Journal of Nephropharmacology

Red cell distribution width as a prognostic marker in diabetes; a pilot cross-sectional study

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A R T I C L E I N F O

A B S T R A C T

Introduction: Red cell distribution width (RDW) is one of the important factors in anisocytosis which is related to impairment of erythropoiesis and degradation of erythrocytes.
Objectives: The aim of this study was to evaluate the use of RDW as a prognostic marker in diabetic patients.
Patients and Methods: This cross-sectional study was conducted on 144 individuals who referred to laboratories in Khuzestan. Of all, 69 persons were diabetic patients and 75 were non-diabetic.
Results: The mean fasting blood sugar (FBS) and RDW coefficient of variation (RDW-CV), were 85.20 ± 9.12 mg/dL and 13.26 ± 0.69% respectively, in the non-diabetic group, and 238.65 ± 70.54 mg/dL and 13.50 ± 0.74% respectively, in the diabetic group. In this study, a significant difference of mean FBS ($P < 0.001$) and mean RDW ($P = 0.04$) between groups were detected.
Conclusion: In our study, a significant relationship between changes in RDW and changes in blood sugar in diabetic patients was detected. Studying RDW in diabetes delineated higher RDW values than in healthy population. Therefore, it can be recommended to apply serum RDW as a prognostic marker for diabetes. However additional studies on this subject are necessary.

Introduction

Red cell distribution width (RDW) is typically measured by automated laboratory tools. It represents the variation in the size of red blood cells (RBCs) (anisocytosis) and the heterogeneity in the volume of RBCs. RDW is calculated as follows; standard deviation of RBC size/ mean corpuscular volume (1).

In other words, RDW represents a numerical measurement of the variation in RBC size. It is a strong prognostic factor in patients with heart failure and in patients with myocardial infarction, before the incidence of any symptom even after matching with hematocrit (2). It is commonly used in the hematologic laboratory for the differential diagnosis of anemia. However, recent evidence suggests that anisocytosis is a common factor in human disorders such as cardiovascular diseases (CVDs), venous thromboembolism, cancer, diabetes, pneumonia, chronic obstructive pulmonary disease, liver and kidney failure, and also in other acute or chronic conditions (3). The normal RDW coefficient of variation (RDW-CV), is between 11.5% to 14.5%. Its elevated level indicates an increase in the variations in cell size (4).

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia that is caused by a defect

in the secretion or action of insulin, or both. Chronic hyperglycemia, which occurs in DM, is associated with dysfunction and disability of organs, especially eyes, kidneys, nerves, heart, and blood vessels. Hyperglycemia has several effects on RBCs, including cell swelling and reduced cell half-life (5). There are two types of DM; 1) type I diabetes that is commonly observed in children and adults and is related to insulin defects, and 2) type II diabetes that occurs in adults and accounts for more than 90% of all cases of diabetes in the world. The risk factors for type 3 diabetes include low activity, obesity, and aging (6). Nowadays, type 2 diabetes is one of the most common and complicated problems of the community. The disease has affected hundreds of millions of people all over the world and has created serious socioeconomic problems. The pathogenesis of type 2 diabetes is associated with the progression of insulin resistance in peripheral tissues and liver, decrease in β cell mass, and deficiency in insulin secretion. Type 2 diabetes is markedly associated with reduction in insulin, which is not only due to the poor performance of pancreatic cells, but also due to the decrease in cell volume. Hyperglycemia has several effects on RBCs, besides formation of glycated hemoglobin, it leads to reduced deformability, changes in mechanical properties of RBCs, increased adhesion, and increased osmotic fragility, leading to changes in erythrocyte structure and hemodynamic characteristics (7, 8). Long-term (chronic) increase in glucose in diabetes is the main cause of angiopathic and neuropathic disorders, retinopathy, weak antioxidant defense system, metabolic disorders, and changes in lipid profiles. DM can be diagnosed by measuring fasting blood sugar (FBS) (>126 mg/dL). Among the symptoms of hyperglycemia, we may note over-drinking, over-urinating, over-eating, and weight loss (9). Diabetes is associated with increased risk of microvascular and macrovascular complications (10, 11). CVD is the leading cause of death among patients with diabetes accounting for 30%–40% of deaths (12, 13). RDW higher than 15% was associated with approximately 10-fold increase in mortality, thus serving as a powerful tool for risk stratification in this high-risk group. The change in RDW could potentially serve as a surrogate marker for all-cause and cardiovascular mortality that could be used in pilot studies of primary and secondary prevention of CVD in diabetes (14).

Objectives
The aim of this study was to evaluate the efficacy of RDW as a prognostic marker in diabetic patients.

Patients and Methods
Patients
This cross-sectional study was conducted on the results of FBS and CBC tests which were conducted on 144 individuals who referred to laboratories in Khuzestan (from 2013 to 2014). In this study, blood was taken to conduct CBC test and to measure blood glucose. After performing the CBC test, the data on a variety of parameters such as such as hemoglobin, hematocrit, mean corpuscular volume (MCV), RDW, mean corpuscular hemoglobin (MCH), and platelets were obtained by a simplex apparatus model KX21. The measurement of serum glucose level was conducted by an auto-analyzer apparatus via enzymatic colorimetric methods (Pars Azmon kit).

Ethical issues
Study-related data was delivered to subjects and informed consent was provided before the study. The research followed the Tenets of the Declaration of Helsinki. The Ethics Committee of Ahvaz Jundishapur University of Medical Sciences approved this study.

Statistical analysis
Statistical analyses were performed using SPSS18 software (SPSS Inc., Chicago, IL, USA). Quantitative continuous variables were indicated by mean ±SD. Independent sample t test was used to compare the significant difference between study groups. Additionally, P values less than 0.05 were considered as the level of significance.

Results
Of 144 individuals who referred to the laboratory, 69 persons were diabetic patients and 75 were non-diabetic. The mean FBS and RDW-CV were 85.20 ± 9.12 (mg/dL) and 13.26 ± 0.69 (%) respectively, in non-diabetic group. In addition, the mean hemoglobin and hematocrit, MCV and RBCs, and platelets were 13.44 ± 1.65 g/dL, 40.42 ± 4.36 %, 85.49 ± 6.12 fl, 4.68 ± 0.59($\times^{106ml}$), and 232.91 ± 59.47 ($\times^{106\mu l}$), respectively in the non-diabetic group (Table 1).

In diabetic group, the mean FBS and RDW were 238.65 ± 70.54 mg/dL and 13.50 ± 0.74 %, respectively. In addition, the mean hemoglobin, hematocrit, MCV, RBC, and platelet were 13.36 ± 1.44 g/dl, 39.96 ± 3.90 %, 86.63 ± 4.45 fl, 4.57 ± 0.48($\times^{106ml}$), and 240.44 ± 67.94 ($\times^{106\mu l}$) respectively (Table 1).

In this study, a significant difference of mean FBS (p <0.001) and mean RDW (P = 0.04) between groups was detected.

Discussion
DM and hyperglycemia have different effects on RBC and HbA1c formation (15). DM is associated with osmotic adhesion (16). DM also causes oxidative stress, which causes red cell deformation, resulting in increased RDW levels (17).

In contrast to our results, in the study by Engström et al, the reduction in RDW was associated with an increase in the prevalence of diabetes. The reduction in RDW can be used as an alternative marker for the decrease in RBC survival (18). In a study by Dada et al in Nigeria, a

Table 1. Results of analysis of various parameters in diabetic and non-diabetic groups

Variable	Groups (mean± SD)		P value
	Diabetics (n=69)	Non-diabetics (n=75)	
FBS (mg/dL)	238.65±70.54	85.20± 9.12	<0.001
RDW (%)	13.50±0.74	13.26±0.69	0.04*
Hb (g/dL)	13.36±1.44	13.44±1.65	0.77
Hct (%)	39.96±3.90	40.42±4.36	0.51
MCV (fl)	86.63±4.45	85.49±6.12	0.20
RBC ($\times^{106ml}$)	4.57±0.48	4.68±0.59	0.22
Plt ($\times^{106\mu l}$)	240.44±67.94	232.91±59.47	0.54

significant relationship between RDW and blood pressure was seen. However, contrary to our finding, no significant relationship between RDW and FBS was detected (6). Moreover, our findings in this study are inconsistent with the findings of other studies, such as the studies by Lee et al (19). In another study, the researchers evaluated RDW and serum BNP (B type natriuretic peptide) levels in diabetic patients with cardiac failure and compared them with healthy subjects. It was found that RDW levels in diabetic patients with cardiac failure were significantly higher than of healthy subjects (4). Finally, in a review study, Shirali et al detected the efficacy of RDW as a prognostic marker for diabetes (20). Similar results were found in Nada study, which RDW was considered as an inflammatory marker with a significant predictive value and is significantly higher in diabetic patients than healthy subjects (21).

Conclusion
In our, a significant relationship between changes in RDW and changes in blood sugar in diabetic patients was detected. Therefore, it can be suggested to apply serum RDW as a prognostic marker for diabetes. However additional studies on this subject are necessary

Limitations of study
This is a pilot study, which requires more investigations by larger studies.

Authors' contribution
SS, MB and SB; idea and writing the manuscript. AAV and MB; Literature Review. SMK; critique and thought. FJ; statistical analysis. All authors read and approved the final manuscript.

Conflicts of interest
The authors declare no conflict of interest.

Ethical considerations
Ethical issues (including plagiarism, misconduct, data fabrication, falsification, double publication or submission, redundancy) have been completely observed by the authors.

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