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Correlation of Red Blood Cell Distribution Width with Coronary Artery Disease

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Abstract

Coronary Artery Disease (CAD) has been amongst the major factors for mortality through-out the world. The red blood cell distribution width (RDW), which is an easily measured indicator of the variation in the size of red blood cell (RBC) (i.e., anisocytosis) could be a new biomarker that reflects a variety of physiological impairments associated with atherosclerosis and CAD and hence the two are correlated in this study. A Cross-sectional Study comprising of 80 people with acute coronary syndrome (ACS), typical and atypical angina, and inducible chest pain by treadmill test were taken. The patients underwent coronary angiography, later were separated into 2 groups depending on the outcomes (CAD group (n=60) and Non-CAD group (n=20)). Clinical data, along with traditional CAD risk variables and RDW, were analysed to determine their relation with CAD. The CAD severity was assessed using the Modified Gensini score. The gender distribution shows male preponderance with 73.75%. Patients with CAD on angiography had significantly higher RDW levels than Non-CAD group (15.52±0.56) vs. (14.66±0.88), with P value <0.001.RDW and Gensini score had a significant positive correlation (r=0.49, P value <0.001). RDW was discovered to be an independent indicator of angiographic CAD in multivariate logistic regression analysis (OR=1.49, 95% CI: 1.41-1.97, P<0.05). When a patient has CAD or an acute coronary syndrome, RDW is a significant risk-factor for cardiovascular incidents. Anisocytosis may be the reason for the reported bad outcomes in this group, or it may only be a marker of several clinical conditions associated with the observed prognosis.

Keywords: Acute coronary syndrome, Coronary artery disease, Modified gensini score, Red blood cell distribution width.

Introduction

Coronary artery disease, also referred to as ischemic heart disease has an insufficient delivery of oxygen as well as blood to the heart (myocardium) which is due to the result of coronary artery obstruction and mismatch of oxygen demand-supply due to creation of plaques in the coronary artery lumen, which obstructs the flow of blood (1).The most prevalent risk factors for the condition include cigarette smoking, hypertension, diabetes, hyperlipidemia, male-sex, lack of physical activity, familial obesity, and unhealthy dietary choices such as low intake of nuts, fish, legumes, fiber, whole grains, vegetables and fruits; excessive or high intake of unhealthy fats, added sugars, processed foods and sodium. It is also dependent on lifestyle and habits like smoking, alcohol consumption, stress, obesity and overweight due to lack of exercise (2, 3). The leading cause of death in India, cardiovascular disease (CVD), is responsible for over 21% of fatalities. Indians have an estimated age-standardized mortality rate of 272 for 100,000 people due to CVD, which is more than the global average of 235 for 100,000 people as per the Global Burden of Disease research (4). The major reason for death in the world is coronary artery disease, brought on by atherosclerosis which usually starts by the formation of fatty streaks along the arterial walls, mostly in adolescence and typically manifests as Acute Coronary Syndrome

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(ACS) or sudden cardiac-death (SCD) due to obstruction of coronaries (5). These risk factors impact the vascular endothelium's usual actions, involving locally controlling the vascular tone, maintaining an anti-thrombotic surface, regulation of adhesion of inflammatory cells and diapedesis. When these defences are lost, aberrant blood cell interactions, luminal thrombus development, and improper constriction occur. As a result, the sub-intimal assembly of fibroblasts, fat, smooth muscle cells and inter-cellular matrix that characterises the atherosclerotic plaque wills eventually form (6). A determination of disease severity can be done by assessing the extent of coronary disease and the left ventricular function. Many diagnostic and prognostic markers were developed in the last decade which enhances the quality of management and improvement in outcome. The RDW plays an important role to assess the cardiovascular disease. It was noted that RDW can be used as an indicator of prognosis in people suffering from heart failure (7). RDW can be used to predict mortality in the overall population as well as in people with a variety of diseases including peripheral vascular disease, obstructive lung diseases as well as renal failure (8, 9). A growing body of research documenting the relation between RDW and outcomes in patients with stable CAD, including those receiving percutaneous coronary intervention (PCI) and those experiencing myocardial-infarction, is available in the literature (MI) (10,11). Our study is planned to evaluate possible correlation between RDW and severity of Coronary Artery Disease among the patients of Eastern India.

Materials and method

A Cross-sectional Study comprised of 80 patients who were admitted to and attended the outpatient clinics at tertiary care hospital, Bhubaneswar in between the time period of January 2021 to July 2022, with acute coronary syndrome (ACS), typical and atypical angina, and inducible chest pain by treadmill test. Before the study began, the Institutional Ethical Committee approval was taken (Ref.no/IEC/IMS.SH/SOA/2021/257). Each participant provided informed written consent.

Inclusion criteria

People older than 18 years, with provisional diagnosis of Acute coronary syndrome, Typical Angina, Atypical Angina, Chest pain with positive treadmill test were taken.

Exclusion criteria

- Anemia where hemoglobin level, less than 12gm/dl in men whereas less than 11gm/dl in women was taken.
- Patients on Blood transfusions.
- Patients with a H/O, coronary artery bypass surgery, percutaneous coronary intervention etc
- Bleeding disorders
- Pregnancy

Detailed H/O risk factors like HTN, Type2 DM, alcohol consumption, smoking, family history of CAD, Obesity were extracted. ECG, 2D-Echo, Treadmill test (when required in patients without ACS) were done. Blood samples were taken to measure RDW CV & SD, fasting lipid profile, Renal Function Test (RFT) and Troponin-I. Coronary angiography was done and the magnitude of the lesion on it is analysed by modified Gensini score (MGS). Patients were then split into 2 categories depending on the outcomes of coronary angiography: Group A (those with CAD) and Group B (those without CAD).

The diameter of the stenosis in a vessel exceeding or equalling 50% was used to define angiographic CAD. Based on the combined total value of 8 proximal-segments of the coronary arterial-tree, MGS determines the severity of the lesion.

According to MGS, the max score can be 32 and minimum being 0 and the severity can be classified as:

1) 1-6: Mild
2) 7-13: Moderate
3) >13: Severe

The RDW-SD& RDW-CV values are then compared with MGS.

Modified Gensini score

Each of the eight coronary segment's most severe stenosis was rated on a scale of 1- 4,

- Stenosis of 1% - 49% - 1
- Stenosis of 50% -74% - 2
- Stenosis of 75% - 99% - 3
- 100% occlusion - 4

We then produce a final score that can range from 0 to 32. Based upon its location and the fraction of involvement of every coronary artery a

multiplication factor is used: for left mainartery -5; left anterior descending artery (LAD): proximal segment -2.5, distal segment-1.5, LAD apical artery-1, Diagonal arteries: primary -1, secondary -0.5, left circumflex artery-proximal segment-2.5, left circumflex mid, distal segments and obtuse marginal artery -1 for each, proximal,mid,distal-1 (RCA) (12).

Statistical Methods

SPSS version 26.0 was utilised for analysis of the statistics (SPSS Inc, Chicago, IL, USA). The analysis of variance (ANOVA) method is used to determine the significance of variables among different groups. The Pearson correlation co-efficient was utilised to investigate the relationship. *p*-values lesser than 0.05 were taken as statistically significant.

Results

80 patients were enrolled in this study. The descriptive analysis was done for both continuous and categorical variables. The gender distribution shows male preponderance with 73.75%. Out of 80 patients 59 were male and 21 were female patients. There were around 67.50% obese patients enrolled in this study. Only 32.50% patients were free from obesity like co-morbidity. Around 46.3% that means 37 patients out of 80 patients had positive family history of CAD. The prevalence of CAD was found as 75% and only 25% had without CAD patients. The prevalence of Diabetes in our study was found to be 73.80% and Prevalence of Hypertension was found to be 62.50%. About the addiction history, it is observed that 56.3% patients had habit of Smoking and 60.0% individuals were consuming alcohol (Table 1).

Table 1: Patient details and distribution of comorbidities and habits present among patients

Factors	Frequency (n)	Percentage (%)
Gender		
Male	59	73.8%
Female	21	26.2%
Obesity		
Present	54	67.5%
Absent	26	32.5%
Family History of CAD		
Present	37	46.2%
Absent	43	53.8%
Prevalence of CAD		
CAD group	60	75%
Non-CAD group	20	25%
Diabetes		
Present	59	73.7%
Absent	21	26.3%
Hypertension		
Present	50	62.5%
Absent	30	37.5%
Smoking habit		
Present	45	56.2%
Absent	35	43.8%
Alcohol intake		
Present	48	60.0%
Absent	32	40.0%

The mean Age was 52.92±5.89 years ranging from minimum 42 years to maximum 63 years. The mean height was 147.99±3.98 cms and mean weight was found to be 59.95±11.94. Again, the mean BMI was found as 27.29±5.01 in our study. The descriptive analysis for haematological and biochemical parameters were depicted through mean and standard deviation (μ±SD). The mean

Haemoglobin was 12.83±0.68 g/dl, the mean RDW-CV was 15.31± 0.75 and the mean RDW-SD was 44.71±3.50. The other parameter like Triglyceride, low density lipoprotein, High density lipoprotein, VLDL, Total cholesterol, serum urea, serum creatinine, Haematocrit, MCH and MCV were mentioned (Table 2).

Assessment of Modified Gensini Score was done among coronary artery disease patients. Around 48.3% (29 0ut of 60) were having score between 7 to 13 which belongs to MGS-2, 41.7% (25 out of 60) having score of more than 13 which indicates they belongs to MGS-3 and only 10% patients had MGS-1 that means they had score in between 1 to 6 (Table 3).

Table 2: Descriptive analysis of general examination and of haematological and biochemical parameters of patients

Factors	Mean (μ)	Standard Deviation (SD)
Age (in years)	52.92	5.89
Height (in cm)	147.9941	3.98993
Weight (in kg)	59.95	11.943
BMI	27.2944	5.01351
Haemoglobin (g/dl)	12.835	0.6833
TG	182.27	10.098
LDL	109.40	11.607
VLDL	46.27	9.299
HDL	39.20	4.900
Total Cholesterol	194.8750	14.15947
Serum Urea	23.60	8.413
Serum Creatinine	0.961	0.1768
RDW-CV	15.3106	0.75279
RDW-SD	44.7114	3.50716
Haematocrit	40.9422	2.66255
MCH(pg/cl)	29.4565	1.19608
MCV(fl)	86.00	7.944
MCHC(g/dl)	33.775	2.0234

Table 3: Distribution of modified Gensini score among CAD patients

Factors	Frequency (n)	Percentage (%)
MGS- score 1 (01-06)	6	10%
MGS-score 2 (07-13)	29	48.3%
MGS-score 3 (>13)	25	41.7%

There was significant association found between Obesity, Familial history of CAD, Hypertension, Diabetes mellitus, Intake of alcohol and Smoking habit among coronary artery disease (p value <0.001) (Table 4).

Applying Independent t-test for comparing mean value of biochemical parameters among Group A (CAD) and Group B (Non-CAD) we observed there was significant disparity found in between mean value of Haemoglobin, RDW-CV and RDW-SD among both the group (p <0.001) (Table 5).

In Table 6 it shows the red cell distribution is positively correlated with severity of CAD (p <0.001) (Table 6).

Discussion

Atherosclerosis, which is a chronic inflammatory condition manifests as ACS or SCD as a result of coronary blockage. The atherosclerotic lesion induces oxidative stress and emits inflammatory factors due to endothelial dysfunction and macrophage accumulation. RDW, a component of red cell indices, is a measure of the variation of size in RBC volume (anisocytosis), which is employed in the differential diagnosis of anemia. The significance of RDW as an indicator of bad prognosis clinically in the context of many disorders, which includes Coronary Artery Disease, has been demonstrated in a number of researches in recent years.

The study participants were split in 2 groups based on the diagnosis of coronary artery disease. There were 60 out of 80 patients suffering from CAD. Similarly other study conducted by Nagula P *et al..* observed the relation of red cell distribution on severity of coronary artery disease by taking 438 CAD patients and 138 Non-CAD patients.

Table 4: Patient distribution of CAD and without CAD patients

Factors	CAD Group	Without CAD Group	P-Value
Male	44 (73.3%)	15 (75%)	0.56
Female	16 (26.6%)	5 (25%)	
Obesity			
Present	52	2	0.000
Absent	8	18	
Family history of CAD			
Present	36	1	0.000
Absent	24	19	
Hypertension			
Present	49	1	0.000
Absent	11	19	
Diabetes Mellitus			
Present	49	10	0.008
Absent	11	10	
Alcohol intake			
Present	45	3	0.000
Absent	15	17	
Smoking Habit			
Present	44	1	0.000
Absent	16	19	

Table 5: Baseline characteristics of the patients with CAD and without CAD group

Variables	CAD (n=60)	Without CAD (n=20)	P-value
Age in years (μ±SD)	52.82± 6.083	53.25±5.42	0.77
Haemoglobin (g/dl)	13.105± .5552	12.025± .2511	0.000
RDW_CV	15.5253± .56483	14.6665± .88502	0.000

RDW_SD	46.2223±2.46198	40.1785± 1.86624	0.000
Haematocrit	40.8837±2.82532	41.1180±2.15529	0.736
MCH (pg/dl)	29.5293±1.34749	29.2380±.49287	0.349
MCV (fl)	85.68±7.588	86.95±9.076	0.540
MCHC (g/dl)	33.760±2.0058	33.820±2.1277	0.909

Table 6: Positive correlation between Red cell width distribution and prediction of Coronary artery disease

Correlations			
		RDW CV	**CAD and Non-CAD Group**
RDW_CV	Pearson Correlation	1	-.497**
	Sig. (2-tailed)		.000
	N	80	80
CAD and Non-CAD Group	Pearson Correlation	-.497**	1
	Sig. (2-tailed)	.000	
	N	80	80
**Correlation is significant at the 0.01 level (2-tailed).			

Likewise, He *et al.,* in 2014 conducted similar study on 128 CAD patients with 24 Non-CAD patients (13). The mean age of present study was 52.82± 6.083 years in CAD group and 53.25 + 5.42 years in Non-CAD group. There is no major disparity seen in age of both groups (p >0.05). But the study conducted by Nagula P *et al.,* shows significant difference in mean age of two groups (13). It was depicted in the results that 53.64 ±10.36 years was the age (mean) of Group A and 49.4± 9.73 years was of Group B with a significant p value of < 0.0001. Predominance of male population was seen in both groups. CAD patients showed a greater age (mean) (61+/-10 vs 54+/-10 years, p=0.016) and male predominance (83.3% vs 23.8%, p<0.001) was found in similar study conducted by Cay S *et al.,* Male preponderance was seen in the study done by Nagula *et. al.,* the various risk factors like presence of obesity, hypertension, diabetes mellitus, history of smoking habit and excessive alcohol consumption were more in CAD group and significantly higher proportion in CAD group as compared to Non-CAD group with p value <0.001. Similar result shown in another study by Nagula *et al.,* 2017 and He *et al.,* 2014 conducted in different geographical area (13, 14).

In angiography, the RDW was correlated positively with greater lesion severity as determined by MGS scores. Comparable Outcomes were reported in Nagula P *et al.,* study (13). They demonstrated how in the ACS group of people, all-cause mortality could be predicted independently by RDW. In their study, it was discovered that the co-relation between RDW-CV and haemoglobin in the entire group was only weakly-negative with r value of 0.1096. Although Hematocrit or packed cell volume readings are within normal ranges and emphasise the RBC size, the CAD group's value is lower than the non-CAD group's. The decrease in value can theoretically be attributed to the elevated levels of anisocytosis as well as micro-cytosis in the CAD group, albeit a peripheral blood-smear has not been performed to corroborate this. The evaluation of the red blood cell indices in the two groups revealed increase in MCHC, decrease in MCV as well as

MCH in Group-A but no such trend seen in Group-B.

In patients presenting with chest discomfort, Lippi *et al.,* 2009, had shown that, RDW with a cut-off value of 14% has a good chance to predict and identify ACS (15, 16). According to Felker*et al.,* study, higher RDW in a patient with CAD increases their likelihood of developing heart failure (17). In a group of 251 people who were admitted to a cardiac unit over the course of a year, Tenekecioglu *et al.,* in 2015, discovered that RDW was helpful in classifying individuals with NSTEACS as NSTEMI (18). Baseline RDW had an increased positive predictive value of atherosclerotic burden and had a strong correlation with MGS.

According to multivariate analysis conducted in research by Cavusoglu *et al.,* the RDW is a potent tool to predict all causes mortality in the ACS subset of patients independently (19). Poludasu *et al.,* in 2008 conducted a retrospective study on 859 patients who underwent Percutaneous intervention (PCI) found result of higher RDW level increases the risk of death in patients undergoing PCI (19-21). Another prospective study by Dabbah *et al.,* in 2010 gave result of increased RDW lead to increase mortality among patients with MI (22). Similarly, Azab *et al.,* carried out a study among 619 patients having Non-ST Elevation MI found that RDW could predict the mortality in long run (23).

This meta-analysis identifies a risk-factor for further mortality and cardiovascular disease (CVD) events in established CAD populations based on the prospective studies that are currently available and the lack of randomized controlled trials (12). Therefore, it is necessary to conduct randomized controlled studies in these patients to ascertain if RDW-modifying treatments could reduce the risk of CVD events. It should be highlighted that the inability to measure RDW using a gold standard limits clinical judgement and treatment options for patients with high RDW concentrations. However, persons in CAD populations with a high RDW concentration should be given additional attention.

When a patient has CAD or an acute coronary syndrome, RDW is a substantial risk-factor for cardiovascular events as well as death. Anisocytosis may be the reason for the reported bad prognosis in this group, or it may only be a marker of several clinical conditions associated with the observed prognosis. RDW offers important information on prognosis in CAD patients, unlike indicators of inflammation as well as oxidative stress, as they are not frequently analysed. In individuals with established CAD, greater RDW concentrations are linked to a higher risk of CVD events and subsequent death. Taking into Consideration, the direction, quality and magnitude of the connections of the included studies, the results show evidence for positive associations, although there might be a possibility of some publication bias. Future research should concentrate on RDW-modifying treatments to shed more insight into the possible underlying mechanisms causing CVD events.

Abbreviations

Nil

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Author contributions

All authors have equally contributed to this study.

Conflict of interest

Nil

Ethical approval

The Institutional Ethical Committee approval was taken with the letter number: (Ref.no/IEC/IMS.SH/SOA/2021/257).

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