



ORIGINAL ARTICLE

Correlation of HbA1c with red cell width distribution and other red cell indices in Type II diabetic females.

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ABSTRACT... Objective: To assess the correlation of HbA1c with hemoglobin concentration, RDW, and other red cell indices in Type II diabetes mellitus female patients. **Study Design:** Cross-sectional study. **Setting:** Department of Physiology, Al Nafees Medical College, and Pakistan Institute of Medical Sciences, Islamabad. **Period:** January 2019 to December 2020. **Material & Methods:** The study included 70 adult female diabetic patients, adhering to International Diabetes Federation guidelines. Exclusion criteria encompassed uncontrolled diabetes, pregnancy, renal issues, cardiac failure, and hemoglobinopathies. Laboratory tests, such as Complete Blood Count and HbA1c measurements, were conducted. SPSS version 23 was used for statistical analysis, employing mean, standard deviation, and Pearson's correlation to assess relationships among HbA1c, hemoglobin, Red Cell Distribution Width (RDW), and other red cell parameters. **Results:** A total of 70 female patients with diagnosed Type II diabetes mellitus were included in our study with a mean age of 40.45 ± 12.70 years. The Mean \pm SD of study variables like HbA1c, hemoglobin, MCV, MCHC, RDW, and FBS of the patients was $5.91 \pm 0.89\%$, 11.23 ± 1.59 gm/dl, 76.32 ± 9.50 fl, 31.02 ± 3.39 mg/dl, 12.78 ± 1.51 and 100.53 ± 15.52 mg/dl respectively. A significant correlation between HbA1c and RDW was found and showed that both variables were positively correlated with each other. ($r = 0.320$, $p = 0.001$). **Conclusion:** RDW correlates with HbA1C in female Type II diabetes patients, suggesting CBC, including RDW, as a cost-effective diagnostic marker alongside HbA1c for glycemic status assessment.

Key words: Diabetes, Diagnostic Marker, HbA1c, RDW.

INTRODUCTION

A chronic progressive metabolic disorder that causes inadequate control of blood glucose levels is called diabetes mellitus.¹ According to the International Diabetes Federation, the number of people suffering from diabetes is increasing day by day drastically and it is estimated that this number can reach up to 592 million by the year 2035.²

The main reason that is causing a drastic rise in the number of patients with this disease is basically urbanization and modernization.³ This drastic rise and increasing incidence of chronic disease causes an increase in macrovascular (coronary artery disease peripheral disease and stroke) and microvascular (diabetic neuropathy, neuropathy, and retinopathy) complications.

In low socio-economic countries diagnosis, management of the disease, follow-ups, and monitoring of the blood glucose level have always remained challenging for the health care providers. Hence, cost-effectiveness in terms of tools used for the assessments is always encouraged and is the need of the hour. HbA1c is a test that has been used for the assessment of blood glucose levels since 2010; however, it was used as a mechanism for the glycemic control assessment before.⁴ Hyperglycemia affects red blood cells in various ways. It changes the biomechanical characteristics of RBCs. It causes reduced deformability and increased adhesion and fragility. All these effects cause a change in hemodynamic characteristics and erythrocyte structure.⁵

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RBC, RDW, and its indices have been used for the diagnosis of various diseases in recent years.^{6,7} The red cell distribution width (RDW) is a part CBC test that measures the variability in the size of the red blood cells (RBC). RDW is used with MCV to help in finding the anemia's causes.^{8,9}

HbA1c increases constantly due to uncontrolled diabetes. The hemoglobin molecule and cytoplasmic environment within each red blood cell can change in terms of function and structure due to the consistent rise in HbA1c. Hence, RDW and RBC and its indices may alter. As diabetes mellitus is associated with increased HbA1c, alteration in RDW can be used for the diagnosis, monitoring, complications, and monitoring of the blood sugar level in diabetic patients. This study aimed to assess the association of HbA1c with hemoglobin concentration, RWD, and other red cell indices.¹⁰

MATERIAL & METHODS

This cross-sectional study was executed in the outpatient department of medicine at Al Nafees Medical College and Pakistan Institute of Medical Sciences, Islamabad from January 2019 to December 2020. The minimum sample size for the study was estimated as 70 diabetic females using a 5% level of significance, 95% confidence interval and 80% power of the test, 6.8% margin of error, and 9.19% prevalence¹¹ of Type II diabetes mellitus among females in Pakistan. Ethical approval of the study was taken from the ethical committee of the hospital (F.2/IUIC-ANMC/EC-132/2019). All the patients who participated signed an informed consent form prior to the study.

The diagnosed Type II diabetic females aged 18 years and above were included in this study through a nonprobability consecutive sampling

method. The diagnostics criterion for diabetes was used as provided by the International Diabetes Federation guidelines. Blood samples were taken in CBC bottles as well as in serum gel bottles. Samples were saved and stored at 4-C to be analyzed for CBC and HbA1c. FBG was taken by glucometer to exclude uncontrolled diabetes. Urine was tested for proteins by Dipstick to exclude cases of diabetic nephropathy. Patients with a history of anemia, uncontrolled diabetes, pregnancy, renal complications, cardiac failure, chronic illness, and hemoglobinopathies were excluded from the study. After an informed consent, the medical history of the patients was taken. The participants underwent a thorough physical examination. The necessary laboratory investigations like CBC, HbA1c, and FBS were also recorded.

Analysis of Data: Data was entered and analyzed in SPSS version 23. Descriptive and inferential statistics were applied for the analysis. As all the variables were in continuous form, mean and standard deviation were calculated for these variables. Pearson Product Moment Correlation was applied to assess the correlations between the study variables. A $p\text{-value} \leq 0.05$ was considered significant and a $p\text{-value} \leq 0.01$ was considered to be highly significant.

RESULTS

A total of 70 female patients with diagnosed Type II diabetes mellitus were included in our study with a mean age of 40.45 ± 12.70 years. Descriptive analysis revealed the mean distribution of all the study variables. The mean of study variables like HbA1c, hemoglobin, MCV, MCHC, RDW, and FBS of the patients was $5.91 \pm 0.89\%$, $11.23 \pm 1.59\text{gm/dl}$, $76.32 \pm 9.50\text{fl}$, $31.02 \pm 3.39\text{mg/dl}$, 12.78 ± 1.51 and $100.53 \pm 15.52\text{mg/dl}$ respectively. (Table-I)

Parameter	Minimum	Maximum	Mean	St. Deviation
HbA1c	4.10	9.50	05.91	0.89
Hemoglobin	7.40	15.10	11.23	1.60
Mean corpuscular volume (MCV)	60.00	97.00	76.32	9.50
Mean corpuscular hemoglobin (MCH)	15.00	39.00	31.02	3.39
Red cell width distribution (RDW)	9.91	16.02	12.78	1.51
Fasting blood sugar (FBS)	63.00	125.00	100.53	15.52

Table-I. Mean distribution of HbA1c, RDW, and another parameter of red cells

The correlation analysis revealed that the HbA1c was negatively correlated with the hemoglobin. ($r=-0.490$, $p\leq 0.0001$) The correlation between MCV and MCHC turned out to be significantly negative. ($r= -0.298$, $p=0.002$ & $r=-0.208$, $p=0.029$ respectively). The FBS revealed in significant relationship with HbA1c showing that a change in hemoglobin will not essentially affect the change in FBS in our study. (Table-II)

indices	r	P-Value
Hemoglobin (Hb)	-0.490	0.0001**
Mean corpuscular volume (MCV)	-0.298	0.002**
Mean corpuscular hemoglobin concentration (MCH)	-0.208	0.029*
Red cells width distribution (RDW)	0.320	0.001**
Fasting blood sugar (FBS)	0.038	0.690

Table-II. Correlation of hemoglobin, RDW, and other red cell indices with HbA1c
**** Highly Significant, * significant**

The correlation between HbA1c and RDW was found to be significant and showed that both variables were positively correlated with each other. ($r= .320$, $p=0.001$)

		HbA1c	RDW
HbA1c	Pearson Correlation	1	.320**
	Sig. (2-tailed)		.001
	N	70	70
RDW	Pearson Correlation	.320**	1
	Sig. (2-tailed)	.001	
	N	70	70

** . Correlation is significant at the 0.01 level (2-tailed).

Table-III. Correlation of RDW and HbA1c

Limitation of the Study

The study’s limitations include the need for more extensive, controlled research to establish the connection between HbA1c and RBC parameters while accounting for potential confounding factors. Additionally, conducting larger, multi-centered studies is warranted to explore this relationship in greater depth.

Inclusion Criteria

Females over 18 years of age will be included

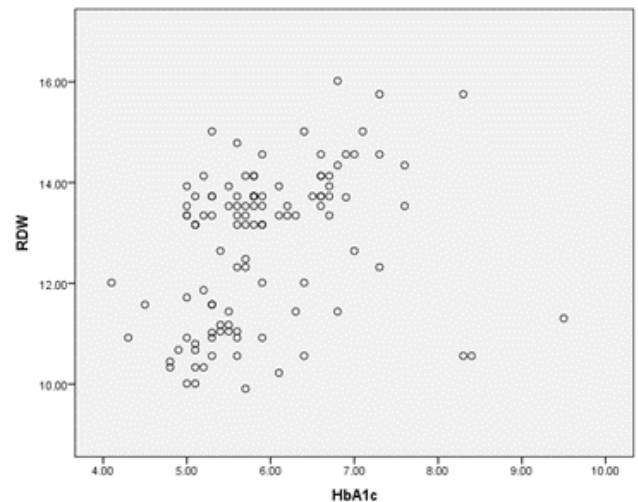


Figure-1. Scatter plot of HbA1c and RDW showing the correlation between them

Exclusion criteria

Patients with uncontrolled diabetes or with renal complications (protein urea), cardiac failure, hemoglobinopathies, and pregnancy will be excluded from the study.

Ethical Consideration

Permission to carry out the proposed study was taken from the ethical review committee of Al Naffees Medical College and PIMS Hospital, Islamabad (Annexure attached)

DISCUSSION

Global T2DM incidence and prevalence vary based on ethnicity and geography, with Japanese, Hispanics, and Native Americans displaying heightened susceptibility.¹²⁻¹³ the precise reasons for these disparities are uncertain, yet potential factors encompass contemporary lifestyle choices promoting obesity, socioeconomic influences, and intricate genetic-environment interactions.¹⁴

Genetic predisposition is a central factor in T2DM risk, as evidenced by recent genome-wide association studies unveiling its complex polygenic nature, with the majority of loci influencing T2DM risk through insulin secretion, and a minority affecting insulin action.¹⁵⁻¹⁶ Certain variants have been classified based on their potential intermediate roles in T2DM pathophysiology, including four associated with

insulin resistance, two leading to reduced insulin secretion and fasting hyperglycemia, nine linked to decreased insulin secretion with normal fasting glycemia, and one affecting insulin processing.¹⁷

During routine investigations of the patients, a test CBC is performed which has some components. RDW is among one of those components. It is a parameter of RBCs that is available without any extra cost. Hence, it can be used as an indicator to measure the variability in the size of the red blood cells.^{18,19} A number of studies have proved that RDW may be used with MCV to help in finding the causes of various disease and their complications.²⁰

In our study, the correlation between HbA1c and RDW was found to be significant and showed that both variables were positively correlated with each other with correlation ($r= 320$, $p<0.01$). Whereas, the same results were produced in another study conducted by Salimon et al. which was conducted on both males and females and showed a significant correlation for the female population ($r=0.40$, $p<0.01$).²¹ Another study by Suryavanshi et al. suggested the same results in their study ($r=0.235$, $p<0.01$).²²

The correlation analysis revealed that the HbA1c was negatively correlated with the hemoglobin. ($r=-0.490$, $p\leq 0.0001$) The correlation between MCV and MCHC turned out to be significantly negative. ($r= -0.298$, $p=0.002$ & $r=-0.208$, $p=0.029$ respectively). There is a huge diversity in the results of previous studies conducted; showing the relationship between these parameters. A study conducted by Koga et al. showed that MCV and MCHC were significantly and negatively associated with HbA1c for premenopausal women ($r= -0.368$, $p=0.0001$ & $r=-0.320$, $p=0.0001$, respectively) whereas for post-menopausal women no significant association was observed ($r=0.019$, $p=0.771$ & -0.104 , $p=0.107$, respectively).²³ In our study, no significant correlation was observed between FBS and HbA1c ($r=0.038$, $p=0.690$) which is comparable to a study conducted by Hussain et al. which revealed that in their study population, no relationship between both variables was

examined ($r=0.098$, $p=0.072$).²⁴

CONCLUSION

It is a fact that diabetes is a life-long disease and patients with this disease always kept asking for a cost-effective way of monitoring this. Moreover, in low socio-economic countries diagnosis, management of the disease, follow-ups, and monitoring of the blood glucose level have always remained challenging for healthcare providers. Hence, cost-effectiveness in terms of tools for the assessment of this disease is need of the hour. In this perspective, the current study was carried out which showed that RDW is significantly correlated with HbA1c. It is an inexpensive test that is freely available and may be used for the assessment of glycemic status. However, more studies on high scales can be conducted to closely observe this relation.

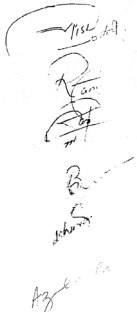
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REFERENCES

1. Hameed I, Masoodi SR, Mir SA, Nabi M, Ghazanfar K, Ganai BA. **Type 2 diabetes mellitus: From a metabolic disorder to an inflammatory condition.** World journal of diabetes. 2015 15; 6(4):598.
2. Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE. **Global estimates of diabetes prevalence for 2013 and projections for 2035.** Diabetes research and clinical practice. 2014; 103(2):137-49.
3. Asif M. **The prevention and control the type-2 diabetes by changing lifestyle and dietary pattern.** Journal of education and health promotion. J Educ Health Promot. 2014; 3: 1-8.
4. **International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes.** Nathan DM. Diabetes Care. 2009; 32:1327-1334.
5. Livshits L, Srulovich A, Raz I, Cahn A, Barshtein G, Yedgar S, Eldor R. **Effect of short-term hyperglycemia on protein kinase C alpha activation in human erythrocytes.** The Review of Diabetic Studies: RDS. 2012; 9(2-3):94.
6. Li N, Zhou H, Tang Q. **Red blood cell distribution width: A novel predictive indicator for cardiovascular and cerebrovascular diseases.** Dis Markers. 2017:2017:7089493.

7. Al-Kindi SG, Refaat M, Jayyousi A, Asaad N, Al Suwaidi J, Abi Khalil C. **Red cell distribution width is associated with all-cause and cardiovascular mortality in patients with diabetes.** *Biomed Res Int.* 2017; 2017:5843702. doi:10.1155/2017/5843702
8. Adeoye S, Abraham S, Erlikh I, Sarfraz S, Borda T, Yeung L. **Anaemia and Haemoglobin A1c level: Is there a case for redefining reference ranges and therapeutic goals?** *BJMP* 2014; 7(1):a706.
9. Montagnana M, Cervellin G, Meschi T, Lippi G. **The role of red blood cell distribution width in cardiovascular and thrombotic disorders.** *Clinical chemistry and laboratory medicine.* 2012; 50(4):635-41.
10. Bhutto AR, Abbasi A, Abro AH. **Correlation of hemoglobin A1c with red cell width distribution and other parameters of red blood cells in type ii diabetes mellitus.** *Cureus.* 2019; 11(8):e5533. Published 2019 Aug 30. doi:10.7759/cureus.5533
11. Meo SA, Zia I, Bukhari IA, Arain SA. **Type 2 diabetes mellitus in Pakistan: Current prevalence and future forecast.** *JPMA. The Journal of the Pakistan Medical Association.* 2016; 66(12):1637-42.
12. Chan, J.C.; Cheung, C.K.; Swaminathan, R.; Nicholls, M.G.; Cockram, C.S. **Obesity, albuminuria and hypertension among Hong Kong Chinese with non-insulin-dependent diabetes mellitus (NIDDM).** *Postgrad. Med. J.* 1993; 69:204-210. [CrossRef]
13. Liu, L.L.; Yi, J.P.; Beyer, J.; Mayer-Davis, E.J.; Dolan, L.M.; Dabelea, D.M.; Lawrence, J.M.; Rodriguez, B.L.; Marcovina, S.M.; Waitzfelder, B.E.; et al. **Type 1 and Type 2 diabetes in Asian and Pacific Islander U.S. youth: The SEARCH for Diabetes in Youth Study.** *Diabetes Care.* 2009; 32:(Suppl. 2), S133-S140. [CrossRef]
14. Haines, L.; Wan, K.C.; Lynn, R.; Barrett, T.G.; Shield, J.P. **Rising incidence of type 2 diabetes in children in the U.K.** *Diabetes Care.* 2007; 30:1097-1101. [CrossRef]
15. Fuchsberger, C.; Flannick, J.; Teslovich, T.M.; Mahajan, A.; Agarwala, V.; Gaulton, K.J.; Ma, C.; Fontanillas, P.; Moutsianas, L.; McCarthy, D.J.; et al. **The genetic architecture of type 2 diabetes.** *Nature.* 2016; 536:41-47. [CrossRef] [PubMed]
16. McCarthy, M.I. **Genomics, type 2 diabetes, and obesity.** *N. Engl. J. Med.* 2010; 363:2339-2350. [CrossRef] [PubMed]
17. Dimas, A.S.; Lagou, V.; Barker, A.; Knowles, J.W.; Magi, R.; Hivert, M.F.; Benazzo, A.; Rybin, D.; Jackson, A.U.; Stringham, H.M.; et al. **Impact of type 2 diabetes susceptibility variants on quantitative glycemic traits reveals mechanistic heterogeneity.** *Diabetes* 2014; 63:2158-2171. [CrossRef] [PubMed]
18. Abraham IV LL, Ramos JD, Cunanan EL, Tiongson MD, Punzalan FE. **Red cell distribution width and mortality in patients with acute coronary syndrome: A meta-analysis on prognosis.** *Cardiology Research.* 2018; 9(3):144.
19. Yaman H, Celik T, Akgul EO, Cayci T, Kurt Y. **Red cell distribution width and acute coronary syndromes.** *International journal of cardiology.* 2010; 145(2):353.
20. Perlstein TS, Weuve J, Pfeffer MA, Beckman JA. **Red blood cell distribution width and mortality risk in a community-based prospective cohort.** *Archives of internal medicine.* 2009; 169(6):588-94.
21. Salimon AH, Patil HA. **Correlation of red blood cell distribution width (RDW) and hemoglobin A1C (HbA1C) levels in diabetic individuals.** *Int J Innov Res Sci Eng Technol.* 2017; 6:8227-39.
22. Suryavanshi C, Manjula SD, Bekur R, Rao RK. **Association of increased levels of glycated hemoglobin with variations in red blood cell parameters in diabetes mellitus.** *International Journal of Advanced Research.* 2015; 3(6):31-7.
23. Koga M, Morita S, Saito H, Mukai M, Kasayama S. **Association of erythrocyte indices with glycated haemoglobin in premenopausal women.** *Diabetic medicine.* 2007; 24(8):843-7.
24. Hussain A, Ali I, Ijaz M, Rahim A. **Correlation between hemoglobin A1c and serum lipid profile in Afghani patients with type 2 diabetes: hemoglobin A1c prognosticates dyslipidemia.** *Therapeutic advances in endocrinology and metabolism.* 2017; 8(4):51-7.

AUTHORSHIP AND CONTRIBUTION DECLARATION

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2	Roomisa Anis	Methodology, Discussion.	
3	Rashad Mahmood	Write up, Data analysis.	
4	Beenish Zafar	Literature review.	
5	Khurram Shehzad Khan	Referencing write-up.	
6	Azhar Ali	Proof reading.	