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**Original Article** 

# "Correlation of red blood cell distribution width with the severity of coronary artery disease—A single center study"



IHJ

Praveen Nagula<sup>\*</sup>, Suneetha Karumuri, Adikesava Naidu Otikunta, Subba Reddy Venkata Yerrabandi

Department of Cardiology, Osmania General Hospital, Afzalgunj, Hyderabad, Telangana 500012, India

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#### ABSTRACT

*Objective:* Coronary Artery Disease (CAD) is the leading cause of morbidity and mortality all around the world. We evaluated the correlation of Red blood cell Distribution Width (RDW) with the severity of lesion on coronary angiography as assessed by Modified Gensini score (MGS) in CAD patients. *Methods:* A total of 576 consecutive patients admitted in Department of Cardiology over a period of one year, who underwent coronary angiography after diagnosis of CAD or presence of angina like chest pain and/or positive treadmill test were enrolled in the study (August 2014–May 2015). Patients were divided into two groups, with CAD (Group A) and without CAD (Group B). The RDW Cofficience of variance (RDW CV) and RDW standard deviation (RDW SD) of each patient, and their correlation with severity of CAD

was assessed. *Results:* Of the total 576 patients enrolled, 438 were in Group A and 138 were in Group B. The mean age of presentation in Group A and Group B was  $(53.64 \pm 10.36 \text{ vs} 49.4 \pm 9.73)$  years (p < 0.0001). The Male and Female ratio overall was 2.42:1. Patients in Group A had significantly elevated RDW CV and RDW SD levels compared with those in Group B [ $(14.59 \pm 1.04)$ % vs ( $13.6 \pm 0.68$ )%, p < 0.0001], [ $(45.78 \pm 4.76)$  vs ( $40.77 \pm 3.01$ ), p < 0.0001 respectively]. A significant positive correlation between RDW CV, RDW SD and MGS was noted (r = 0.33, p < 0.0001) (r = 0.43, p < 0.0001) respectively. On multivariate logistic regression analysis, RDW was demonstrated to be an independent predictor for angiographic CAD (OR = 4.17, 95% CI 3.05-5.69, p < 0.0001). On receiver operating characteristic curve (ROC) analysis, an RDW value of 14.3% was identified as an effective cut off point in diagnosing CAD with a sensitivity of 58.9% and specificity of 84.8%.

*Conclusions*: RDW is an independent predictor of CAD and severity of coronary stenosis, suggesting that it can be a readily available marker for prediction and severity of CAD.

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#### 1. Introduction

Coronary Artery Disease, due to atherosclerosis is the most common cause of death worldwide. Atherosclerosis is a chronic inflammatory disorder with long asymptomatic period for years and usually manifests as acute coronary events with occlusion of coronaries. RDW, a measure of heterogeneity of red blood cell size, is usually used in the differential diagnosis of anemia.<sup>1</sup> In the recent years, there is increased interest in the role of increased RDW as a risk marker of various cardiovascular diseases for example heart failure<sup>2</sup> and coronary artery disease.<sup>3</sup> We have

\* Corresponding author.

assessed the RDW in patients presenting with chest pain and correlated its relation with severity of lesion as assessed by Modified Gensini score (MGS) on angiography.

### 2. Methods

#### 2.1. Study population

The study was carried out in Department of Cardiology, Osmania General Hospital, Hyderabad between August 2014– March 2015. After analyzing 1835 patients presenting with chest pain, a total of 576 consecutive patients have been enrolled in the study.

#### 2.2. Inclusion criteria

Patients with Age >18 years, with diagnosis of

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*E-mail addresses:* drnagulapraveen@yahoo.com, drpraveennagula@gmail.com (P. Nagula), suneethaleo@gmail.com (S. Karumuri), oadikesavanaidu@gmail.com (A.N. Otikunta), dryvsreddy@yahoo.co.in (S.R.V. Yerrabandi).

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#### 1 Acute Coronary Syndrome (ACS) [ST segment Elevation Myocardial Infarction (STEMI), Non ST elevation Acute Coronary Syndrome (NSTEACS)]

ACS was defined as presentation with symptoms of ischemia in association with ECG changes (ST segment deviation elevation or depression, T wave inversion, and new Qwave), positive cardiac enzymes and regional wall motion abnormalities on echocardiography (absent in patients with unstable angina, with intracoronary lesion on angiography in most of the cases).

- 2 Typical Angina, described as substernal chest discomfort lasting for less than 20 min precipitated by stress and relived by rest or nitroglycerin
- 3 Atypical angina with conventional risk factors (i.e. diabetes mellitus, hypertension, obesity, family history of CAD, chronic smoking, chronic alcohol intake) or
- 4 Chest pain with treadmill test positive for inducible ischemia (i.e. new ST depression at the start of exercise, new ST depression >2 mm in multiple leads, hypotensive response to exercise, development of heart failure or sustained ventricular arrhythmias during the study, prolonged interval after exercise (>5 min) before the ischemic changes return to baseline) were included in the study.

#### 2.3. Exclusion criteria

Patients with anemia i.e with Hemoglobin level of < 12gm/dl in males and < 11gm/dl in females were excluded.<sup>4</sup>

The patients with previous history of Percutaneous Coronary Intervention (PCI), Coronary Artery Bypass Grafting (CABG) surgery, Valvular Heart Disease, Bleeding disorders, Chronic Kidney Disease (CKD), on Estrogen Replacement Therapy (ERT), Anemia and Blood transfusions, Liver disease, Pregnancy, Thrombotic Thrombocytopenic Purpura were excluded from the study.

Institutional ethical committee has approved the study.

Each patient has been enrolled after obtaining written and informed consent.

A detailed evaluation of demographic data of each patient, presence of risk factors (hypertension, diabetes mellitus, smoking, alcohol intake, family history of premature CAD, obesity) clinical examination, with electrocardiography (ECG), echocardiography (2d ECHO) and the treadmill test whenever required i.e in patients without ACS has been done. Venous blood sample for RDW has been collected at the time of admission from the antecubital vein by atraumatic puncture and value was assessed by SYSMEX 2.0 analyzer within an hour of collection of sample. Blood was collected in a tube containing EDTA for measurement of red cell indices. The reference value of RDW in our laboratory was 11.5-13.5%. Transthoracic echocardiography was performed with Phillips I3 machine using 3-5 MHz transducer on each patient after admission to the intensive cardiac care unit. Each patient underwent coronary angiography either by transradial or transfemoral route using 5F Optitorque catheter in the former and 6F Judkins catheters in the latter within 24 h after hospital admission. The severity of lesion on angiography has been assessed by MGS.

After coronary angiography patients were divided into two groups, those with CAD (Group A) and those without CAD (Group B). Angiographic CAD was defined as the diameter of the stenosis in a vessel reaching more than or equal to 50%. Severity of lesion is by MGS, based upon the total added value of the eight proximal segments of coronary arterial tree. Maximum score is 32 and minimum is 4. Mild, moderate, severe is for scores of 1–6, 7–13 and >13 respectively (**Appendix A.1**). The RDW CV, RDW SD values were correlated with MGS.

#### 2.4. Statistical analysis

Statistical analysis was carried out using Medcalc (Belgium). Continuous variables are expressed as mean  $\pm$  standard deviation (SD). Categorical variables are expressed as percentages. Students *t*-test or analysis of variance was used to compare parametric continuous variables. To compare categorical variables, the chi-square ( $\chi$ 2) test was used. Correlation of two variables were examined by Pearson r correlation coefficient. Receiver operating characteristic (ROC) curves for RDW values were plotted to determine the optimal cut off point for use in clinical decision making. Multivariate logistic regression analysis was used to identify the independent predictors of angiographic CAD. A p value <0.05 was considered significant statistically. Tables, bar diagrams, pie diagrams were illustrated wherever possible.

#### 3. Results

Total number of patients included in the study were 576. In CAD group (hereby Group A) there were 438 patients and in without CAD group (hereby Group B) were 138. The mean age of presentation in the whole cohort was  $52.6 \pm 10.38$  years. The range of age of patients was 22 years to 84 years. On group analysis, the mean age of presentation in Group A was  $53.64 \pm 10.36$  years whereas in Group B was  $49.4 \pm 9.73$  years (p < 0.0001). Males were predominant than the females (70.8% vs 29.2%) with a sex ratio of 2.42:1. The difference in mean hemoglobin levels between the two groups was statistically insignificant  $(13.66 \pm 0.71 \text{ vs } 13.63 \pm 0.54,$ p=0.65). In Group A, the most common risk factor was hypertension seen in 287 (65.5%), followed by smoking in 243 (55.5%) and diabetes in 189 (43.2%) patients. Patients in Group A had significantly elevated RDW CV levels compared to Group B  $[(14.59 \pm 1.04)\%$  vs  $(13.6 \pm 0.68)\%$ , p < 0.0001]. The RDW SD levels were also significantly elevated [ $(45.78 \pm 4.76)$  vs  $(40.77 \pm 3.01)$ , p < 0.0001]. The red cell indices when analysed showed no significant difference in the mean hematocrit (Hct) and mean corpuscular hemoglobin (MCH) values between the two groups but significant difference with regards to mean values of the mean corpuscular volume (MCV), and mean corpuscular hemoglobin concentration (MCHC). The baseline characteristics of patients in both groups are shown in Table 1.

The most common diagnosis in Group A was Anterior wall STEMI in 180 (42%), the next common diagnosis was NSTEACS seen in 112 (26%) patients (Table 2). The patients in CAD group were stratified according to the MGS and the baseline characteristics along with the RDW CV and RDW SD have been analysed (Table 3). The RDW CV value increased along the score values of 1–6, 7–13 and >13 (14.53  $\pm$  0.88, 14.55  $\pm$  1.07, 14.68  $\pm$  1.10) respectively (p < 0.0001). A significant positive correlation between RDW CV for the presence or absence of angiographic CAD (n = 576, r = 0.40, p < 0.0001) and with severity of CAD (n = 438, r = 0.33, p < 0.0001) was seen on Pearson correlation analysis. The correlation of hemoglobin levels in the whole cohort with RDW CV was – 0.109, a weak negative correlation noted.

On subgroup analysis in CAD group (Group A) according to the diagnosis in comparison with group B (n = 138, 13.60  $\pm$  0.68), the RDW CV was increased in all subgroups i.e AWSTEMI (n = 180,14.79  $\pm$  4.86,p = 0.0041), NSTEACS (n = 112,14.65  $\pm$  1.02, p = 0.0001), IW STEMI (n = 72, 14.84  $\pm$  5.46,p = 0.0091), Stable angina (n = 65, 14.25  $\pm$  2.46,p = 0.0089).

In multivariate logistic regression analysis, RDW was demonstrated to be an independent predictor for angiographic CAD (OR = 4.17, 95% Cl 3.05–5.69, P < 0.0001) (Table 4). On ROC analysis, an RDW value of 14.3% was identified as an effective cut off point in diagnosing CAD with a sensitivity of 58.9% and specificity of 84.8%

#### Table 1

Baseline characteristics of the patients with CAD and without CAD (Group A and Group B).

Variables (n,%)	CAD (n=438)	without CAD (n = 138)	P value
Age of presentation (yrs) mean $\pm$ SD	$53.64 \pm 10.36$	49.4± 9.73	<0.0001
Males	332 (75.8)	76 (55.07)	0.7
Hypertension	287 (65.5)	90 (31.5)	< 0.0001
Diabetes mellitus	189 (43.2)	38 (27.5)	< 0.0001
Alcohol intake	189 (43.2)	50 (36.2)	< 0.0001
Smokers	243 (55.5)	59 (13.5)	< 0.0001
Family h/o CAD	61 (13.9)	17 (12.32)	< 0.0001
RDW CV (mean $\pm$ SD,%)	$14.59 \pm 1.04$	$13.71\pm0.84$	< 0.0001
RDW SD (mean $\pm$ SD,fl)	$45.78 \pm 4.76$	$42.77\pm3.01$	< 0.0001
Hemoglobin levels (gm/dl)	$13.66\pm0.71$	$13.63\pm0.54$	0.65
Hematocrit (%)	$\textbf{39.89} \pm \textbf{4.77}$	$40.65 \pm 4.24$	0.09
MCV (fl)	$88.22 \pm 4.21$	$90.27 \pm 5.28$	< 0.0001
MCH (pg/cl)	$\textbf{30.21} \pm \textbf{2.57}$	$\textbf{30.30} \pm \textbf{1.88}$	0.70
MCHC (g/dl)	$34.24 \pm 2.27$	$33.53 \pm 1.16$	0.0004
Male: Female	3.13:1	1.22:1	

Abbreviations: n – number,% – percentage, yrs – years, SD – standard deviation, CAD – coronary artery disease,RDW – red blood cell distribution width,CV – coefficience of variance, fl – femto liters,gm/dl –gram per deciliter, p value – calculated probability, MCV- mean corpuscular volume,MCH – Mean corpuscular hemoglobin, MCHC – mean corpuscular hemoglobin concentration,pg/cl – pictogram per cell.

#### Table 2

Proportion of patients in CAD group (Group A):.

Diagnosis	Males	Females	Total (%)
AWSTEMI	138	42	180 (41)
IWMI/PWMI/RVMI	48	24	72 (16)
NSTEACS	82	30	112 (26)
CSA	57	08	65 (15)
ICMP	7	2	09 (2)
Total	332	106	438 (100)

Abbreviations: AWSTEMI – Anterior wall ST segment elevation myocardial infarction, IWMI – Inferior wall myocardial infarction, PWMI – Posterior wall myocardial infarction, RVMI – Right ventricular myocardial infarction, NSTEACS – Non ST segment elevation acute coronary syndrome, CSA – chronic stable angina, ICMP – ischemic cardiomyopathy.

with area under curve (AUC) being 0.793 (Figs. 1 and 2). The positive predictive value (PPV) of RDW was 85.42%.

#### 4. Discussion

Atherosclerosis is a chronic inflammatory disease, subclinical for most of the years, starting as fatty streaks in the arterial walls in the teenage years and usually presents in most of the scenarios as

 Table 3

 Baseline characteristics of patients stratified according to Modified Gensini Score (MGS) in Group A

(MG3) III GIOUP A.				
Variables n (%)	MGS 01-06	MGS 07–13	MGS >13	p value
No.of pts Age (mean ± SD.yrs)	$\begin{array}{c} 118 \; (26.9) \\ 53.05 \pm 10.06 \end{array}$	$\begin{array}{c} 174 \; (39.7) \\ 53.6 \pm 10.4 \end{array}$	$\begin{array}{c} 146~(33.3)\\ 53.68\pm11.22 \end{array}$	0.32
(mean ± 5D,913) Male RDW (mean ± SD,%)	$\begin{array}{c} 86~(72.9)\\ 14.53\pm0.88 \end{array}$	140 <i>(80.5)</i> 14.55 ± 1 0.07	$\begin{array}{c} 106~(72.6)\\ 14.68\pm1.10 \end{array}$	0.0012 <0.0001
Hemoglobin (gm/dl) Smokers Family h/o Diabetes mellitus Hypertension Alcoholic	$13.4 \pm 0.45 \\ 67 (56.8) \\ 10 (8.5) \\ 47 (39.8) \\ 72 (61.0) \\ 56 (47.5) \\ \end{cases}$	$\begin{array}{c} 13.6 \pm 0.83 \\ 101 \; (58.0) \\ 28 \; (16.0) \\ 73 \; (42.0) \\ 113 \; (64.9) \\ 83 \; (47.70) \end{array}$	$14.2 \pm 0.89 75 (51.4) 23 (15.6) 69 (47.3) 102 (69.9) 50 (34.2)$	0.99 0.0012 0.002 0.0012 0.002 0.002

#### Table 4

Multivariate regression analysis of various parameters for prediction of CAD.

Variables	95% CI	OR	P value
Age	1.01-1.06	1.03	0.0035
Male	1.83-4.04	2.54	< 0.0001
Smoking h/o	0.45-1.45	0.8	0.47
Family h/o	0.69-1.42	0.9	0.93
Diabetes mellitus	0.32-0.90	0.5	0.02
Hypertension	0.52-1.53	0.8	0.67
RDW CV	3.05-5.69	4.17	< 0.0001
RDW SD	1.6633	2.35	< 0.0001
Alcoholic	0.42-1.39	0.7	0.38

Abbreviations: h/o - history, RDW - red blood cell distribution width, CV - coefficience of variance, SD <math>- Standard deviation, CI - confidence interval, OR - odds ratio.

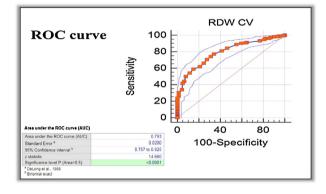
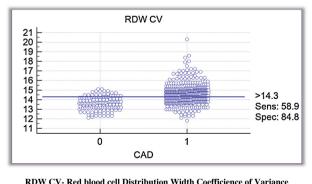


Fig. 1. Receiver Operating Characteristic (ROC) curve of RDW.

acute coronary syndrome or sudden cardiac deaths due to coronary occlusion.  $^{\rm 5}$ 

The atherosclerotic lesion is responsible for oxidative stress and release of inflammatory mediators as a result of endothelium dysfunction and macrophage accumulation.<sup>5</sup> Red blood cell distribution width (RDW) is the measure of the range of variation in size of red blood cell volume (anisocytosis) used in the differential diagnosis of anemia as part of red cell indices. In recent years, numerous studies have noted the importance of RDW as a predictor of poor clinical outcomes in the settings of various diseases, including coronary artery disease (CAD).

The mechanisms put forth for the explanation of increased RDW in atheroslcerosis are many, among them a few are



RDW CV- Red blood cell Distribution Width Coefficience of Variance
 0 – without CAD, 1- with CAD, sens – sensitivity, spec -specificity

Fig. 2. Scatter Diagram of RDW CV among the patients (Group B and Group A).

- The subclinical inflammation and pro inflammatory mediators are responsible for decrease in erythropoietin from the renal mesangial cells, as a result of suppression of Epo gene transcription, which leads to anisocytosis and microcytosis of red blood cells leading to anemia. Due to increase in the number of premature red blood cells in the peripheries, the RDW increases.<sup>6</sup>
- The other mechanism proposed is the oxidative stress, causing early damage of the RBCs resulting in microcytosis and thereby increased RDW.<sup>7</sup>
- Functional iron deficiency anemia can be seen as a result of increased synthesis of hepcidin in liver. Hepcidin, a peptide hormone is found in the heart and its expression is increased in hypoxia and inflammation. An increased level of hepcidin inhibits the absorption of the iron from the intestinal epithelium and blocks release of iron from the macrophages. [8]
- Decreased red blood cell deformability among patients with higher RDW values impairs blood flow through the microcirculation, resulting in the diminution of oxygen supply at the tissue level, particularly among patients suffering from myocardial infarction treated with urgent revascularization.<sup>9</sup>

The mean age of presentation was more in Group A compared to Group B, but is earlier than in the developed countries, emphasizing the early occurrence of the CAD in Indians as seen in INTERHEART study.<sup>10</sup> Males were predominant in both groups. The risk factors of CAD were more in Group A compared to Group B. The confounding bias of the increased risk factors among the CAD group causing the increased RDW in them is removed by multiregression analysis, which showed that increased RDW is an independent predictor of presence or absence of CAD. The RDW showed a positive correlation with increased severity of lesion in angiography assessed by MGS along the tertiles mild, moderate and severe. The RDW was found to be an independent predictor of all cause mortality in ACS subset of patients.<sup>11</sup>

The correlation of RDW CV with hemoglobin in the whole cohort was found to be weakly negative (r = -0.1096). The Hct or packed cell volume, the value emphasizing the size of the Red blood cells is decreased in the CAD group compared to the without CAD group though both the values are within normal limits. The decrease in the value can be explained theoretically due to the increased anisocytosis and microcytosis in the CAD group though the peripheral blood smear for confirmation have not been done. The red cell indices have been evaluated in both groups which showed decreased MCV, MCH and increased MCHC in Group A but not in Group B. Decreased MCV and MCH can be explained by the microcytosis and anisocytosis whereas the increased MCHC shows it not be related to the iron deficiency anemia where the MCHC will be decreased. The peripheral blood smear and vitamin B12,folate, iron levels have not been assessed in these patients.

Lippi et al.,<sup>12</sup> showed that the RDW with cut off value of 14% has a predictive value in diagnosing ACS in patients presenting with chest pain (sensitivity of 79% and a specificity of 50%). Increased RDW in a patient with CAD, leads to increased risk of Heart failure as shown by Felker et al. in 2007.<sup>2</sup> RDW was found to be useful in triaging patients with NSTEACS as NSTEMI in a cohort of 251 patients admitted to coronary care unit over one year period by Erhan Tenekecioglu et al.<sup>13</sup> Baseline RDW correlated well with MGS and was having increased positive predictive value of atherosclerotic burden. The RDW has been reported to be a predictor of coronary heart disease events and all cause mortality in various cardiovascular conditions.<sup>14</sup> In a study by Cavusoglu et al., the RDW was found to be a strong independent predictor of all- cause mortality in the ACS subset of patients based on multivariate analysis.<sup>11</sup> Tonelli et al., reported that among patients with CAD and without heart failure, mortality rates were significantly more in patients with elevated RDW.<sup>3</sup>

In our study, we have evaluated the RDW in CAD patients (all along the spectrum from stable angina to ACS), the first study in Indian Population to the best of our knowledge. The number of patients were more compared to the other studies. Indians have a low level of hemoglobin compared to the western population and hence have a high RDW value. The cutoff value of Hb <13 gm/dl in males and <12 gm/dl in females for diagnosis of anemia overdiagnoses the anemia in Indian Subcontinent as shown in a study by Deepak K et al.<sup>4</sup> Hence we have taken the value of <12 gm/dl in males and <11 gm/dl in females as cutoff for anemia.

In conclusion, RDW is an inexpensive blood parameter which can be obtained at the time of complete blood count and helps in risk stratification of patients with chest pain well before the time period taken for the rise of troponins to be detected peripherally.

#### 5. Limitations

It is a single center study with no follow up. Only hemoglobin levels and red cell indices were measured in the present study whereas the parameters such as serum iron, B12, folate were not assessed. The hepcidin levels have not been evaluated. The peripheral blood smear of cases with increased RDW was not studied.

#### 6. Conclusion

RDW is an effective easily available marker for the assessment of severity of coronary artery disease and helps in risk stratification of CAD patients for further events.

#### **Conflicts of interest**

Authors have no conflicts of interest to declare.

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#### Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ihj.2017.04.007.

#### References

- Perkins SL. Examination of blood and bone marrow. In: Greer JP, Foerester J, Lukens JN, Rodgers GM, Paraksevas F, Glader BE, eds. Wintrobe's Clinical Hematology. 11th ed. Salt Lake City: Utah: Lippincott Wilkins & Williams; 2003:5–25.
- Felker GM, Allen LA, Pocock SJ, et al. Red cell distribution width as a novel prognostic marker in heart failure;data from the CHARM program and the Duke databank. J Am Coll Cardiol. 2007;50:40–47.
- Tonelli M, Sacks F, Arnold M, Moye L, Davis B, Pfeffer M. Relation between red blood cell distribution width and cardiovascular event rate in people with coronary disease. *Circulation*. 2008;117:163–168.
- Pasupala Deepak K, Reddy PS. When is a South Indian really anemic? Ind J Clin Biochem. 2014;29(4):479–484.
- Tuttolomondo A, Di Raimondo D, Pecoraro R, Arnao V, Pinto A, Licata G. Atherosclerosis is an inflammatory disease. *Curr Pharm Des.* 2012;18 (28):4266–4268.
- 6. Heyman S, Hirsch E, Anker SD, et al. Inflammation as a therapeutic target in heart failure: a scientific statement from the Translational Research

Committee of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2009;11:119–129.

- 7. Berliner JA, Navab M, Fogelman AM, et al. Atherosclerosis basic mechanism. Oxidation, inflammation and genetics. *Circulation*. 1995;91:2488–2496.
- Merle U, Fein E, Gehrke SG, Stremmel W, Kulaksiz H. The iron regulatory peptide hepcidin is expressed in the heart and regulated by hypoxia and inflammation. *Endocrinology*. 2007;148:2663–2668.
- Bujak K, J. Wasilewski, T. Osadnik, et al. The Prognostic role of Red blood cell distribution width in coronary artery disease: a review of pathophysiology Disease Markers. Hindawi Publishing Corporation; 2015 [Volume].
- Ajay Vamadevan S, Prabhakaran Dorairaj. Coronary heart disease in Indians: implications of the INTERHEART study. *Indian J Med Res.* 2010;132 (November):561–566.
- Cavusoglu E, Chopra V, Gupta A, et al. Relation between red blood cell distribution width (RDW) and all cause mortality at two years in an unselected population referred for coronary angiography. *Int J Cardiol.* 2010;141(2):141– 146.
- 12. Lippi G, Filippozzi L, Montagnana M, et al. Clinical usefulness of measuring red blood cell distribution width on admission in patients with acute coronary syndromes. *Clin Chem Lab Med.* 2009;47(3):353–357.
- 13. Tenekecioglu E, Yilmaz M, Can Yontar Osman, et al. Red blood cell distribution width is associated with myocardial injury in non ST elevation acute coronary syndrome. *Clinics*. 2015;70(1):18–23.
- Zalawadiya SK, Veerana V, Niraj A, Pradhan J, Afonso L. Red cell distribution width and risk of coronary heart disease events. *Am J Cardiol.* 2010;106 (7):988–993.