship between RDW and coronary artery lesions severity in their study of ACS patients. Isik T et al.[16] demonstrated a significant correlation between RDW and the SYNTAX score ($r=0.55$, $P<0.001$) in patients with stable CAD undergoing elective angiography. Similar findings were reported by Nagula P et al.[14] In the light of all above studies it is concluded that RDW being a readily available, inexpensive test can be of value to predict the presence of CAD along with its severity that can help in risk categorization and management of CAD patients.

Here are some limitations in this study. First, this was one center study with a small sample size, so its findings cannot be generalized and applicable to entire population thus necessitating further large scale multicentre studies. Secondly, only hemoglobin was measured and other factors that can affect RDW value like iron, vitamin B 12 and folic acid levels were not measured in our study population. Thirdly, RDW levels were measured only once at admission and did not further measured during index hospitalization.

CONCLUSION

We found a strong and positive correlation between mean RDW and mean SYNTAX score in patients of non-ST elevation myocardial infarction. RDW is associated with both presence and severity of coronary artery disease suggesting the application of this cheap and readily available marker to anticipate the severity of coronary artery disease.

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