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Original Research Article

Correlation analysis of red cell distribution width with HbA1c in Type 2 Diabetes Mellitus patients

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Abstract

Background: Red cell distribution width (RDW) have been found to be altered in uncontrolled diabetic patients because of consistent increase in HbA1c values that are known to induce functional and structural changes in Hb and an alteration in its cytoplasmic environment. Alteration in RDW may have a role in the diagnosis and monitoring of glycemic status along with its complications.

Objective: Present study aims towards analysis of correlation of red cell distribution width with HbA1c in T2DM patients.

Methodology: Present study was a case control study in which total 50 cases and 50 controls were recruited. Controls were the healthy non-diabetic patients and cases involved patients with diabetes. Patients were categorized as diabetic and non-diabetic as per American Diabetes Association Diagnostic Criteria. 3ml blood sample was obtained to analyze the RDW and HbA1c.

Results: The mean age of patients was 59.54±10.78 in the cases and was 55.40±15.63 in control group. The mean HbA1c was 10.79±2.45 was significantly high in cases compared to 5.59±0.31 in controls. The mean RDW was 13.69±1.31 in cases and 13.40±1.17 in controls which do not differ significantly. In diabetes patients, a non-significant positive correlation was observed between the HbA1c and RDW with the correlation coeffect of 0.027.

Conclusion: In present study, a non- significant correlation was observed between the RDW and HbA1c in diabetes patients. A multicentric study with a large sample size is required to establish diagnostic significance of RDW in diabetes patients.

Keywords: Diabetes, RDW, HbA1c

Introduction

Microvascular and macrovascular complications of T2DM pose an increased risk to the health of the patient, therefore, it becomes extremely crucial for health care providers to adopt a holistic approach which includes dietary and lifestyle modification, adequate exercise, appropriate medications, regular monitoring of blood glucose levels, timely follow-up and a thorough assessment of complications [1]. The glycated hemoglobin i.e., HbA1c has been used

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to check for control of blood sugar levels. HbA1c values are not affected by any of the drugs that are conventionally used or any acute stress that tends to influence the metabolism of blood glucose levels. In addition to this, there are other advantages too over fasting blood glucose levels such as the biological variability of HbA1c is quite low and it is less influenced by pre- analytical factors [2].

As a valuable test, HbA1c helps in glycemic control and gives an estimate of blood glucose levels over the preceding three to four months i.e., 12-16 weeks since the life-span of RBCs is approximately 120 days. The total duration of hyperglycemia and concentration of blood glucose levels primarily determine HbA1c concentration. Furthermore, there are several other adverse effects of raised blood glucose levels on the red blood cells besides the glycosylation of hemoglobin that eventually led to change in the structure of erythrocytes and characteristics of hemodynamics. These effects are an increase in the osmotic fragility of RBCs, an increase in the adhesive properties, reduction in the deformability and change in the mechanical properties [3].

In recent years, red cell distribution width (RDW) has been studied as a diagnostic and prognostic marker in various diseases like peripheral artery disease and cardiovascular mortality. RDW, one of the parameters of CBC has recently been studied & found to be increased in a number of health conditions like cardiovascular disease, cancer, infections & diabetes [4, 5].

The range in the size and volume of red blood cells (circulating erythrocytes) gives a measurement of RDW. The word 'width' refers to the difference in the size between the largest and the smallest red blood cell and not the individual red blood cell size. If the red blood cells are all about the same size, it means RDW is low. On the other hand, if both very small and very large red blood cells are present, RDW will be high. Normal range of RDW is between

12.2 to 16.1 percent for women and 11.8 to 14.5 percent for men. High or normal RDW had been seen in number of conditions like different types of anemia, heart, liver & kidney diseases, cancer etc. It is a component of routine complete blood count (CBCs) & can be measured by most hematologic analysers. It can be used as a potential screening tool. To differentiate between the causes of anemia, traditionally it has been used along with mean corpuscular volume (MCV) [6].

RDW have been found to be altered in uncontrolled diabetic patients because of consistent increase in HbA1c values that are known to induce functional and structural changes in Hb and an alteration in its cytoplasmic environment. The microvascular complications of Diabetes Mellitus are known to be more prevalent when HbA1c values are high, so an alteration in RDW may have a role in the diagnosis & monitoring of glycemic status along with its complications. Present study aims to analyze the correlation between HbA1c with RDW in T2DM patients.

Methodology

Study design: Present study was a single centric, observational, case control, hospital-based study conducted by taking the 50 healthy controls and 50 diabetic cases. Patients were categorized as diabetic and non-diabetic as per American Diabetes Association Diagnostic Criteria which is as follows: Fasting Blood Glucose >/=126mg/dL or 2 hr post-prandial blood sugar >/=200mg/dL or HbA1C>/=6.5% or in a patient with classical symptoms of hyperglycemia or hyperglycemic crisis, Random Blood Sugar >/=200mg/dL.

Blood sample: 3 ml blood sample was taken to analyze the RDW and HbA1c levels. HbA1c was done using HbA1c Flex reagent cartridges and is based on a turbidimetric inhibition immunoassay (TINIA) principle. Fasting Blood Glucose, 2-hour Post-Prandial Blood Glucose, Random Blood Glucose was done by Hexokinase Method. RFT- BUN was measured using a Urease UV/GLDH method. RDW was analysed using five chamber

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automated analyser sysmex XN- 550.

Statistical analysis: The statistical analysis was carried out using SPSS 27.0. For quantitative variables, mean and standard deviation was used as measures of central tendency and variability respectively. For qualitative variable, fraction of total and percentages was calculated. Chi-square test was used to compare two qualitative groups and unpaired t-test was used to compare two quantitative groups. Pearson's correlation was used to analyze correlation between two quantitative variables. A p value <0.05 was considered as significant.

Results

The mean age of patients was 59.54±10.78 in the cases and was 55.40±15.63 in control group with no significant difference between the two groups. In cases, there were 21 females and 29 males whereas in controls, there were 26 females and 24 males but the difference between the two groups is not significant. In cases, the number of illiterate patients was significantly high compared to the controls. Marital status revealed that 38 cases and 45 controls were married and rest of patients were unmarried or widow with no significant difference between the two groups. Significantly a greater number of patients in control group belonged to the rural area compared to the cases (Table 1).

Table 1: Sociodemographic determinants of cases and controls.

Variable	Subgroup	Case	Control	P value
Mean age		59.54±10.78	55.40±15.63	0.126
Gender	Female	21	26	0.316
	Male	29	24	
Education	Illiterate	23	5	0.007*
	Primary	6	5	
	Secondary	15	27	
	Graduation	6	12	
Marital status	Married	38	45	0.145
	Unmarried	1	1	
	Widow	11	4	
Locality	Rural	3	20	0.000*
	Urban	47	30	

The mean FBS was 215.30±89.16 in cases which is significantly high compared to 96.50± 4.84 in controls. The mean 2h-PP was 252.40±70.40 in cases which is significantly high compared to 143.56±14.44in controls. The mean RBS was 311.12±144.86 in cases which is significantly high compared to 164.80±19.17 in controls. The mean HbA1c was 10.79±2.45 in cases which is significantly high compared to 5.59±0.31 in controls. The mean RDW was 13.69±1.31 in cases and 13.40±1.17 in controls which do not differ significantly.

Table 2: Blood glucose, HbA1c and RDW in cases and controls.

Variable	Case	Control	P value
FBS	215.30±89.16	96.50±4.84	0.000*
2h-PP	252.40±70.40	143.56±14.44	0.000*
RBS	311.12±144.86	164.80±19.17	0.000*
HbA1c	10.79±2.45	5.59±0.31	0.000*
RDW	13.69±1.31	13.40±1.17	0.296

In diabetes patients, a non-significant positive correlation was observed between the HbA1c and RDW with the correlation coeffect of 0.027.

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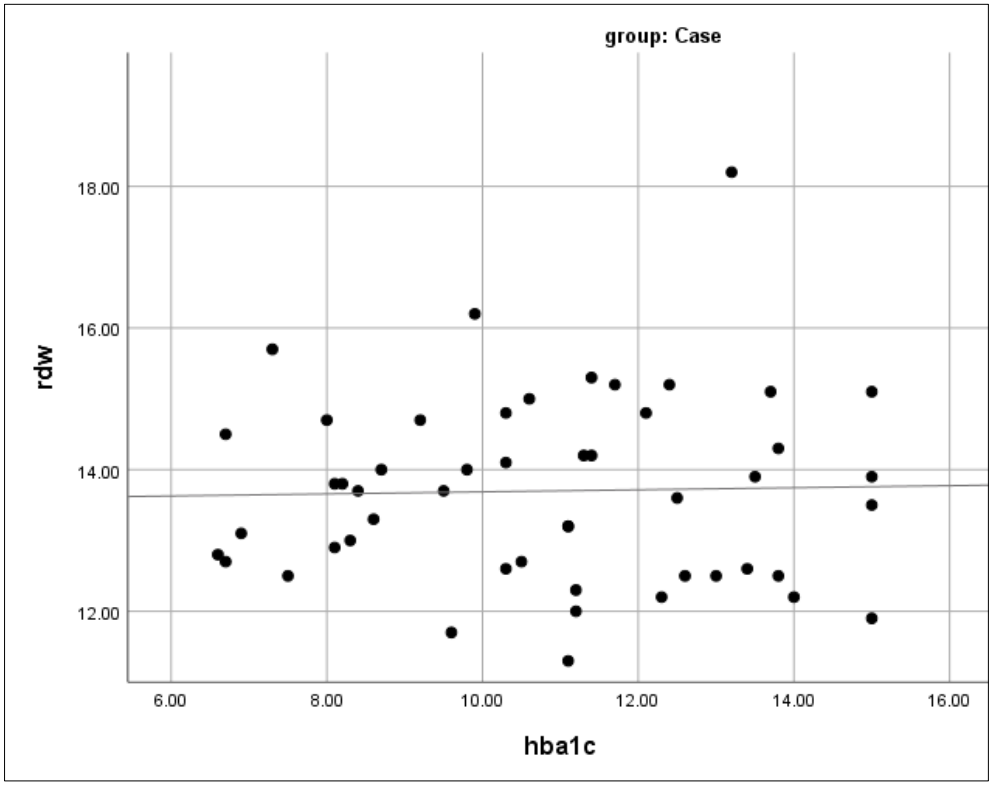

Fig 1: Correlation between the RDW and HbA1c.

Discussion

Red cell distribution width (RDW) is one of the parameters of Complete Blood Count test and has been studied as a potential diagnostic and prognostic surrogate marker in various diseases, given its advantage of being an easily available, cost-friendly and a routinely done test. Recent research has demonstrated that the red cell distribution width (RDW) and other complete blood count indices can be used as prognostic markers because they are correlated with HbA1c and diabetic complications; therefore they can be used as a predictive marker for diabetic control [7, 8]. However, some authors have disputed the role of RDW in diabetes mellitus [9, 10].

Since the initial studies of red cell distribution width's (RDW's) predictive usefulness in patients with heart failure, the evidence linking it to an elevated risk of mortality has been stronger. Additionally, it has been said to be able to predict cardiovascular and overall mortality on its own in a variety of high-risk categories as well as in the general population [11, 12]. Additionally, it has been demonstrated to be a major predictor of death in a wide range of diseases including cancer, obesity, and renal diseases [13]. Because of this, several researchers claimed that a correlation between RDW and diabetes prognosis may be present [7].

The relationship between RDW and HbA1C was also observed in a study by G. Lippi *et al*. in 2515 patients over the age of 65. RDW was found to have a significant relationship with HbA1C in Southern European individuals over 65. In DM development risk prediction, RDW may be a new parameter according to their study [14]. RDW and HbA1C correlation was assessed in a study by V. Veranna *et al*. in healthy adults. RDW was found to be a predictor of the onset of T2DM in healthy adults without history of diabetes [15].

Another study found that, regardless of other risk variables, low RDW levels were associated with an increased incidence of DM. It was found to be a potential contributing marker in assessing the disease's risk of onset in people with DM development risk [16].

In the present study, RDW and HbA1c did not show a statistically significant correlation

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among diabetes patients. Similarly, RDW and HbA1c were not shown to be significantly correlated in a study conducted by Demir *et al*. in 2016 [17].

RDW and HbA1C have been found to have a close relationship in studies with much larger patient populations; the reason we were unable to detect this relationship may have been due to the small patient population in our groups. It is too soon to determine the significance of RDW in diabetic patients and that many more studies are necessary before a clear consensus can be reached. Therefore, further research on this topic involving larger patient population is required.

Conclusion

Present study was a single centric, prospective, case-control study which analysed the diagnostic significance of RDW in Type 2 Diabetic patients and their correlation with HbA1c. The comparison of the case and control group revealed no significant difference in mean RDW. Correlation analysis among cases revealed a statistically non-significant positive correlation of HbA1c with the RDW. Since it was a single centre study with a small number of patients, we require further studies taking a large population as study sample in order to have more clarity and arrive at a consensus whether simple blood parameters like RDW can be used as a diagnostic marker to know the glycemic status and predict complications due to Diabetes Mellitus.

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ISSN 2515-8260 Volume 10, Issue 02, 2023

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