Association of the Red Cell Distribution Width with Complete Blood Count, Glycated Hemoglobin and Vitamin D in Patients with Type 2 Diabetes Mellitus- Across Sectional Study

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The current study was aimed to assess the association of the Red Cell Distribution Width (RDW) with Glycated haemoglobin (HbA1C) and Vitamin D in Patients with Type 2 Diabetes Mellitus to provide insight into the potential physiological mechanisms and predictive significance of RDW fluctuations in patients with heart failure who are diabetic. Material &Methods: The cross-sectional design of this study was utilized to investigate a cohort of 150 patients who had received a diagnosis of type 2 diabetes mellitus. The assessment centered on the evaluation of comorbidities, red cell distribution width (RDW), and glycemic management in addition to vitamin D levels. Information was gathered via questionnaires, encompassing demographic details as well as medical history. Blood samples were assessed for RDW, total blood count, HbA1c, and Vitamin D concentrations using automated analyzers. The statistical analysis was performed utilizing version 27 of SPSS. Results: The study found low relationships between HbA1c and Vitamin D (r = -0.033, p = 0.691), RDW and HbA1c (r = -0.046, p = 0.573), and RDW and Vitamin D (r = -0.128, p = 0.118). Furthermore, Vitamin D had diverse connections with CBC values, suggesting a complex link within the setting of type 2 diabetes mellitus. Conclusion: The findings of the current study indicated an association between the RDW and RBCs, Hb and Red blood cell indices (HCT, MCV, MCH and MCHC) in patients with T2DM. The RDW could therefore serve as potential marker for the management of patients with T2DM.

Keywords: Glycated Hemoglobin; Vitamin D; Red Cell Distribution Width.

A regular complete blood count can yield the Red Cell Distribution Width (RDW), a helpful statistic for assessing the variability in red blood cell volume. The size of circulating erythrocytes varies, with higher levels observed in conditions including recent bleeding, iron deficiency anaemia [1,2]. Apart from its traditional use in the investigation of blood diseases, RDW is a significant predictor

of adverse cardiovascular outcomes in the general population as well as in certain patient subgroups [3]. Elevated RDW levels have been strongly linked to increased rates of cardiovascular morbidity and death in patients undergoing percutaneous coronary procedures, heart failure, and coronary artery disease (CAD), according to many studies. In addition, diabetes mellitus accelerates the development of atherosclerosis, increasing the risk of cardiovascular issues. Diabetes mellitus is characterized by elevated oxidative stress and inflammation in blood vessels[4]. The relationship between RDW and diabetes mellitus has been the subject of recent research, which highlights RDW's potential as a predictor of long-term mortality in diabetic patients from all causes. The association between RDW and diabetes includes a variety of comorbidities, including peripheral artery disease, neuropathy, and nephropathy, in addition to the cardiovascular effects [5]. Studying the intricate relationship between RDW and these issues is crucial, particularly in the case of people with type 2 diabetes who have frequently been exposed to high blood sugar levels. Notably, there has been a growing emphasis on examining RDW in connection to macro- and microvascular issues related to diabetes[6]. Previous studies have indicated a significant association between high RDW levels and an increased risk of heart failure and nephropathy in individuals with diabetes. However, nothing is now known about the potential association among a particular population of people with type 2 diabetes, RDW, peripheral vascular disease, and peripheral neuropathy [7]. Also Hyperglycemia in diabetes can indeed result in elevated fibrinogen levels, a condition known as hyperfibrinogenemia. This heightened fibrinogen can initiate the coagulation cascade, potentially leading to atherothrombotic events characterized by the formation of blood clots within the arteries. These complications can be particularly severe in women, potentially contributing to pregnancy-related issues [8-10]. Ahigh Red Cell Distribution Width (RDW) are associated with poorer blood sugar regulation, lower vitamin D levels, and an increased risk of diabetic complications, including peripheral vascular disease, neuropathy, and nephropathy, in people with type 2 diabetes mellitus[11]. Furthermore, we suggest that RDW may serve as a prognostic marker for adverse cardiovascular events in a high-risk diabetic cohort requiring laser treatment for proliferative diabetic retinopathy. This study aims to rectify this shortcoming by conducting a comprehensive evaluation of the relationship between RDW and complications associated with the type 2 diabetes mellitus patients.

The relationship between RDW and T2DM has been studied for several years, and there are no consistent results. to assess the association of the Red Cell Distribution Width (RDW) with Glycated Haemoglobin (HbA1C) and Vitamin D in Patients with Type 2 Diabetes Mellitus to provide insight into the potential physiological mechanisms and predictive significance of RDW fluctuations in patients with heart failure who are diabetic.

MATERIALS AND METHODS

The current study used is a cross-sectional analysis. The research sample consists of diabetic individuals who are between the ages of 20 and 79. Between April and June of 2022, the data gathering took place. To collect relevant information, participants were provided with a well-designed questionnaire that inquired about their demographics, the medical history of their families, the duration of their diabetes, and any ailments that were present at the same time. It was possible to conduct a more in-depth analysis of the information that was gathered thanks to the structured questionnaire, which proved to be an efficient instrument for obtaining essential patient characteristics. The inclusion criteria were satisfied by every single person who had been diagnosed with type 2 diabetes mellitus and who sought medical treatment. To preserve the study's impartiality and validity, the researchers did not include patients who were pregnant, patients who were under the age of 18, or patients who did not provide their consent.

To determine the HbA1c and Complete Blood Count (CBC) values, tests were performed on blood samples that were collected using EDTA tubes. In addition, a second blood sample of two millilitres was collected into a tube containing lithium heparin to determine the levels of 25-hydroxyvitamin D. It is necessary to utilize certain tubes for particular analyses to minimize the risk of cross-contamination and ensure

that the results of the tests are accurate. When investigating the platelet indices parameters, the Beckman Coulter UniCel DxH-800/900, which is a very effective five-part auto analyzer, was utilized. Every sample may be evaluated using this analyzer, which can evaluate 23 parameters. In addition, the Beckman Coulter DXC AU 700 analyzer was utilized to carry out the HbA1c test, whilst the Cobas 6000e/601 analyzer was utilized to carry out the 25-hydroxyvitamin D assay. Both analyzers were utilized all during the testing process. In recent years, the highly sophisticated analyzers have garnered a substantial amount of interest because to the outstanding precision they possess and the consistent transmission of exact laboratory data that they accomplish.

It was with the assistance of the Statistical Package for Social Science (SPSS) version 27 that the analysis of the data was carried out, which is a software program that is frequently utilized for statistical applications. During the process of analysis, many statistical methods were utilized, including correlation analysis, descriptive statistics, and the Mann-Whitney U-test, amongst others. Within the population of individuals who have been diagnosed with type 2 diabetes mellitus, the deployment of these methodologies made it possible to conduct an in-depth investigation of the links that exist between vitamin D levels, glycemic control, RDW, and comorbidities. A particular criterion of significance was specified as a p-value that was lower than 0.05. This was done to determine whether any of the detected linkages were statistically significant.

In its most basic form, this all-encompassing strategy entails a methodical process of data collection and analysis, which guarantees the dependability and accuracy of the results. Understanding the complexities of RDW and its intricate relationship to type 2 diabetes mellitus requires a firm foundation, which may be established through the combination of stringent inclusion/exclusion criteria, ethical concerns, and sophisticated laboratory technologies. In a way that is complementary to one another, each of these components contributes to the construction of this foundation. The objective of the effort is to make a significant contribution to the understanding of the scientific community by employing the methodical implementation of this stringent technology. The

findings of this study have the potential to have a substantial impact on clinical practices and treatment for those who are coping with diabetes-related diseases.

RESULTS

Demographic Distribution

Patients who had been diagnosed with type 2 diabetes mellitus were included in the study, and the genders were distributed in an approximately equal manner. The total number of participants was 150. 45.3% of the total participants were female, while 54.7% were male. The female participants made up most of the total. 74.7% of the sample population was composed of individuals aged 50 and over, as indicated by the age distribution, which exhibited a strong majority of individuals older than 50. There were 16.0% of participants who fell into the age range of 41-50 years, 6.7% of individuals who fell into the age range of 31-40 years, and 2.7% of participants who fell into the age range of 21-30 years. Regarding the diabetic duration, in most cases (62%) they were diagnosed with diabetic for more than 5 years and (38%) were less than 5 years. According to T2DM Complications (40%) they didn't have any complications and (60%) they had complications (Table 1).

Correlations of RDW with HbA1c, Vitamin D, and CBC Parameters

The following variables showed several statistically significant negative correlations with RDW: Mean Corpuscular Volume (MCV) ($r = -0.339$, $p = 0.000$), Mean Corpuscular haemoglobin (MCH) ($r = -0.401$, $p = 0.000$), Red Blood Cell count (RBC) ($r = -0.210$, $p = 0.010$), haemoglobin (HB) ($r = -0.434$, $p = 0.000$), Haematocrit (HCT) ($r = -0.384$, $p = 0.000$), and MCHC ($r = -0.306$, $p = 0.000$). The statistically significant negative connections that were discovered indicate that a variety of CBC parameters had lower values in correlation with greater levels of RDW.

Correlations of HbA1c with Vitamin D and CBC Parameters

The examination into the existence of a correlation between glycemic control (HbA1c), vitamin D, and complete blood count levels revealed associations that were primarily weak and negligible. Taking into consideration the fact that

the correlation between HbA1c and Vitamin D was found to be weakly negative (r = -0.033, p = 0.691), it can be concluded that there is no substantial linear connection between the management of glycemic levels and Vitamin D levels (Table 3). In the same vein, HbA1c revealed weak and statistically insignificant relationships with additional CBC parameters, such as RBC, RDW, HB, HCT, Platelets, and WBC. These connections were shown in the same manner as the previous one. The results of the study reveal that there is no significant linear link between the parameters of the CBC that were analyzed and the glycemic control that was determined by the HbA1c test.

Correlations of Vitamin D with CBC Parameters

According to the findings, there is a significant positive correlation (r = 0.156) between vitamin D and red blood cells (RBC), which indicates that higher levels of vitamin D are associated with a higher number of RBC. Vitamin D also shown significant inverse correlations with RDW (r = -0.128, p = 0.118), HCT (r = -0.386, p = 0.000), and MCHC (r = -0.203, p = 0.013). These findings were supported by statistical analysis

Table 1. Distribution of demographic data, Complications and Family history

		Frequency	Percent
Gender	Female	68	45.3
	Male	82	54.7
Age	21-30	4	2.7
	31-40	10	6.7
	41-50	24	16.0
	>50	112	74.7
Diabetic Duration	Less than 5 years	57	38.0
	More than 5 years	93	62.0
T2DM Complications	None	60	40.0
	Cardiovascular disease	6	4.0
	Diabetic foot	1	.7
	Hypertension	20	13.3
	Kidney disease	30	20.0
	Neuropathy	1	.7
	Kidney disease, Hypertension	32	21.3
Family History with T2DM	No	47	31.3
	Yes	103	68.7

Table 2. Correlations of RDW with HbA1c, vitamin D, and CBC

	RDW	
	Pearson Correlation	P. value
HbA1c	-.046	0.573
Vitamin D	-.128	0.118
RBC	-.210	0.010**
HB	-.434	0.000**
HCT	-.384	0.000**
MCV	-.339	0.000**
MCH	-.401	0.000**
MCHC	-.306	0.000**
Platelets	-.016	0.845
WBC	.131	0.110

Table 3. Correlations of HbA1c with Vitamin D and CBC

	HbA1c	
	Pearson Correlation	P. value
Vitamin D	-.033	0.691
RBC	-.050	0.542
RDW	-.046	0.573
HB	.038	0.646
HCT	.018	0.827
MCV	-.013	0.874
MCH	.033	0.692
MCHC	.024	0.768
Platelets	-.067	0.418
WBC	.130	0.114

Table 4. Correlations of Vitamin D with CBC

	Vitamin D	
	Pearson Correlation	P. value
RBC	.156	0.056
RDW	-.128	0.118
HB	.404	0.000**
HCT	.386	0.000**
MCV	.043	0.602
MCH	.114	0.165
MCHC	.203	0.013*
Platelets	.024	0.770
WBC	-.101	0.221

(Table 4). The findings of this study suggest that there is a connection between increasing levels of vitamin D and decreased RDW values, decreased haematocrit, and decreased mean corpuscular haemoglobin concentration [MHC].

DISCUSSION

Diabetes mellitus (DM) is an epidemic disorder that affects roughly 463 million people. 90% of those suffer from type 2 diabetes. According to some future studies are expected to reach 700 million cases of diabetes documented by 2045. Diabetes includes various complications, including nephropathy, neuropathy, changes in the angiogenic response and cardiovascular disease [13-14]. The data indicates that the most commonly occurring complications are cardiovascular disease, diabetic foot, hypertension, renal disease, and neuropathy (Table1). Notably, it acknowledges the prevalence of multiple complications, emphasizing that 30% of individuals diagnosed with T2DM experience two or more challenges. These results are consistent with broader research trends, as evidenced by a study published in Diabetes Care which reveals that a significant proportion (68%) of individuals with T2DM encounter at least one difficulty, with nearly a quarter (24%) contending with two or more problems. This underscores the intricate and interconnected characteristics of problems linked to type 2 diabetes mellitus (T2DM), emphasizing the need for a comprehensive approach to understanding and managing these diverse health obstacles.

It is recognized that the correlation between type 2 diabetes mellitus (T2DM) complications and various demographic factors— such as gender, age, and duration of diabetes— varies. This notion is supported by data published in PLOS Medicine, which indicates that individuals who were elderly, male, and had a prolonged medical history of diabetes had an increased risk of developing cardiovascular disease, renal disease, and neuropathy [15]. It is of the utmost importance to consider personalized risk assessments and actions that are tailored to the specific attributes of every patient.

Upon scrutinizing the research concerning the correlation between red cell distribution width (RDW) and various variables including glycemic control, vitamin D supplementation, and complications associated with type 2 diabetes mellitus (T2DM), intriguing observations emerge. The weak and statistically insignificant inverse relationship between RDW and HbA1c indicates that there may not be a direct correlation between RDW levels and the regulation of blood sugar levels. This finding aligns with existing knowledge and underscores the need for more sophisticated metrics to predict glycemic outcomes.

The correlation study indicates that Vitamin D and RDW have a moderately negative relationship. While lacking statistical significance, this suggests the potential existence of a pattern that warrants further examination. Subsequent investigations may delve deeper into the intricate relationship between RDW and Vitamin D levels, given the well-established importance of Vitamin D in various physiological processes and its correlation with complications associated with Type 2 Diabetes Mellitus (T2DM)[16].

Quantitative changes in RDW, in patients with T2DM are also evident in some existing reports [17-19]. The results of the correlation analysis reveal negative relationships between RDW and CBC parameters, such as RBC, HB, HCT, MCV, MCH, and MCHC, which are statistically significant. Increased levels of RDW are correlated with reduced values in various parameters, indicating potential irregularities in the dimensions and morphology of red blood cells. This finding provides evidence in favor of the notion that an elevated RDW could serve as a potential

sign of haematological changes associated with complications of type 2 diabetes mellitus. Chowta et al. studied the hemogram profile of 2 groups of elderly diabetics < 60 years &> 60 years and found that the RDW of patients > 60 years had a higher value than the younger group which was statistically significant (p-value 0.002) which can be correlated with our study [20].

By shedding light on the relationships between RDW and glycemic control, Vitamin D, and T2DM complications, the correlation results resolve the initial study concerns. While the correlation between RDW and glycaemic control is not robust and statistically significant, the associations with CBC parameters suggest a potential link between RDW and haematological changes associated with type 2 diabetes mellitus.

The study offers valuable insights into the prevalence of complications linked to Type 2 Diabetes Mellitus (T2DM), emphasizing the considerable incidence of diverse issues among those affected. The correlation analysis between RDW and additional biomarkers provides a comprehensive understanding of the possible associations between haematological changes and glycemic control [21]. Regarding the other parameters HbA1c, vitamin D, TWBCs and Platelets have shown no significant correlation with RDW. There is diversity in the results of previous studies regarding the correlation of these parameters and HbA1c; a study by Abdul Rabb et al Their study highlighted that RDW has a significant correlation with HbA1c[22]. Regarding the association between Vitamin D and RDW one study conducted by Otero et al concluded that in a nationwide sample of non-hospitalized adults within the United States, low 25OHD was associated with increased likelihood of elevated RDW [23].

To preventing or delaying the onset of problems associated with type 2 diabetes mellitus (T2DM), it is necessary to do more research in order to identify possible risk factors and design therapies that are specifically targeted, as suggested by these results. The results of this study improve our understanding of the complex interplay among metabolic regulation, haematological markers, and complications in individuals with type 2 diabetes mellitus (T2DM).

Study Limitations

Small cases number in the study and all sample were collected from single hospital in Ajman which confines its applicability to a specific demographic within the Ajman area only in UAE and thereby limits its generalizability; therefore, further studies with larger samples are recommended.

Also, we recommended to compare the red cell distribution in diabetic patients with different health complications.

Future Directions

Additional research is necessary to include studies that span over a longer period of time and include a broader range of demographics, in order to achieve a more thorough and complete knowledge. Through the examination of genetic variables, lifestyle impacts, and modern imaging methods, it is feasible to get a more thorough comprehension of the complex interaction of aspects that lead to issues related to type 2 diabetes mellitus.

CONCLUSION

The Red blood cells and their parameters are affected by T2DM and shows altered function and structure. The findings of the current study indicated a strong association between the RDW and RBCs, Hb and Red blood cell indices (HCT, MCV, MCH and MCHC) in patients with T2DM and the RDW could therefore serve as potential marker for the management of patients with T2DM.

ACKNOWLEDGMENT

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