Original Article

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Correlation of Red Cell Distribution Width with Severity of Cardiovascular Diseases

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ABSTRACT

Objectives: To determine the correlation of red cell distribution width (RDW) with severity of cardiovascular diseases.

Methodology: This study was conducted at the Department of Pathology, Aziz Fatima Medical and Dental College, Faisalabad, over a period of one year from October 2019 to September 2020. A total of 150 participants were included in the study consisting of 75 patients of cardiovascular disease in case group and 75 participants without any cardiovascular disease in control group. All patients in the study underwent trans radial or transfemoral rout coronary angiography using 5F optitorque catheter for trans radial rout or 6F Judkins catheters for transfemoral rout. All the patient had angiography within 24 hours of admission in the hospital.

Results: The patients who were diagnosed with Coronary artery Disease (CAD) had significantly higher mean age (51.45 ± 11.29 years) as compared (44.56 ± 9.45 years) to group B without out CAD. There were 53 (70.67%) males in group A, and 42 (56%) males in group B. The rate of hypertension (61.33%) was significantly higher among patient who diagnosed with CAD. The mean value of RDW CV was found significantly (p-value < 0.05) raised among patients of CAD (14.36 ± 1.02vs. 13.52 ± 0.89). The RDW SD was also significantly higher in group A (43.67 ± 4.39 vs. 41.65 ± 3.46, p-value = 0.002) in comparison to group B. Age and male gender were found to be a significant (p-value < 0.05) contributor for CVD with an odds ratio of 1.18 and 3 respectively.

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.

Key Words: Cardiovascular disease, RDW CV, RDW SD, Biomarker.

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Introduction

The most common cause of death worldwide is coronary artery disease due to atherosclerosis. A chronic inflammatory disorder is termed atherosclerosis, which occurs in a long period consisting of years without showing any symptoms. Generally, it ends up with occlusion of coronaries and manifests an acute coronary event. The measure of heterogeneity in the size of red blood cells is called red cell distribution width (RDW) and is mostly used in diagnosis of anemia. The use of RDW as risk marker for various cardiovascular diseases like coronary artery disease and heart failure is increasing in recent years.[1]

In earlier studies red cell distribution width has been shown to have a strong association with prognosis of the patients having a cardiovascular condition like heart failure and Coronary artery disease (CAD).[2,3] Although there is a strong evidence for prognostic importance of RDW in coronary artery diseases like systolic heart failure, but findings related to the association of RDW with heart function have variation among them. Independent correlation of RDW has been reported by different studies with findings of echocardiography in diastolic dysfunction after adjustment of other risk factors.[4] The results from another study showed that increased RDW level was found to be associated with worsening heart function. But the

correlation of RDW with cardiac variables in heart failure in patients having normal ejection fraction is unknown.[5]

Red cell distribution width is commonly used as a routine measure as part of standard complete blood count (CBC). The measure of variation in size of circulating erythrocytes is called red cell distribution width and is utilized in diagnosis of anemia. Increased levels of RDW are indicators of inflammation and oxidative stress and have a strong association with poor prognosis in stable and unstable cardiac events.[6]

Coefficient of variation of red cell volume distribution is termed as RDW and is calculated by dividing standard deviation with mean cell volume. High variation in size of erythrocytes is indicated by higher value of RDW and more homogeneous population of red blood cells show a lower value of RDW. The increased RDW level has been found to have a significant relationship with various other pathophysiological mechanisms including ineffective erythropoiesis, nutritional deficiencies, impaired iron mobilization, decreased hemoglobin level, inflammation, and oxidative stress.[7,8]

Cardiovascular morbidity and mortality can be predicted by increased RDW in patients having cardiac diseases like acute and chronic heart failure, pulmonary arterial hypertension, and coronary artery disease.[9] All the heart diseases related to vasculopathy are generally characterized as cardiovascular diseases (CVDs). The CVDs include atherosclerosis, heart failure, myocardial infarction, hypertension, and stroke. The recent improvement in medication and devices could not decrease the morbidity and mortality in CVDs patients.[10]

The prognosis evaluation of patients with CVDs is a challenge for cardiologists because assessment and stratification of risk is very difficult among these patients. The diagnosis of CVDs mainly depends upon imaging modalities, clinical judgment, and some biochemical parameters, but proper indexes which could be routinely employ in clinic are very limited. Such biomarkers are vital for diagnosis, early prevention, and treatment strategies. Clinicians are seeking such biomarkers for years to prevent cardiovascular and cerebrovascular events. One of such biomarkers can be red blood cell distribution width (RDW), which can be easily obtained from standard complete blood count.[11]

Many studies have shown a powerful association of RDW with severity and progression of CVDs, which is even stronger than previously identified risk factors. Hence RDW level can be used as predictive indicator of morbidity and mortality in patients of CVDs. However, underlying mechanisms are unclear till now. This present study was conducted to identify the association between RDW and CVDs in our population.

Methodology

Patients presenting with acute coronary syndrome, typical and atypical angina, or chest pain were selected for the study from the Department of Pathology, Aziz Fatima Medical and Dental College, Faisalabad. The study was conducted in a period of one year from October 2019 to September 2020. Approval of the study was taken from Ethics review committee of hospital. Non-probability consecutive sampling technique was used to select the study sample. Informed written consent was taken from all participants after brief description about the study. Confidentiality of the data was maintained.

A total of 150 participants were included in the study consisting of 75 patients of cardiovascular disease in cases group and 75 participants without any cardiovascular disease in control group. The sample size was calculated by WHO sample size calculator on the basis of 5% level of significance, 80% power of test, 1.9 population standard deviation, and mean value of RDW CV of 14.59 in cases and 13.71in control group.[1] Patients of both genders, having age from 18 to 65 years presenting with acute coronary syndrome, typical and atypical angina, or chest pain at the time of admission were included in the study. The patients presenting with anemia, history of PCI or coronary artery bypass grafting, acute myocardial infarction, renal disease, malignancy, and prior blood transfusions were excluded from the study.

Information on demographic characteristics including age, gender, risk factors like diabetes mellitus, hypertension, smoking, obesity, and family history of CAD were recorded. The details of clinical examination based on electrocardiography (ECG), echocardiography was noted in patients with and without cardiovascular disease. Venous blood sample was taken from antecubital vein through atraumatic puncture to assess the value of red cell distribution width (RDW) for all participants. The instrument used for this purpose was SYSMEX 2.0 automated analyzer and all the samples were processed within an hour of sample collection. The red cell indices were calculated from blood collected in a tube having EDTA.

All the patients in the study underwent trans radial or transfemoral rout coronary angiography using 5F optitorque catheter for trans radial rout or 6F Judkins catheters for transfemoral rout. All the patient had angiography within 24 hours of admission in the hospital.

MGS was used to assess the severity of lesion on angiography. On the basis of the results of angiography patients were divided into two groups first group A was consisted of patients with CAD (with diameter of stenosis ≥ 50% in the vessel) and second group B, consisted of patients without CAD. All the collected data was entered and analyzed with SPSS v. 25. Descriptive statistics like mean ± SD were calculated for quantitative variables and frequency with percentages were presented for qualitative variables. Independent sample t-test and chi-square tests were used to compare means and proportions between both groups. p-value < 0.05 was taken significant.

Results

The patients who were diagnosed with CAD had significantly higher mean age (51.45 ± 11.29 years) as compared (44.56 ± 9.45 years) to group B without out CAD. There were 53 (70.67%) males and 22 (29.33%) females in group A, 42 (56%) males and 33 (44%) females in group B without any statistically significant (p-value > 0.05) difference. The rate of hypertension and diabetes mellitus was significantly higher among patients who diagnosed with CAD (61.33% vs. 40%, p-value = 0.009) and (48% vs. 29.33%, p-value < 0.05) respectively.

The rate of smokers was also significantly higher among patient of CAD (48% vs. 21.33%, p-value = 0.000) as compared to patients without CAD. The rate of positive family history for CAD was 17.33% among patients diagnosed with CAD and in this rate was 9.33% in patients without CAD as elaborated in table I.

The mean value of red blood cell distribution width (RDW) CV was found significantly (p-value < 0.05) raised among patients of CAD (14.36 ± 1.02) as compared to (13.52 ± 0.89) patients without CAD. The red blood cell distribution width SD was also found to have increased mean value among patients of CAD (43.67 ± 4.39 vs. 41.65 ± 3.46, p-value = 0.002) in comparison to patients without CAD. There was no significant (p-value > 0.05) difference in mean hemoglobin level of patients of CAD (12.98 ± 0.98) and patients without CAD (13.24 ± 0.69).

Table I: Distribution of Demographic Characteristics of the patients

Characteristics	Group A (With CAD) N(%)	Group B (Without CAD) N(%)	P-value
Age of patient at presentation			
Mean ± SD	51.45 ± 11.29	44.56 ± 9.45	0.000*
Gender of the patient			
Male	53(70.67)	42(56.00)	0.062
Female	22(29.33)	33(44.00)	
Hypertension			
Yes	46(61.33)	30(40.00)	0.009*
No	29(38.67)	45(60.00)	
Diabetes Mellitus			
Yes	36(48.00)	22(29.33)	0.019*
No	39(52.00)	53(70.67)	
Smoking status of the patient			
Smoker	39(48.00)	16(21.33)	0.000*
non-smoker	36(52.00)	59(78.67)	
Family history of CAD			
Yes	13(17.33)	7(9.33)	0.149
No	62(82.67)	68(90.67)	

** Significant at 5% level of significance*

Table II: Comparison of Hematological Parameters between both groups

Group A (With CAD)		Group B (Without CAD)		P-value
Mean	**SD**	**Mean**	**SD**	
Red Blood Cell Distribution Width (RDW) CV (%)				
14.36	1.02	13.52	0.89	0.000*
Red Blood Cell Distribution Width (RDW) SD (fl)				
43.67	4.39	41.65	3.46	0.002*
Hemoglobin (gm/dl)				
12.98	0.98	13.24	0.69	0.062
Hematocrit (%)				
38.78	4.62	40.58	4.49	0.017*
MCV (fl)				
87.79	3.98	89.87	4.76	0.004*
MCH (Pg/cl)				
30.18	2.21	30.42	1.65	0.452
MCHC (g/dl)				
34.38	2.18	33.45	1.28	0.002*

** Significant at 5% level of significance*

The mean value of hematocrit was found to be significantly (p-value < 0.05) decreased among patients of CAD (38.78 ± 4.62) in comparison to patients without CAD (40.58 ± 4.49). The mean values of MCV and MCH were found to be significantly (p-value < 0.05) decreased among patients of CAD as compared to patients without CAD. The mean value of MCHC was noted to be significantly (p-value > 0.05) higher in patients of CAD (34.38 ± 2.18vs 33.45 ± 1.28) as elaborated in table II.

The multivariate logistic regression analysis showed that age was significant (p-value < 0.05) contributor for CVD with an odds ratio of 1.18, showing a very little but significant impact of increasing age on angiographic CAD. The male gender showed a quite high impact on the positive finding of angiographic CAD, indicating a 3 times higher risk of angiographic CAD among males. According to the multivariate analysis, smoking, positive family history for CAD, and hypertension did not show any significant impact on angiographic CAD. It was found that RDW CV was an independent and significant (p-value < 0.05) risk factor for CAD with an odds ratio of 5.31. Similarly, RDW SD was a significant (p-value < 0.05) risk factor for angiographic CAD with an odds ratio of 3.55 as elaborated in table III.

Table III: Multivariate Logistic Regression analysis

Characteristics	Odds Ratio	P-value	95% CI
Age	1.18	0.004*	1.04 - 1.45
Gender (male)	3.01	0.000*	2.35 - 5.01
Smoking (Yes)	1.01	0.336	0.39 - 1.06
Family history (+ve)	0.90	0.731	0.4 - 1.20
Diabetes Mellitus (Yes)	1.30	0.034*	0.5 - 1.82
Hypertension (Yes)	0.80	0.560	0.3 - 1.10
RDW CV	5.31	0.000*	4.45 - 6.78
RDW SD	3.55	0.038*	2.06 - 5.38

* *Significant at 5% level of significance*

Discussion

The measure of variation in size of circulating erythrocytes is termed as red blood cell distribution width. This parameter is routinely used for differential diagnosis of anemia and it is a routine part of complete blood count. There is a strong and independent association of RDW with risk of adverse outcomes in patients having heart disease. This relationship remains the same even after adjustment for hematocrit.[12]

The potential mechanisms behind this relationship of red blood cell distribution width with poor prognosis and outcome among heart patients are not clear. The severity and extent of CAD is associated with inflammatory markers and these inflammatory markers are linked with high level of RDW. The bone marrow's response to erythropoietin could be affected due to the weakening of iron metabolism which could be disturbed by inflammation due to a high level of RDW. The erythrocytes could be impaired by oxidative stress and this damage decreases the survival of erythrocyte leading to elevated level of RDW. So, chronic inflammation and oxidative stress could be major contributor to adverse outcomes.[13,14]

In this present study, the patients who were diagnosed with CAD had significantly higher mean age (51.45 ± 11.29 years) as compared (44.56 ± 9.45 years) to patients without out CAD. There was male dominance in both groups of this study with (70.67%) in group A and (56%) in group B. The rate of hypertension was significantly higher among patients who were diagnosed with CAD. Results are similar with literature which says that higher age and hypertension is a major contributor for CAD.[15] Similarly, a review article by Gao *et al.,* 2019 revealed that male gender has a twofold higher chance of CAD in comparison to females.[16]

Some studies have revealed a strong relationship of RDW value with long term poor outcomes in both acute and chronic conditions like heart failure, acute myocardial infarction, stroke, stable angina, and peripheral artery disease. There was no difference in these results even after adjusting for multiple potential confounders like anemia. The RDW level showed an association with the presence and complexity of coronary artery disease.[17,18]

The results of this present study showed that the mean value RDW CV (14.36 ± 1.02 vs. 13.52 ± 0.89, p-value < 0.05) and RDW SD (43.67 ± 4.39 vs. 41.65 ± 3.46, p-value = 0.002) were found significantly raised among patients of CAD as compared to patients without CAD. There was no significant (p-value > 0.05) difference in mean hemoglobin level of patients with CAD (12.98 ± 0.98) and patients without CAD (13.24 ± 0.69). These results are parallel to previous studies showing increased RDW level among patients with CAD. The chance of incidental coronary event increase with an increase in RDW level and a cohort study found a 1.8 times increased chance of fatal acute coronary event after adjusting for several covariates. No significant association of RDW was observed with an incidence of non-fatal coronary event.[19,20]

The results of this present study showed that the mean values of hematocrit, MCV and MCH were found to be significantly (p-value < 0.05) decreased among patients of CAD in comparison to patients without CAD. The mean value of MCHC was noted to be significantly (p-value > 0.05) higher in patients of CAD (34.38 ± 2.18) as compared to (33.45 ± 1.28) in patients without CAD. Similar results were found by Nagula P, et al 2017, who found a significant decrease in hematocrit, MCV and MCH level among confirmed cases of CAD. The decrease

in MCV and MCH could be a result of microcytosis and anisocytosis but the increase in MCHC differentiates it from anemia where MCHC will be decreased.[1,21]

The enhanced erythrocytes destruction and deranged erythropoiesis can cause increase in red blood cell distribution width. The risk of poor outcome among patients of stable CAD can be stratified, simply by RDW value. A risk model based upon complete blood count including hematocrit value, platelet count, white blood cell count, mean corpuscular volume, mean corpuscular hemoglobin concentration and RDW value was used by some studies to predict mortality risk among suspected cardiovascular disease patients.[22]

The inflammation in patient with CAD can be predicted by increased RDW level. Which can be an indicator of poor prognosis in patients of CAD and can be used as principal pathophysiological observation. The severity and characteristics of inflammation may have correlation with elevated RDW. The increased level of RDW among patients of confirmed CAD could be the result of aggravated inflammatory status.[23]

Some epidemiological studies support this evidence that patients with CVDs have more chances of having anisocytosis and elevated RDW levels. But many clinical studies have revealed the association of RDW with various disease incidences, severity, and outcomes. This relationship of RDW with cardiovascular diseases may be mediated by some other factors and RDW is just the combined effect of these factors. It still needs to be clarified.

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. RDW should be used in combination with more specific cardiovascular clinical parameters, to obtain a multi-biomarker profile, which might be more appropriate.

References

1. Nagula P, Karumuri S, Otikunta AN, Yerrabandi SRV. Correlation of red blood cell distribution width with the severity of coronary artery disease a single center study. Indian Heart J. 2017;69(6):757-61. https://doi.org/10.1016/j.ihj.2017.04.007
2. Uyarel H, ErgelenM, Cicek G, KayaMG, Ayhan E, Turkkan C, et al. Red cell distribution width as a novel prognostic marker in patients undergoing primary angioplasty for acute myocardial infarction. Coron Artery Dis 2011;22:138-44. https://doi.org/10.1097/MCA.0b013e328342c77b
3. Van Kimmenade RR, Mohammed AA, Uthamalingam S, van der Meer P, Felker GM, Januzzi Jr JL. Red blood cell distribution width and 1-year mortality in acute heart failure. Eur J Heart Fail 2010;12:129-36. https://doi.org/10.1093/eurjhf/hfp179
4. Parizadeh SM, Jafarzadeh-Esfehani R, Bahreyni A, Ghandehari M, Shafiee M, Rahmani F, et al. The diagnostic and prognostic value of red cell distribution width in cardiovascular disease; current status and prospective. Biofactors. 2019;45(4):507-16. https://doi.org/10.1002/biof.1518
5. Holmstrom A, Sigurjonsdottir R, Hammarsten O, Gustafsson D, Petzold M, Fu MLX. Red blood cell distribution width and its relation to cardiac function and biomarkers in a prospective hospital cohort referred for echocardiography. Eur J Intern Med. 2012;(23):604–9. https://doi.org/10.1016/j.ejim.2012.05.005
6. Isik T, Kurt M, Tanboga IH, Ayhan E, Gunaydin ZY, Kaya A, et al. The impact of admission red cell distribution width on long-term cardiovascular events after primary percutaneous intervention: A four-year prospective study. Cardiol J. 2016;23(3):281-8. https://doi.org/10.5603/CJ.a2015.0080
7. Salvagno GL, Sanchis-Gomar F, Picanza A, Lippi G. Red blood cell distribution width: a simple parameter with multiple clinical applications. Crit Rev Clin Lab Sci. 2015;(52):86–105. https://doi.org/10.3109/10408363.2014.992064
8. Turcato G, Zorzi E, Prati D, Ricci G, Bonora A, Zannoni M, et al. Early in-hospital variation of red blood cell distribution width predicts mortality in patients with acute heart failure. Int J Cardiol. 2017;243:306-10. https://doi.org/10.1016/j.ijcard.2017.05.023
9. Baggen VJM, van den Bosch AE, van Kimmenade RR, Eindhoven JA, Witsenburg M, Cuypers JAAE, et al. Red cell distribution width in adults with congenital heart disease: A worldwide available and low-cost predictor of cardiovascular events. Int J Cardiol. 2018;260:60-5. https://doi.org/10.1016/j.ijcard.2018.02.118
10. Laslett LJ, Alagona P Jr, Clark BA 3rd, Drozda JP Jr, Saldivar F, Wilson SR, Poe C, Hart M. The worldwide environment of cardiovascular disease: prevalence, diagnosis, therapy, and policy issues: a report from the American College of Cardiology. J Am Coll Cardiol. 2012;60(25):S1-49. https://doi.org/10.1016/j.jacc.2012.11.002
11. Li N, Zhou H, Tang Q. Red Blood Cell Distribution Width: A Novel Predictive Indicator for Cardiovascular and Cerebrovascular Diseases. Dis Markers. 2017;2017:7089493. https://doi.org/10.1155/2017/7089493
12. Tonelli M, Sacks F, Arnold M, Moye L, Davis B, Pfeffer M; for the Cholesterol and Recurrent Events (CARE) Trial Investigators. Relation Between Red Blood Cell Distribution Width and Cardiovascular Event Rate in People with Coronary Disease. Circulation. 2008;117(2):163-8. https://doi.org/10.1161/CIRCULATIONAHA.107.727545

13. Salvagno GL, Sanchis-Gomar F, Picanza A. Red blood cell distribution width: a simple parameter with multiple clinical applications. Crit Rev Clin Lab Sci 2015;52:86–105. https://doi.org/10.3109/10408363.2014.992064
14. Bao D, Luo G, Kan F, Wang X, Luo J, Jiang C. Prognostic value of red cell distribution width in patients undergoing percutaneous coronary intervention: a meta-analysis. BMJ Open. 2020;10(9):e033378. https://doi.org/10.1136/bmjopen-2019-033378
15. Weber T, Lang I, Zweiker R, Horn S, Wenzel RR, Watschinger B, et al. Hypertension and coronary artery disease: epidemiology, physiology, effects of treatment, and recommendations: A joint scientific statement from the Austrian Society of Cardiology and the Austrian Society of Hypertension. Wien Klin Wochenschr. 2016;128(13-14):467-79. https://doi.org/10.1007/s00508-016-0998-5
16. Gao Z, Chen Z, Sun A, Deng X. Gender differences in cardiovascular disease. Med Novel Technol Devic. 2019;(4):100025. https://doi.org/10.1016/j.medntd.2019.100025
17. Ye Z, Smith C, Kullo IJ. Usefulness of red cell distribution width to predict mortality in patients with peripheral artery disease. Am J Cardiol. 2011;107:1241-5. https://doi.org/10.1016/j.amjcard.2010.12.023
18. Isik T, Ayhan E, Kurt M, Tanboga IH, Kaya A, Aksakal E. Is red cell distribution width a marker for the presence and poor prognosis of cardiovascular disease? Eurasian J Med. 2012;44(3):169-71. https://doi.org/10.5152/eajm.2012.39
19. Borne Y, Smith JG, Melander O. Red cell distribution width in relation to incidence of coronary events and case fatality rates: a population-based cohort study. Heart 2014; 100:1119-24. https://doi.org/10.1136/heartjnl-2013-305028
20. Fava C, Cattazzo F, Hu ZD, Lippi G, Montagnana M. The role of red blood cell distribution width (RDW) in cardiovascular risk assessment: useful or hype? Ann Transl Med. 2019 Oct;7(20):581. https://doi.org/10.21037/atm.2019.09.58
21. Ma FL, Li S, Li XL, Liu J, Qing P, Guo YL, et al. Correlation of red cell distribution width with the severity of coronary artery disease: a large Chinese cohort study from a single center. Chin Med J (Engl). 2013;126(6):1053-7.
22. Khalil A, Shehata M, Abdeltawab A, Onsy A. Red blood cell distribution width and coronary artery disease severity in diabetic patients. Future Cardiol. 2019;15(5):355-66. https://doi.org/10.2217/fca-2018-0066
23. Li W, Li X, Wang M, Ge X, Li F, Huang B, et al. Association between red cell distribution width and the risk of heart events in patients with coronary artery disease. Exp Ther Med. 2015;9(4):1508-14. https://doi.org/10.3892/etm.2015.2244