

# ARTICLE

## ASSESSMENT OF THE RELATION BETWEEN RED CELL DISTRIBUTION WIDTH AND ATRIAL FIBRILLATION IN TYPE-2 DIABETIC PATIENTS

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## ABSTRACT

We aimed to investigate the level of red cell distrubition width(Rdw), in type-2 diabetic patients with atrial fibrillation. Patients aged 18 to 80 years old who were admitted to the internal medicine and cardiology outpatient clinics were enrolled. The data of the patient were retrospectively scanned from hospital database. 105 people were included in the study as 63 patients with diabetes mellitus and atrial fibrillation and 42 patients with diabetes mellitus and no atrial fibrillation. It was found that the age factor was statistically significant in men, women, and all patients between the groups, and Hb, hba1c, and LDL were statistically significant in men and all patients. The level of Rdw is investigated in 2 groups of diabetic patients with and without atrial fibrillation. However, there was no significant difference between the two groups.

Keywords: Atrial fibrillation, Diabetes mellitus type-2, Red cell distribution width.

## АБСТРАКТ

Цель исследования - изучить уровень ширины дистракции эритроцитов (Rdw) у больных сахарным диабетом 2-го типа с фибрилляцией предсердий. В исследование были включены пациенты в возрасте от 18 до 80 лет, поступившие в поликлинику внутренних болезней и кардиологическую клинику. Данные о пациентах ретроспективно сканировались из базы данных больницы. В исследование были включены 105 человек: 63 пациента с сахарным диабетом и фибрилляцией предсердий и 42 пациента с сахарным диабетом и отсутствием фибрилляции предсердий. Установлено, что фактор возраста был статистически значимым у мужчин, женщин и всех пациентов между группами, а Hb, hba1c и ЛПНП - у мужчин и всех пациентов. Исследован уровень Rdw в 2 группах больных сахарным диабетом с фибрилляцией предсердий и без нее. Однако достоверных различий между двумя группами не выявлено.

**Ключевые слова** : Фибрилляция предсердий, сахарный диабет типа 2, ширина распределения красных клеток.

## **INTRODUCTION**

Diabetes is a chronic metabolic disease observed with hyperglycemia due to insulin deficiency or peripheral insulin resistance, the frequency of which increases exponentially day by day. The causes such as advanced age, people's increasing sedentary life, and obesity have a role in this increase <sup>1</sup>. The prevalence of Type 2 Diabetes is increasing all over the world. It is estimated that 642 million people will be affected in 2040 <sup>2</sup>. It ranks sixth among disability-causing diseases, according to a 2015 study <sup>3</sup>.

Cardiovascular complications are very important, particularly in terms of morbidity and mortality in patients with diabetes. Atrial fibrillation (AF) is the most common one among arrhythmias. C. J. Ostgren et al reported that AF was monitored more frequently in patients with diabetes than in non-diabetics<sup>4</sup>. Diabetes is a risk factor for the development of atrial fibrillation, also the presence of diabetes in patients with AF is a condition that increases mortality in terms of thrombotic events and AF complications.

AF is also important for its consequences such as stroke and heart failure <sup>5, 6</sup>. It is more common in men than in women, and more common in developed countries than in developing countries. In addition, its frequency increases with age 7Atrial remodeling, which sets the stage for the formation of AF, can occur 3 ways: Structurally, electrically, or in functionally. Although this condition is not clearly explained in diabetes mellitus, some cases are focused on. The first of these is left ventricular diastolic dysfunction, which is common in patients with diabetes mellitus, the second is fibrosis of the atrium, resulting in loss of elasticity and atrial enlargement<sup>8</sup>. As a result of all these, the occurrence of arrhythmia becomes easier. In addition, when insulin resistance and increased sympathetic activity in diabetics are joined to this, the formation of AF in diabetics is triggered. If the diabetic patient also has poor glucose control, the complications increase 9.

RDW (red cell distrubition width), is a quantitative measure of the variability in the

sizes of erythrocytes <sup>10</sup>. It shows anisocytosis. In circulation, it is normally between 80-100 fl. It is found by dividing the standard deviation erythrocyte volumes by the mean of corpuscular volume. Hematological devices automatically calculate and give RDW during a complete blood count <sup>11</sup>. But in various anemias or in cases that affect the production of ervthrocytes, the heterogeneity in these values occurs. So, it is used in the differential diagnosis of anemia such as of normocytic and microcytic anemias. It is especially important in the differential diagnosis of iron deficiency anemia from the other reasons of micocvtic anemias such as thalassemia an other hemoglobinopathies. RDW is an inexpensive, easy method that is utilized in routine tests of almost all patients.

#### **MATERIAL AND METHOD**

Patients aged 18-80 years who were admitted to the internal medicine and cardiology outpatient clinics of Sabuncuoğlu Serefeddin Training and Research Hospital of Amasya University between 2020-2022 were enrolled in our study. The data of the patients were retrospectively scanned with the help of our hospital database. Patients with anemia and infection were excluded from the study. Patients with impaired renal function. impaired liver function, heart valve disease or surgery, or undergoing ablation were not included in the study. The patients were divided into 2 groups. Also, 105 people were included in the study as 63 patients with diabetes mellitus and atrial fibrillation and 42 patients with diabetes mellitus and no atrial fibrillation. The relationship between red cell disruption width (RDW, erythrocyte distribution width) and atrial fibrillation was examined between these groups. The red cell restriction width (RDW) values, HbA1c (hemoglobin A1c) values indicating 3-month sugar control, and other routine examinations that were already examined in their routine requested laboratory controls were accessed with the hospital database. For our study, Tokat Gaziosmanpasa University Research Hospital's ethical board approval was taken.

Detailed descriptive statistical information is presented in Table 1. GraphPad Prism version 7.00 was used for statistical analysis (GraphPad Software, La Jolla California USA).

## RESULT

The results were obtained at the 95% confidence interval, and the statistical significance level was p<0.05. Data of a total of 105 patients were used. There were 41 female

and 22 male patients in the group with diabetes and AF. But, 24 female and 18 male patients were enrolled in the group with diabetes but no AF. The differences between the groups were determined using the student's t-test for multivariate tests and the Mann-Whitney U test for non-multivariate tests. The presence of the relationship of atrial fibrillation with RDW in patients with diabetes was analyzed by logistic regression analysis.

	The group with diabetes and AF			The group with diabetes but no AF			P-value		
		Mean	Std. dev.	Std. error		Mean	Std. dev.	Std. error	
	Female (n:41)	67.63	10.07	1.573	Female (n:24)	56.58	10.42	2.127	0,0002 *
Age	Male (n:22)	70,95	10,99	2,343	Male (n:18)	58,67	11,92	2,810	0,0004 *
5	Total (n:63)	68,79	10,44	1,315	Total (n:42)	57,48	11,00	1,697	<0.0001 *
	Female (n:41)	8491	2775	433,3	Female (n:24)	8163	2445	499,1	0,2191
WBC	Male (n:22)	7953	2291	499,9	Male (n:18)	8550	2272	535,6	0,5349
	Total (n:63)	8309	2614	332,0	Total (n:42)	8329	2352	362,9	0,6478
	Female (n:41)	13,23	1,444	0,2255	Female (n:24)	13,59	1,144	0,2336	0,2862
Hb	Male (n:22)	13,20	1,696	0,3702	Male (n:18)	14,52	1,701	0,4009	0,0252 *
	Total (n:63)	13,22	1,520	0,1931	Total (n:42)	13,99	1,466	0,2262	0,0247 *
	Female (n:41)	263902	77070	12036	Female (n:24)	279000	71426	14580	0,3597
Plt	Male (n:22)	253000	79486	17345	Male (n:18)	247111	48792	11500	0,6506
	Total (n:63)	260210	77418	9832	Total (n:42)	265333	64064	9885	0,3526
	Female (n:41)	13,81	1,781	0,2781	Female (n:24)	13,50	1,371	0,2798	0,4390
RDW	Male (n:22)	14,23	2,083	0,4545	Male (n:18)	13,63	2,052	0,4837	0,0627
	Total (n:63)	13,95	1,882	0,2390	Total (n:42)	13,56	1,675	0,2584	0,0959
Uba1a	Female (n:41)	7,63	1,366	0,2134	Female (n:24)	8,108	1,923	0,3926	0,4388
Hba1c	Male (n:22)	10,70	12,29	2,681	Male (n:18)	9,283	2,313	0,5451	0,0483 *

Table 1: Statistical results of parameters between groups

	Total (n:63)	8,671	7,271	0,9234	Total (n:42)	8,612	2,154	0,3323	0,0441*
	Female (n:41)	172,7	73,17	11,43	Female (n:24)	158,5	42,93	8,763	0,6584
Glucose	Male (n:22)	163,0	46,99	10,78	Male (n:18)	209,4	78,56	18,52	0,0621
	Total (n:63)	169,6	65,75	8,489	Total (n:42)	180,3	65,13	10,05	0,3231
Ldl	Female (n:41)	114,2	48,46	8,310	Female (n:24)	129,2	41,56	8,483	0,1273
	Male (n:22)	88,21	33,48	7,680	Male (n:18)	120,2	33,59	7,918	0,0073 *
	Total (n:63)	104,9	45,13	6,198	Total (n:42)	125,3	38,17	5,890	0,0062 *
	Female (n:41)	163,0	82,91	14,43	Female (n:24)	177,2	81,09	16,55	0,3451
Tg	Male (n:22)	136,8	90,49	20,76	Male (n:18)	160,8	65,09	15,34	0,1526
	Total (n:63)	153,5	85,82	11,90	Total (n:42)	170,2	74,25	11,46	0,1144

\* It indicates that it is statistically significant, p<0.05.

 Table 2: Logistic regression analysis

	Odds ratio	CI	P value
RDW	0,2478	0,007381 to 5,652	0,2826

RDW: Red Blood Cell Distribution Width

As a result of logistic regression analysis, it was found that RDW is not associated with atrial fibrillation (Rdw Odds ratio:0.2478 CI: 0.007381 to 5.652 p<0.05) (Table 2). ROC curve analysis was not performed because the RDW data did not give significant results in the intergroup comparison.

#### DISCUSSION

In our study, we investigated the level of RDW in 2 groups of type-2 diabetic patients with and without atrial fibrillation. However, we did not find any significant difference between both groups.

It was found that the age factor was statistically significant in women, men, and all patients between the groups, Hb was statistically significant in men and all patients, HbA1c was statistically significant in men and all patients, and LDL was statistically significant in men and all patients. Other parameters did not show a statistically significant difference.

In recent studies, it has been shown that there is an association between high RDW levels and atrial fibrillation. S.Qingmiao et al. reviewed the studies conducted on AF and RDW up to the year 2016 in their metaanalysis<sup>12</sup>. In total, they examined 12 studies and 2721 patients. They reported that high levels of RDW increased the risk of AF.

In the Tromso study conducted between 1994 and 2013 by Hald E.M et al. RDW values and AF development were examined in 26.111 patients. They found an increase in both the incidence of AF and ischemic events as the RDW value increased. Especially they found it in low MCV( Mean corpuscular volume) levels<sup>13</sup>. In a study conducted on 1894 patients with an average duration of 13.6 years, researchers found RDW and AF to be related. Cersit S. et al. conducted a study on 112 patients with acute coronary syndrome and found that the level of RDW was significantly higher in patients with acute coronary syndrome and AF<sup>14</sup>.

One important reason of our conclusion is not in accordance with the other studies may be : which size of erithrocytes were in the majority with high RDW levels? Small cells or large cells. It is important because in some studies it is shown that high RDW levels with low MCV more significant than with high ratio of MCV<sup>13</sup>. So we think according to MCV more detailed studies will be usefull for this issue.

## **CONCLUSION**

In our study, patients were the cases already exposed to inflammation, high glucose, and glycosylated end products for a while because they were diabetic. However, since our study was retrospective, we did not know how long they had diabetes and atrial fibrillation. In addition, CRP and other inflammatory markers were not studied. These were the limitations of our study. They may have been a factor in our inability to find RDW statistically significant. More detailed studies with inflammatory markers and covering more cases will shed light on the issue.

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#### **DECLARATIONS**

The authors declare that there is no conflict of interest regarding the publication of this paper. Author contribution: Conceived and designed the analysis; A.Dilara Demir. Collected the data; Orhan Demir and A.Dilara Demir. Performed the analysis; A.Dilara Demir and Orhan Demir. Wrote the paper; A.Dilara Demir and Orhan Demir.

# REFERENCES

K.Kaku. Pathophysiology of Type 2 Diabetes and Its Treatment Policy. [Internet]. 2010 February JMAJ 53(1): 41-46, 2010

- International Diabetes Federation. IDF Diabetes 2. Atlas. 7th edn. 2015.
- 3. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet . [Internet]. 2016 october 388: 1545-602. DOI : https://doi.org/10.1016/S0140-6736(16)31678-6
- 4 C.J.Ostgren, J. Merlo, L. Rastam, U. Lindblad. Skaraborg Hypertension and Diabetes Project, "Atrial fibrillation and its association with type 2 and hypertension in a diabetes Swedish community," Diabetes, Obesity & Metabolism. [Internet]. 2004 Augst ; 6 (5) : 367-374. https://doi.org/10.1111/j.14628902.2004.00358.x
- 5. Thrall G, Lane D, Carroll D, Lip GY. Quality of life in patients with atrial fibrillation: A systematic review. Am J Med. [Internet]. 2006 May;119(5):448.e1-19. DOI:https://doi.org/10.1016/j.amjmed.2005.10.05
- 6. Wang TJ, Larson MG, Levy D, Vasan RS, Leip EP, Wolf PA et al. Temporal relations of atrial fibrillation and congestive heart failure and their joint influence on mortality: The framingham heart study. Circulation. [Internet]. 2003 Jun 17;107(23):2920-5. DOI: https://doi.org/10.1161/01.CIR.0000072767.8994 4.6E
- 7. Chugh S.S, Havmoeller R, Narayanan K, Singh D, Rienstra M , Benjamin E.J , et al. Worldwide Epidemiology of Atrial Fibrillation: A Global Burden of Disease [Internet]. 2010 Study. Circulation. 2014 Feb 25;129(8):837-47. DOI: https://doi.org/10.1161/CIRCULATIONAHA.113.0 05119
- 8. Otani K, Takeuchi M, Kaku K, Haruki N, Yoshitani H,Tamura M et al. Impact of diastolic dysfunction grade on left atrial mechanics assessed by twodimensional speckle tracking echocardiography. J Soc Echocardiogr [Internet]. 2010 Am Sep;23(9):961-7. DOI: https://doi.org/10.1016/j.echo.2010.06.023

Kato T, Yamashita T, Sekiguchi A, Sagara K, 9. Takamura M, Takata S, et al. What are arrhythmogenic substrates in diabetic rat atria? J Electrophysiol. Cardiovasc [Internet]. 2006 Aug;17(8):890-4. DOI: https://doi.org/10.1111/j.15408167.2006.00528.x

10. K. Clarke, R. Sagunarthy, S. Kansal, "RDW as an additional marker in inflammatory bowel

- disease/undifferentiated colitis." Digestive Diseases and Sciences. [Internet]. 2008 Sep;53(9):2521-3. DOI: https://doi.org/10.1007/s10620-007-0176-8
- 11. Lippi G, Pavesi F, Bardi M, Pipitone S . Lack of harmonization of red blood cell distribution width (RDW). Evaluation of four hematological analyzers. Clin Biochem[Internet]. 2014 Aug;47(12):1100-3.

DOI:https://doi.org/10.1016/j.clinbiochem.2014.0 6.003

- Shao Q, Korantzopoulos P, Letsas K.P, Tse.G, Hong J, Li.G,et al. Red blood cell distribution width as a predictor of atrial fibrillation . J Clin Lab Anal. [Internet].2018 Jun; 32(5): e22378. DOI: https://doi.org/10.1002/jcla.22378
- 13. Eryd S.A , Borné Y, Melander O, Persson M, Smith JG, Hedblad B et al. Red blood cell distribution width is associated with incidence of atrial fibrillation. J Intern Med. [Internet]. 2014 Jan;275(1):84-92. DOI: https://doi.org/10.1111/joim.12143
- 14. Cerşit S, Kalçik M., Öcal L, Bayam E. Association between atrial fibrillation and red cell distribution width in patients with acute coronary syndrome. Medeniyet Medical Journal [Internet]. 2018; 33(2): 89-93 DOI: https://doi.org/10.5222/MMI.2010.50224

https://doi.org/10.5222/MMJ.2018.58234