ORIGINAL RESEARCH

The relationship between red blood cell distribution width and blood pressure in patients with type 2 diabetes mellitus in Lagos, Nigeria

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Background: High red blood cell distribution width (RDW) is related to impairment of erythropoiesis, reflecting chronic inflammation and increased levels of oxidative stress, both of which are telltale signs of type 2 diabetics. The aim of this study was to evaluate the relationship between the RDW and fasting blood sugar/blood pressure, and compare the results from diabetics with nondiabetic controls.

Methods: This was an unmatched case-control study involving 200 participants consisting of 100 diabetics and 100 nondiabetic controls. Blood (4.5 mL) was collected from all of the diabetics and nondiabetic controls, and placed into EDTA anticoagulant tubes. A full blood count was performed using the Sysmex KX-21N, a three-part auto analyzer able to run 19 parameters per sample, including RDW. Blood pressure was measured during sample collection and in a sitting position.

Results: The mean fasting blood sugar level was 95.20±30.10 mg/dL in the controls, and 147.85±72.54 mg/dL in the diabetics. The mean blood pressures for diabetics was 138/90 mmHg and for non-diabetics 120/80 mmHg. The mean RDW-SD (RDW standard deviation) was 46.44±4.64 fl in the controls, and 46.84±3.18 in the diabetics. The mean RDW-CV (RDW coefficient of variation) was 14.74%±1.94% in controls, and 14.80±0.71 for diabetics. No statistically significant correlation was found between the RDW-SD and fasting blood sugar/blood pressure in the diabetics. A statistically significant positive correlation was found between the RDW-CV and blood pressure in the diabetics.

Conclusion: A positive correlation between the RDW-CV and blood pressure was established in the diabetics in this study.

Keywords: RDW, fasting blood sugar, type 2 DM

Background

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia, and resulting from defects in insulin secretion, insulin action, or both.[1] The chronic hyperglycemia occurring in DM is associated with long-term damage, as well as dysfunction and failure of different organs, especially in the eyes, kidneys, nerves, heart and blood vessels.[1] The World Health Organization (WHO) estimates that about 347 million people worldwide are presently living with DM.[2] Of this figure, approximately 80% are from low and medium income countries.[3] WHO also projects that by 2030, DM will be the seventh leading cause of death worldwide.[4] There are two main types of DM: type 1 which usually develops in childhood and adolescence, and is insulin dependent; and type 2 which develops in adulthood and represents more than 90%

of cases worldwide. Risk factors for type 2 DM include sedentary lifestyle, obesity, and old age.

Diagnosis of DM can be made with a simple fasting plasma glucose test with values ≥126 mg/dL (7.0 mmol/L) being diagnostic of DM (fasting is defined as no caloric intake for at least 8 hours).[5] In the presence of symptoms of hyperglycemia (polyuria, polydipsia, polyphagia, weight loss), a casual plasma glucose level of >200 mg/dL (11.1 mmol/L) is diagnostic.[5]

Recently, various researchers have proposed that type 2 DM is connected to a state of subclinical chronic inflammation.[6,7] It may be that abnormal levels of chemokines released by the expanded adipose tissue in obesity activates monocytes, and increases the secretion of proinflammatory adipokines. Such cytokines in turn enhance insulin resistance in adipose and other tissues, thereby increasing the risk of type 2 DM.[8,9]

The red blood cell distribution width (RDW) is a measure of variation in size of the circulating erythrocytes (anisocytosis)[10] which is routinely obtained from a standard automated complete blood count. High RDW indicates the presence of anisocytosis which is related to impairment of erythropoiesis and degradation of erythrocytes,[10] reflecting chronic inflammation and increased levels of oxidative stress, both of which are telltale signs in type 2 diabetics, and this may significantly contribute to development of atherosclerotic diseases.[11,12]

Many recent studies have investigated changes in RDW in association with cardiac and noncardiac related deaths.[13–19] Most of these studies report a positive correlation of RDW with the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels – an increase in the RDW during inflammation, similar to that seen in other inflammatory parameters. Malandrino et al[20] recently reported a positive correlation between a high RDW and increased incidence of both macro- and microvascular complications in DM patients without marked vascular complications.

The aim of this study was to evaluate the relationship between the RDW and fasting blood sugar/blood pressure, and compare with nondiabetic controls.

Methods
Study population
The research was approved by the Ethics Review Committee of Lagos State University Teaching Hospital (LASUTH). This was a case-control study consisting of 100 type 2 DM patients receiving treatment, attending the diabetic clinic of the LASUTH, and 100 nondiabetic controls consisting of medical students, nurses and doctors in the same institution. During

the study period between June to September 2013, all patients who gave informed consent and satisfied the study inclusion criteria were recruited into the study. They were asked to fill structured questionnaires including demographic information, height, weight, last fasting blood sugar, blood pressure, drug history, and family history of diabetes. All the diabetics were on oral hypoglycemic and antiplatelet drugs, like clopidogrel and vasoprin tablets, and some were on antihypertensive and lipid lowering drugs. Information on family history of diabetes was also obtained from the controls and they were subjected to fasting blood sugar testing before enlistment.

Sample collection
Blood was withdrawn with minimal stasis from the antecubital vein using a dry sterile disposable syringe and needle. Blood (4.5 mL) was dispensed into EDTA anticoagulant tubes. The specimens were labeled with subject's age, sex, and identification number. The EDTA samples were kept at room temperature until processed within 4 hours of collection.

Laboratory analysis
A full blood count was performed using the SysmexKX-21N (Sysmex Corporation, Kobe, Japan), a three-part auto analyzer able to run 19 parameters per sample, including hemoglobin concentration, packed cell volume, red blood cell concentration, mean corpuscular hemoglobin, mean cell volume, mean corpuscular hemoglobin concentration, white blood cell and platelet count, and mean platelet volume. Standardization, calibration of the instrument, and processing of the samples were carried out according to the manufacturer's instructions.

Well-mixed blood samples were aspirated, by leaving the equipment sampling probe in the blood sample and then pressing the start button. Approximately 20 µL of blood was aspirated by the auto analyzer. The results of the analysis were displayed after about 30 seconds.

Statistical analysis
Data were analyzed using SPSS version 16.0 (SPSS Inc., Chicago, IL, USA). The continuous variables were given as means ± standard deviation (SD). The Pearson chi-squared test was used to test for association between discrete variables. The P-value was considered to be statistically significant when less than 0.05.

Results
A total of 200 participants were enrolled into the study – consisting of 100 diabetics and 100 nondiabetic controls.

The mean age of the control group was 32.38±6.44 years, with a minimum age of 17 years, and a maximum age of 70 years. The mean age of the type 2 DM group was 62.35±9.84 years, the minimum was 34 years old, and the maximum 90 years old. The overall female:male ratio was 68% to 32%. In the type 2 DM participants, 73% were female, and 27% were male. In the nondiabetic participants, 63% were female, and 37% were male (Table 1).

In the diabetic group, the mean body mass index was 32.10±4.85 kg/m², and the mean fasting blood sugar level was 147.85±72.54 mg/dL. In the nondiabetic group, the mean body mass index was 25±5.23 kg/m², and the mean fasting blood sugar was 95.20±30.10 mg/dL. The minimum blood pressure of the diabetics was 100/90 mmHg, maximum was 200/90 mmHg, and the mean was 138/90 mmHg. Amongst the diabetics, a total of 45 out of 100 (45%) gave a positive family history of type 2 diabetes, while 55% had no family history of diabetes. Only 5% of the controls gave a positive family history of diabetes. The mean duration of diabetes in the type 2 DM group was 8.81±7.06 years. The RDW-CV (RDW coefficient of variation) in the control group was 14.74±1.94, and 14.80±0.71 in the type 2 DM group. The RDW-SD (RDW standard deviation) was 46.44±4.64 in the control group, and 46.84±3.18 in the type 2 DM group (Table 2).

Both the RDW-SD and the RDW-CV were not statistically significantly correlated with the fasting blood sugar level in the type 2 DM group; P-values were 0.10 and 0.55 respectively; Spearman's rho values were −0.61 and −0.12 respectively. The RDW-SD was not statistically significantly correlated with blood pressure; P=0.99; Spearman's rho of 0.11. A statistically significant correlation was achieved between the RDW-CV and the blood pressure of type 2 DM patients; P=0.02, Spearman's rho of 0.02. RDW-SD and the RDW-CV values were not statistically significantly correlated

Table 1 Sociodemographic data of participants

Parameters	Diabetics (n=100)	Nondiabetic controls (n=100)
Mean age (years)	62.35±9.84	32.38 ±66.44
Sex		
Female	73	63
Male	27	37
Educational status		
No education	22	0
Primary only	16	0
Secondary	24	0
Tertiary	38	100
Mean body mass index (kg/m²)	32.1±4.85	25.0±5.23

Table 2 Mean red blood cell distribution width and fasting blood sugar

Parameters	Diabetics (n=100)	Nondiabetic controls (n=100)
RDW-CV (%)	14.80±0.71	14.74±1.94
RDW-SD (fl)	46.84±3.18	46.44±4.64
FBS (mg/dL)	147.85±72.54	95.20±30.10

Abbreviations: RDW-CV, red blood cell distribution coefficient of variation; RDW-SD, red blood cell distribution standard deviation; FBS, fasting blood sugar.

with the duration of diagnosis of diabetes in the patients; P-values were 0.8 and 0.38 respectively; and Spearman's rho of 0.096 and −0.035 respectively.

Tukey's post hoc analysis could not be performed between the RDW-CV and blood pressure because at least one group had fewer than two cases, the significant level of 0.29 was obtained with test of homogeneity of variance.

Discussion

DM affects a sizeable proportion of the working population, and has economic consequences for both the individual and the society as a whole. Thus, the monitoring of DM in order to prevent complications is urgently needed. The RDW, a widely available and inexpensive test conducted as part of the complete blood cell count, measures the degree of anisocytosis. It is calculated as follows:

$$RDW\text{-}CV = (\text{Standard deviation of red blood cell volume} \div \text{mean cell volume}) \times 100$$

The normal range for the RDW-CV is 11.5%–14.5%, and higher values indicate greater variations in cell sizes.[21] High RDW indicates a high degree of anisocytosis which is associated with distortion and degradation of erythropoiesis,[21] reflecting chronic inflammation and an increased level of oxidative stress.[22]

DM increases vascular inflammation and oxidative stress while vascular inflammation affects erythropoiesis and deformability of red blood cells thus elevating RDW levels.[23] RDW is strongly associated with chronic inflammation and is a strong indicator of risk of cardiovascular mortality in people with cardiovascular diseases, DM, as well as in the general population.[13,14,18,24]

Increased RDW may also arise as a result of anemia. Thus, causes like iron deficiency, and megaloblastic anemia with associated micro- or macrocytosis are potential confounders because our participants were not screened for iron, vitamin 12, nor folic acid. However, the effect of such confounders is negligible as all the participants selected for the study were

healthy individuals (control group) and diabetics without complications or obvious comorbidities as at the time of the study. The effect of other causes of chronic inflammation such as tuberculosis, cancers, and connective tissue disorders as confounders is similarly negligible.

The mean age of diagnosis of type 2 DM among adults aged 18–79 years in the US between 1997 and 2011 was 54 years,[25] and is similar to the 62.35±9.84 years obtained in our study; however this value doubles the mean age of our controls of 32.38±6.44 years. All controls used for this study were relatively young men and women working in our institution including nurses, doctors, and medical students, which are not representative of the general population; this could impact on results obtained and is a possible limitation of the study. However, the sex distribution in the type 2 DM group and the control group was similar, with approximately 2:1 female:male in both cases.

Our type 2 DM study population had relatively well controlled diabetes, hence RDW-CV and RDW-SD of the type 2 DM group (14.80±0.71 and 46.84±3.18) was almost the same with control values (14.74±1.94 and 46.44±4.64). Also, the mean fasting blood sugar of 147.85±72.54 mg/dL in diabetics compared well with the nondiabetic controls of 95.20±30.10 mg/dL. These closely related results in our study may be accounted for by the fact that the majority of diabetics enrolled had long been on treatment before this study, and their medications performed well.

We found no significant association between the RDW and the duration of diabetes. This finding is in contrast with the findings of studies by Lee and Partley,[26] Malandrino et al[20] and Heba et al[27] who found significant associations between the RDW and macrovascular complications of DM, suggesting that RDW may be a predictor of the onset of diabetic macrovascular complications.

Also in contrast to the studies of Malandrino et al[20] and Sherif et al,[27] our results showed a statistically insignificant negative correlation between RDW and fasting blood sugar levels in diabetics. While in keeping with many other studies,[28–31] a statistically significant positive correlation was achieved between RDW and blood pressure in our patients.

Elevated RDW had been reported as a prognostic marker reflecting an underlying inflammatory state.[28] High RDW was strongly associated with poor clinical outcomes in patients with heart failure,[28] coronary artery disease,[29,30] pulmonary hypertension[31] and peripheral arterial disease.[32] Increased RDW was also associated with increased mortality in diabetic patients with coronary artery disease treated with percutaneous coronary intervention.[33]

Conclusion
We could only establish a statistically significant correlation between RDW and blood pressure, not between RDW and fasting blood sugar. Some of the limitations of this study could have impacted our results.

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Disclosure
The authors have no conflicts of interest in this work.

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