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Research letter

Correlation between red blood cell distrubition width and glycated hemoglobin in diabetic and nondiabetic patients

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Abstract: *Aim* — Our aim in this study is evaluating the red blood cell distrubition width (RDW) and glycated hemoglobin (HbA1C) relation in nondiabetic and diabetic people who applied to our hospital and showing the usability in disease follow-up.
Material and Methods — Main data of this research is the data of patients (diabetic and nondiabetic) who applied to internal diseases polyclinic between July 1, 2013 and November 31, 2014 and whose RDW, HbA1C, white blood cell, hemoglobin, and hematocrit were controlled. 82 diabetic and 32 nondiabetic patients were included in this study.
Results — No statistically significant difference was observed between the diabetic and nondiabetic groups in age, male and female distribution and RDW. No statistically significant correlation was observed between RDW and age and HbA1C in order in the nondiabetic group. While a correlation which is statistically significant and in the same direction was determine between age and RDW among the diabetic group, a statistically significant correlation was not between HbA1C and RDW. Among all cases a correlation which is statistically meaningful and in the same direction was detected between age and RDW. But a statistically significant correlation was not found between HbA1C and RDW among all cases.
Conclusion — According to the available results, no statistically significant correlation was determined between HbA1C and RDW in the nondiabetic patients, diabetic group or in total. But in order to provide more clearance, we believe that studies with more patients would be useful.

Keywords: red blood cell distrubition width**,** glycated hemoglobin, diabetic patients, nondiabetic patients

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Introduction

It is a metabolic disease characterized with persistent hyperglycemia due to diabetes mellitus (DM), inappropriate glucose use or insufficient insulin production of pancreas. There is a defect in insulin effect, secretion or both [1, 2]. As obesity and sedentary life style is common in the society, DM type 2 frequency is increasing [3]. It is estimated that the DM prevalence which was 2.8% in 2000 in all age groups around the world would be 4.4% in 2030. It is estimated that the total number of people with DM which is equal to 171 million would increase to 366 million in 2030 [4].

Glycemic control is a must in DM. Glycemic control is the main target of treatment in protection against organ damage and other complications of DM. Glycated hemoglobin (HbA1C) follow-up is made in order to measure the efficiency of the treatment in DM and observe the glycemic control [5]. HbA1C is formed as the result of non enzymatic reaction of glucose to hemoglobin. It provides information on the average blood glucose levels of past 8-12 weeks in DM treatment [7]. HbA1C is the golden standard in glycemic control of patients. It is necessary for optimal patient care. Medicine treatment is also used to show the effect of exercise and diet on glycemia [6].

Red blood cell distrubition width (RDW) is the symbol of red blood cell volume distribution width coefficient of variation. May be considered as heterogeneity index and is the equivalent of anisocytosis observed in peripherical blood smear [10]. Concentration of acute phase reactants and inflammation mediators such as interleukin-6 (IL-6), tumour necrosis factor alpha (TNF-alpha) gets higher in type 2 diabetic patients [8]. As RDW is related to many hematological and nonhematological diseases, it is also correlated with inflammatory markers such as high sensitivity C-reactive protein (hsCRP), erythrocyte sedimentation rate, IL-6, soluble transferrin receptor, soluble tumour necrosis factor (TNF) receptor I and soluble TNF receptor II [9]. The latest studies have reported that RDW is an independent prognostic marker strong in many pathophysiological cases such as cardiovascular disease, pulmonary disease, rheumatoid arthritis and progressive inflammatory diseases and even cancer [11].

In this study we examined the RDW and HbA1C levels in nondiabetic and type 2 diabetic patients who applied to our

polyclinic between July 1, 2013 and November 31, 2014. We examined the relationship between RDW and HbA1C level.

Material and Methods

Patients who applied to internal diseases polyclinic in our hospital between July 1, 2013 and November 31, 2014 were included in the study through Amasya University Sabuncuoğlu Şerefeddin Education and Research Hospital patient database. All patients who applied to the hospital with any complaint were included in the study.

This study was approved by Amasya University Sabuncuoğlu Serefeddin Education and Research Hospital (Amasya, Turkey) in the scientific meeting.

A total of 82 diabetic patients consisting of 26 males and 56 females and 32 nondiabetic patients consisting of 16 males and 16 females were included in this study (114 patients in total). Average age was 57.8±15.8 in the nondiabetic group and 60.2±10.9 in the diabetic group (data presented as mean and standard deviation).

Exclusion criteria were determined this way. Patients with anaemia, heart failure, kidney failure, hypothyroid and hyperthyroid were not included in the study. Liver enzymes and blood creatine of the patients included in the study were normal. Hemoglobin (g/dl), hematocrit (HCT) (%), mean corpuscular volume (MCV) (fL), mean corpuscular hemoglobin (MCH) (pg), mean corpuscular haemoglobin concentration (MCHC) (gHb/dL) were in normal range.

SPSS for Windows 11.5 package programme was used for data analysis. Whether the distribution of constant variables was in accordance with the normal distribution was examined with Kolmogorov Smirnov test. Defining statistics were shown as mean ± standard deviation or median (minimum-maximum) for constant variables and nominal variables were shown as case number and percent (%).

The importance of difference was examined with Student t test for mean values among groups and with Mann Whitney U test for median values. Nominal variables were evaluated by Chi-square test of Pearson. Whether there is a statistically significant relationship between constant variables was investigated using correlation test of Spearman.

Multi variable linear regression analysis was used to investigate if DM had a statistically significant changing effect on RDW when a correction was made according to age, gender and HbA1C. Regression coefficient of each variable and 95% confidence intervals were calculated. Results were accepted statistically meaningful for P<0.05.

Results

A statistically significant difference was not observed in the criteria below between diabetic and nondiabetic patients (*Table* 1):

- Age (p=0.428),
- Gender distribution (p=0.069),
- RDW (p=0.540).

HbA1C level of diabetic group compared to the nondiabetic group was significantly higher statistically (p<0.001) (*Table* 1).

Table 1. Demographical and clinical characteristics of cases in studied groups

Variables	*Nondiabetic patients*	*Diabetic patients*	*p-value*
Age, years	57.8±15.8	60.2±10.9	0.428†
Gender:			
- Male, no. (%)	16 (50.0%)	26 (31.7%)	0.069‡
- Female no. (%)	16 (50.0%)	56 (68.3%)	
RDW, %	13.3±0.81	13.2±0.67	0.540†
HbA1C, %	5.3 (4.8-5.9)	7.7 (6.0-14.9)	<0.001

† – Student's t test; ‡ – Pearson's Chi-Square test; without marker – Mann Whitney U test.

Table 2. Spearman's correlation coefficients and importance levels between age, HbA1C and RDW among all studied patients and subgroups

Groups	*Age*	*HbA1C*
Nondiabetic patients	r=0.202, p=0.266	r=0.192, p=0.293
Diabetic patients	r=0.245, p=0.026	r=0.027, p=0.810
All patients	r=0.224, p=0.016	r=0.002, p=0.984

Table 3. RDW levels (%) according to gender among all studied patients and subgroups

Groups	*Male*	*Female*	*p-value*†
Nondiabetic patients	13.2±0.73	13.4±0.90	0.566
Diabetic patients	13.3±0.68	13.2±0.68	0.746
All patients	13.2±0.69	13.2±0.73	0.993

† – Student's t test.

Table 4. Examining the effect of DM on RDW with multivariable linear regression analysis when correction was made according to age, gender and HbA1C

Variables	*Regression coefficient (B)*	*95% CI*	*p-value*
DM	- 0.147	-0.529 – 0.235	0.448
Age	0.014	0.003 – 0.024	0.011
Female factor	0.027	-0.250 – 0.303	0.849
HbA1C	0.006	-0.074 – 0.085	0.891

CI, confidence interval.

No statistically significant correlation was observed between RDW and age and HbA1C in order in the nondiabetic group (p>0.05) (*Table* 2). In the diabetic group, a correlation which is statistically meaningful and in the same direction was detected between age and RDW (r=0.245, p=0.026) (*Table* 2). A statistically significant correlation was not found between HbA1C and RDW among the diabetic patients (p=0.801) (*Table* 2).

Among all cases a correlation which is statistically meaningful and in the same direction was detected between age and RDW (r=0.224, p=0.016). But a statistically significant correlation was not found between HbA1C and RDW among all cases (*Table* 2).

A statistically significant difference was not observed between males and females in average RDW levels in nondiabetic and diabetic groups, as well as in all patients (p=0.566, p=0.746 and p=0.993, respectively) (*Table* 3).

According to multiple variable linear regression analysis, it was observed that didn't have statistically significant effect on RDW when age, gender and HbA1C's effects were kept constant (*Table* 4). When correction was made according to other probable factors as the result of linear regression analysis with multiple variables, it was observed that age was an independent factor on estimating the change in RDW level (*Table* 4).

According to the available results, no statistically significant correlation was determined between HbA1C and RDW in the nondiabetic group, diabetic group or in total.

Discussion

RDW is an easy, affordable and routinely used test [12]. It was used in the distinctive diagnosis of anaemia for years [13]. Studies investigating the relationship between RDW and cardiovascular diseases, inflammatory diseases and DM were made recently. In many studies it was reported that RDW was the risk marker of cardiovascular mortality and morbidity. RDW was considered as a prognostic marker reflecting the underlying inflammatory event. It can be used in the evaluation of determining microvascular and macrovascular complications of DM [14].

In a study made by Heba Sherif et al., the relation between RDW and type 2 DM vascular complications and the connection of this with hsCRP which is another inflammatory marker was investigated. In the study on DM patients, it was observed that RDW values were related to progressive cardiovascular disease and nephropathy. This relation is independent from anaemia, anaemia treatment and DM duration [15]. In middle aged adults, inflammation markers are related to DM development. Autoimmunity may explain this relation partially [8].

In a study of G. Lippi et al., the RDW and HbA1C relation was examined in 2515 patients over 65 years of age. In patients over 65 years of age in Southern Europe, it was observed that RDW had an important connection with HbA1C. Possibility of a new parameter was observed in DM development risk prediction [16]. Again in a study of V. Veranna et al. examined RDW and HbA1C relation in a healthy adult. It was observed that in a healthy adult without DM, RDW is predicative of HbA1C disease development [17].

In another study, it was observed that low RDW levels were related to increased DM incidence independently from other risk factors. It was determined as a possible contributing marker in evaluating the development risk of the disease in individuals with DM development risk [18]. D.S. Liu et al. observed that RDW and RDW/MCV rate was correlated to ketoacidosis in patients with diabetic ketoacidosis. It was observed that ketoacidosis RDW/MCV rate was a healthier and more sensitive marker compared to RDW [19].

We also didn't observe a statistically significant correlation between RDW and age and HbA1C in order among nondiabetic patients in our study (p>0.05). Among diabetic patients, we detected a correlation which is statistically meaningful and in the same direction between age and RDW (r=0.245, p=0.026). But we couldn't find a statistically significant correlation between HbA1C and RDW among diabetic patients (p=0.801).

Among all cases a correlation which is statistically meaningful and in the same direction was detected between age and RDW (r=0.224, p=0.016), but again we couldn't find a statistically significant correlation between HbA1C and RDW among all cases.

It was observed that when age, gender and HbA1C effects were stabilized, DM didn't have a statistically significant changing effect on RDW and age was a independent factor in predicting the change in RDW level. According to the available results, we didn't determine a statistically significant correlation between HbA1C and RDW in the control group, case group or in total.But hyperglycemia has several effects on red blood cells (RBC)s, besides formation of HbA1C. It leads to change in erythrocyte structure, hemodynamic parametres, increased osmotic fragility and also reduces RBC life span [20]. In studies made with much more patients, a close relation was found between RDW and HbA1C, the reason that we couldn't find such a relation may be the low number of patients in the groups and more extensive studies with more patients are needed on this subject.

Conclusion

We didn’t determine statistically significant correlation between Glycated hemoglobin and red blood cell distrubition width. We believe that studies with more patients would be useful.

Conflict of interest: none to declare.

References

1. Singh M, Shin S. Changes in erythrocyte aggregation and deformability in diabetes mellitus: a brief review. *Indian J Exp Biol* 2009; 47(1): 7-15. (PMID: 19317346)
2. Dada OA, Uche E, Akinbami A, Odesanya M, John-Olabode S, Adediran A, et al. The relationship between red blood cell distribution width and blood pressure in patients with type 2 diabetes mellitus in Lagos, Nigeria. *J Blood Med* 2014: 5: 185–189. (doi: 10.2147/JBM.S67989) (PMID: 25278786)
3. Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 2001; 344: 1343-1350. (doi: 10.1056/NEJM200105033441801) (PMID: 11333990)
4. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care* 2004; 27(5): 1047-1053. (doi: 10.2337/diacare.27.5.1047) (PMID: 15111519)
5. Ghazanfari Z, Niknami S, Ghofranipour F, Larijani B, Agha-Alinejad H, Montazeri A. Determinants of glycemic control in female diabetic patients: a study from Iran. *Lipids Health Dis* 2010; 9: 83. (doi: 10.1186/1476-511X-9-83) (PMID: 20701805)
6. Musenge EM, Manankov A, Mudenda B, Michelo C. Glycaemic control in diabetic patients in Zambia. *Pan Afr Med J* 2014; 19: 354. (doi: 10.11604/pamj.2014.19.354.5264) (PMID: 25932067)
7. Pasupathi P, Manivannan P, Uma M, Deepa M. Glycated haemoglobin (HbA1C) as a stable indicator of type 2 diabetes. *Int J Pharm Biomed Res* 2010; 1(2): 53-56.
8. Schmidt M, Duncan BB, Sharrett AR, Lindberg G, Savage PJ, Offenbacher S, et al. Markers of inflammation and prediction of diabetes mellitusin adults (atherosclerosis risk in communities study). *Lancet* 1999; 353: 1649-1652. (doi: 10.1016/S0140-6736(99)01046-6) (PMID: 10335783)
9. Zöller B, Melander O, Svensson P, Engström G. Red cell dıstrıbutıon wıdth for predıctıng cardıovascular dısease: a lıterature revıew. *European Medical Journal* 2014; 2: 61-70.
10. Aulakh R, Sohi I, Singh T, Kakkar N. Red cell distribution width (RDW) in the diagnosis of iron deficiency with microcytic hypochromic anemia. *Indian J Pediatr* 2009; 76(3): 265-268. (doi: 10.1007/s12098-009-0014-4) (PMID: 19205647)
11. Yao J, Lv G. Association between red cell distribution width and acute pancreatitis: a cross-sectional study. *BMJ Open* 2014; 4: e004721. (doi: 10.1136/-2013-004721)
12. Zöller B, Melander O, Svensson P, Engström G. Red cell distribution width and risk for venous thromboembolism: a population-based

cohort study. *Thromb Res* 2014; 133(3): 334-339. (doi: 10.1016/j.thromres.2013.12.013) (PMID: 24393657)

13. Ku NS, Kim HW, Oh HJ, Kim YC, Kim MH, Song JE, et al. Red blood cell distribution width is an independent predictor of mortality in patients with gram-negative bacteremia. *Shock* 2012; 38(2): 123-127. (doi: 10.1097/SHK.0b013e31825e2a85) (PMID: 22683729)
14. Malandrino N, Wu WC, Taveira TH, Whitlatch HB, Smith RJ. Association between red blood cell distribution width and macrovascular and microvascular complications in diabetes. *Diabetologia* 2012; 55(1): 226-235. (doi: 10.1007/s00125-011-2331-1) (PMID: 22002006)
15. Sherif H, Ahmed NR, Radwan M, Hamdy E, Reda R. Red cell distribution width as a marker of inflammation in type 2 diabetes mellitus. *Life Science Journal* 2013; 10(4): 32-39.
16. Lippi G, Targher G, Salvagno GL, Guidi GC. Increased red blood cell distribution width (RDW) is associated with higher glycosylated hemoglobin (HbA1C) in the elderly. *Clin Lab* 2014; 60(12): 2095-2098. (PMID: 25651746)
17. Veeranna V, Zalawadiya SK, Panaich SS, Ramesh K, Afonso L. The association of red cell distribution width with glycated hemoglobin among healthy adults without diabetes mellitus. *Cardiology* 2012; 122(2): 129-132. (doi: 10.1159/000339225) (PMID: 22813786)
18. Engström G, Smith JG, Persson M, Nilsson PM, Melander O, Hedblad B. Red cell distribution width, haemoglobin A1c and incidence of diabetes mellitus. *J Intern Med* 2014; 276(2): 174-183. (doi: 10.1111/joim.12188) (PMID: 24471821)
19. Liu DS, Jin Y, Ma SG, Bai F, Xu W. The ratio of red cell distribution width to mean corpuscular volume in patients with diabetic ketoacidosis. *Clin Lab* 2013; 59(9-10): 1099-1104. (PMID: 24273933)
20. Nada AM. Red cell distribution width in type 2 diabetic patients. *Diabetes Metab Syndr Obes* 2015; 8: 525-533. (doi: 10.2147/DMSO.S85318) (PMID: 26586957)

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