Indonesian Journal of Medicine (2024), 09(01): 45-51
Masters Program in Public Health, Universitas Sebelas Maret

Original Research
Open Access

# Correlation between HbA1c Levels and Red Distribution Cell Width in Type 2 Diabetes Mellitus Patients

**Hadiyatur Rahma[1)], Jelita Siregar[2)], Santi Syafril[3)], Ratna Akbari Ganie[2)], Dewi Indah Sari Siregar[2)], Almaycano Ginting[2)]**

[1)]Faculty of Medicine, Universitas Islam Sumatera Utara
[2)]Department of Clinical Pathology Faculty of Medicine, Universitas Sumatera Utara/ H. Adam Malik General Central Hospital, Medan, North Sumatera, Indonesia
[3)]Department of Internal Medicine, Endocrine Metabolic Diabetes Division Faculty of Medicine, Universitas Sumatera Utara/ H. Adam Malik General Central Hospital, Medan

*Received: 27 September 2023; Accepted: 6 December 2023; Available online: 10 January 2023*

## ABSTRACT

**Background:** HbA1c is used as a parameter for diagnosis and monitoring of diabetes mellitus (DM). Apart from that, HbA1c, red blood cells also experience changes which result in changes in erythrocyte structure and hemodynamic characteristics. The parameter that changes in this case is red cell distribution width (RDW). This study aimed to analyze correlation between HbA1c levels and RDW in type 2 DM patients.
**Subjects and Method:** This a cross sectional study conducted at H. Adam Malik General Central Hospital, Medan, North Sumatera, Indonesia, from December 2022-April 2023. Total sample of 75 type 2 DM patients was selected consecutively. The dependent variable was RDW. The independent variable was HbA1c. Data of RDW and HbA1c were collected from complete blood count test. Data were analyzed using the Spearman correlation.
**Results:** HbA1c was negatively associated with RDW, but it was statistically non-significant (r= -0.08; p= 0.508).
**Conclusion:** HbA1c is negatively associated with RDW, but it is statistically non-significant.

**Keywords:** diabetes melitus, HbA1c, red cell distribution

**Correspondence:**
Hadiyatur Rahma. Faculty of Medicine, Universitas Islam Sumatera Utara, Medan, Indonesia. Email: hadiyatur.rahma@fk.uisu.ac.id. Mobile: +628535-9071255.

**Cite this as:**
Rahma H, Siregar J, Syafril S, Ganie RA, Indah D, Siregar S, Ginting A (2024). Correlation between HbA1c Levels and Red Distribution Cell Width in Type 2 Diabetes Mellitus. Indones J Med. 09(01): 45-51. https://doi.org/10.26911/theijmed.2024.09.01.07.



## BACKGROUND

Diabetes Mellitus (DM) is a metabolic disease characterized by chronic hyperglycemia that occurs due to abnormalities in insulin secretion, insulin action or both. Indonesia ranks among the countries with a significant number of Diabetes Mellitus (DM) cases in Southeast Asia, with approximately 10.7 million individuals affected, constituting 9.2% of the population (Saedi et al, 2019). The prevalence of type 2 DM in Indonesia in 2018 was reported to be 2%,

based on diagnoses made by doctors in individuals aged 15 years and older (Basic Health Research, 2019). One of the parameters used in monitoring DM currently is HbA1c, namely glycated hemoglobin, which is also used in diagnosing DM. The HbA1c value depends on the blood glucose value and the duration for which hyperglycemia (blood glucose levels above normal values) occurs. HbA1c is used as a parameter for diagnosis and monitoring of DM because of the effect of hyperglycemia on changes in hemoglobin. Apart from HbA1c, red blood cells also apparently experience changes in the form of decreased deformability, increased cell adhesion, increased osmotic fragility which results in changes in erythrocyte structure and hemodynamic characteristics (Tsilingiris et al., 2021).

A high RDW score implies poor erythropoiesis, red blood cell disintegration, chronic inflammation, and oxidative stress. RDW and HbA1c which have a positive relationship are mentioned in various studies on DM and are considered to have a role in the course of the disease and its complications. Routinely measuring RDW values can be used as a practical biomarker in assessing risk in DM patients (Jahan et al, 2018)

A study in Pakistan on 119 type 2 DM patients found a positive and significant correlation berween HbA1c and RDW (r= 0.193; p= 0.035), while other hematological parameters, such as MCV, hemoglobin and platelets were not correlated with RDW (Bhutto, Abbasi and Abro, 2019).

Other study in Dhaka, Bangladesh-India on 80 type 2 DM patients also showed a positive correlation between RDW and HbA1c levels (r=0.45; p=0.001) (Jahan et al., 2018). Another study that compared the correlation of RDW and HbA1c levels in male (r= 0.40) and female (r= 0.04) (Jahan et al, 2018).

A study in Chennai, India with a sample of 610 Type 2 DM patients reported a significant relationship between RDW and HbA1c (OR= 1.36; p= 0.003) (Biswas and Srinivasan, 2020).

A study conducted in Athens, Greece, with a sample size of 100 healthy individuals and 83 Type 2 DM patients found a significant positive correlation between RDW and HbA1c on people with normal blood sugar (r=0.31; p=0.001) vs type 2 DM (r= -0.28; p=0.011) (Tsilingiris et al, 2021). A study by Wang et a. (2020) reported that RDW value was associated with the risk of DM is (HR= 1.31; 95% CI= 1.16 to 1.48).

Previous study have differrent results and study in Indonesia is scarce. This study aimed to examine the correlation between HbA1c and RDW in type 2 DM.

## SUBJECTS AND METHOD

### 1. Study Design

This was a cross sectional study conducted at H. Adam Malik General Central Hospital, Medan, North Sumatera, Indonesia, from December 2022-April 2023.

### 2. Population and Sample

A sample of 75 type 2 DM patients aged 30-60 years old was selected consecutively. Patients with hematological disorders (i.e acute, chronic anemia, aplastic anemia, hemoglobinopathy), chronic liver disease, chronic kidney disease, or chronic infectious diseases (i.e malaria, tuberculosis, or malignancies) were excluded.

### 3. Study Variables

The dependent variable was RDW. The independent variable was HbA1C.

### 4. Operational Definition of Variables

**Type 2 diabetes mellitus** is a metabolic disease characterized by chronic hyperglycemia with clinical symptoms with HbA1c >6.5% using standardized methods.

**HbA1c** is hemoglobin glycated with blood glucose. Hyperglycemia if the HbA1c level is

> 6.5%.

**Red cell distribution width (RDW)** is the variability of erythrocyte cell shape and size.

**5. Study Instrument**

Patients were analyzed using interviews to obtain data on subject characteristics including age, gender, family history of diabetes mellitus.

**6. Data Analysis**

Correlation between HbA1C and RDW was examined using Spearman correlation.

**7. Research Ethics**

This study has received approval from the Ethics Commission of the Faculty of Medicine, University of North Sumatra with letter number of 157/KEPK/USU/2023 and the R&D Installation of H. Adam Malik Hospital Medan with letter number of LB.02.02/XV.III.2.2.2/970/2023.

## RESULTS

The subjects who participated in this research were 75 people, overall aged 55-60 years (56%) with an average age of 53 years. The gender of the research subjects was more men, namely 50 people (66.17%) than women, namely 25 people (33.3%). The research subjects who had a family history of suffering from DM were 58 people (77.3%) while 17 people (22.6%) had no family history of suffering from DM. A family history of DM was inherited from the father as many as 15 people (25.8%), and inherited from the mother's side as many as 18 people (31%) and inherited from the father's and mother's sides as many as 25 (43.2%).

Hemoglobin, HbA1c and RDW levels are not normally distributed, so the median value is a measure of centrality and the minimum-maximum is a measure of data spread. The median hemoglobin level is 13.4 (12.1-17.5) g/dL, the median HbA1c level is 8.3 (6.6-15.6) and the median RDW value is 12.9 (11.2-17.8). The Sperman correlation test was used because HbA1c and RDW were not normally distributed, with an r value of -0.078 (p=0.508). There is no correlation between HbA1c and RDW.

**Table 1. Sample characteristics**

| Variable | Characteristics | N= 75 | % |
|---|---|---|---|
| **Age (years old)** | 30-34 | 1 | 1.3 |
| | 35-39 | 0 | 0 |
| | 40-44 | 7 | 9.3 |
| | 45-49 | 9 | 12 |
| | 50-54 | 16 | 21.4 |
| | 55-60 | 42 | 56 |
| **Gender** | Male | 50 | 66.7 |
| | Female | 25 | 33.3 |
| **Family history of DM** | DM | 58 | 77.3 |
| | Non-DM | 17 | 22.7 |
| **Family member diagnosed with DM** | Father | 15 | 25.8 |
| | Mother | 18 | 31 |
| | Father and Mother | 25 | 43.2 |

**Table 2. Laboratory results of type 2 DM patients**

| Variable | N | Mean | Median | SD | Min. | Max. |
|---|---|---|---|---|---|---|
| Hemoglobin (g/dL) | 75 | 13.84 | 13.4 | 1.19 | 12.1 | 17.5 |
| HbA1c (%) | 75 | 9.04 | 8.3 | 2.30 | 6.6 | 15.6 |
| RDW (%) | 75 | 13.34 | 12.9 | 1.45 | 11.2 | 17.8 |

**Table 3. Spearman correlation examined HbA1c Levels and RDW in patients with Type 2 DM**

| Independent variable | r | p |
|---|---|---|
| RDW | -0.08 | 0.508 |

## DISCUSSION

In table 1, it is found that the age of the research subjects is in the age range of 30-60 years with an average age of 53 years. The gender of the research subjects was found to be more male than female, namely 50 males (66.7%) and 25 females (33.3%). In line with research conducted by Bhutto AR which assessed the correlation between HbA1c where the majority of research subjects were men, namely 62.2% (Bhutto et al., 2019). However, based on global diabetes prevalence data according to the IDF, it was found that the prevalence of diabetes was the same between men and women (Sun et al, 2022).

In this study, 58 subjects had a family history of DM. The risk of developing type 2 diabetes mellitus in a family depends on genetic and environmental factors. Individuals who have one parent with a history of diabetes have a 40% risk of developing diabetes and a risk of up to 70% if both parents suffer from diabetes (Prasad and Groop, 2015)

As can be seen in table 2, the HbA1c level of the subjects in this study was 8.3% with a fairly wide minimum and maximum range, namely 6.6% to 15.6%. This shows a high HbA1c level > 6.5 which indicates poor blood sugar control. The results of this study are different from the results of research conducted by Asmamaw et al, where in patients with poor blood sugar control, red blood cell count (RBC count) and hemoglobin levels were significantly ($p<0.005$) reduced in patients with HbA1c ≥7% (Asmamaw et al, 2021). Meanwhile MCV, MCH and RDW were significantly ($p<0.005$) increased in diabetes patients with HbA1c levels ≥7% (Tsilingiris et al, 2021).

In table 2, the RDW levels of the research subjects are with a median value of 12.9% and a minimum-maximum value of 11.2-17.8%. The RDW levels in the subjects of this study showed normal RDW levels. RDW is a small part of routine blood tests and reflects the degree of erythrocyte volume heterogeneity. Increased RDW indicates deregulation of erythrocyte homeostasis which is thought to be related to various underlying metabolic disorders, including inflammation and oxidative stress. This difference in red blood cell size ultimately increases RDW. Hyperglycemia, insulin resistance, and hyperinsulinemia, which are the main clinical abnormalities in DM, promote inflammation, oxidative stress, and other pathophysiological abnormalities ( Ke Xiong et al., 2023 ).

In table 3, the correlation between RDW and HbA1c is an inverse correlation ($r= -0.087$) with a p value = 0.508. This shows that the inverse correlation is very weak and not statistically significant. In line with research conducted by Demir, no significant correlation was found between RDW and HbA1c in diabetic or non-diabetic patients (Demir et al., 2016). Likewise, other studies did not find a significant correlation between RDW and HbA1c in diabetes patients (Gahlot et al, 2023). This can occur due to the influence of erythrocyte age on HbA1c. However, in other studies, a statistically significant correlation was found between RDW and HbA1c ($r= 0.193$; $p=0.035$) (Bhutto et al., 2019). Likewise, research conducted by Asmamaw, obtained significant correlation results

between erythrocyte cell count, MCV, MCH and RDW with HbA1c in diabetes mellitus patients (Asmamaw et al, 2021).

Geriatric age is also thought to influence the age of red blood cells. Inflammation or chronic inflammatory conditions that occur in old age are thought to induce the formation of Reactive Oxygen Species (ROS). ROS can cause a decrease in red blood cells. The average age of the subjects in this study was 53 years, which is included in the middle age classification according to WHO. This is thought to be one of the factors in the RDW values of research subjects still tending to be normal (Rohrig, 2016).

This research, with an insignificant correlation, could be caused by an increase in HbA1c in type 2 diabetes mellitus, hyperglycemia which can cause glycation will result in the formation of advanced glycation end products (AGEs products/ Advance Glycation End products) (Indyk et al., 2021). The end result of this glycation process causes changes in protein structure so that it is resistant to the degradation process, which ultimately causes the accumulation of cross-linked products in cells and body tissues. However, erythrocyte glycation, oxidative stress, increased pro-inflammatory cytokines have not been able to cause erythrocyte deformability, osmotic fragility, and have not caused changes in erythrocyte structure so that RDW is still within the normal range. An increase in HbA1c in type 2 diabetes mellitus is not accompanied by a change in RDW values. The pathway is so complex that hyperglycemia, chronic inflammation and other factors influence it so that it does not disrupt the structure and shape and size of erythroncytes. The priority of this research is that the researchers hypothesized that there is a correlation between HbA1c and RDW, that the RDW value can describe glycemic control together with the HbA1c value in helping screen for DM. The limitation of this study lies in the unexamined confounding factors during the sampling process, notably BMI (Body Mass Index). Obesity, being a potential contributor to metabolic syndrome, can exert an influence on blood sugar levels. Chronic inflammation, intricately linked to oxidative stress, hyperglycemia, and elevated HbA1c, may be exacerbated by obesity. Thus, it is essential to acknowledge the potential impact of unexplored variables, such as BMI, on the observed outcomes of this research. Variables contributing to oxidative stress, such as smoking habits, alcohol consumption, and lifestyle factors, present challenges for researchers. Additionally, the inclusion of vitamin C in the study poses a limitation, as its impact on HbA1c levels is often overlooked. It is imperative for researchers to address the influence of vitamin C on HbA1c levels when evaluating the outcomes of their studies, recognizing it as a potential confounding factor that requires careful consideration.

This study concluded that there was no significant correlation between HbA1c levels and RDW in type 2 diabetes mellitus.

## AUTHOR CONTRIBUTIONS

Jelita Siregar and Santi Syafril contributed to the conception or design of the work. Ratna Akbari Ganie, Dewi Indah Sari Siregar, and Almaycano Ginting reviewed and gave critical suggestion for important intellectual content of manuscript. Hadiyatur Rahma run data analysis and interpreted the data.

## ACKNOWLEDGEMENT

We are very grateful the database providers Pubmed, Google Scholar, and Science Direct.

**FINANCIAL AND SPONSORSHIP**

This study is self-funded.

**CONFLICT OF INTEREST**

There is no conflict of interest in this study.

## REFERENCE

Asmamaw M, Sime T, Kene K, Fekadie Baye M, Teshome M, Zawdie B (2021). Cell parameters as a biomarker for long-term glycemic control monitoring among type 2 diabetic patients in Southwest Ethiopia: A cross-sectional study. Diabetes Metab Syndr Obes. 30(14) :4993-5000.

Bhutto AR, Abbasi A, Abro AH (2019). Correlation of hemoglobin a1c with red cell width distribution and other parameters of red blood cells in Type II Diabetes Mellitus. Cureus. 11(8):-e5533. DOI: 10.7759/cureus.5533.

Biswas A, Srinivasan C (2020). Correlation of red blood cell distribution width (RDW) and hemoglobin A1C (HbA1c) levels, in patients with type 2 diabetes mellitus. Int. J. Res. Pharm. Sci. 11(1): 1160-4.

Demir AD, Dumaz ZH, Kilinc C, Guckan R (2016). Correlation between red blood cell distrubition width and glycated hemoglobin in diabetic and nondiabetic patients. 5(3):e0301. DOI: 10.1-5275/rusomj.2016.0301.

Gahlot D, Krishna R, Cheema M, Chawla S, Verma S (2023). Correlation analysis of red cell distribution width with HbA1c in type 2 diabetes mellitus patients. Eur.j.mol.clin.med. 10(2): 2086-2091. ISSN 2515-8260.

Indyk D, Bronowicka-Szydełko A, Gamian A, Kuzan A (2021). Advanced glycation end products and their receptors in serum of patients with type 2 diabetes. Sci Rep. 11(1):13264. DOI: 10.1038/s41598-021-92630-0.

Jahan N, Firoz A, Uddin F, Ahmed N, Sultana T, Paul D, Islam S et al. (2018). Association of red cell distribution width and hba1c in type-2 diabetes melitus. IOSR Journal of Dental and Medical Sciences. 17(8) :17-21. DOI: 10.1186/s12888-014-0216-9.

Ke-Xiong, Chenbo Xu, Xilling Shou, Meng-ya Dong (2023). Relation of Red Cell Distribution Width to Glucose Metabolism and Adverse Long-Term Prognose inPatients with Acute Coronary Syndrome. Diabetes Metabolic Syndrome and Obesity. I6: 6I-70. DOI: 10.2147/DMSO.S395923.

Prasad RB, Groop L (2015). Genetics of type 2 diabetes-pitfalls and possibilities. Genes (Basel). 6(1): 87-123. DOI: 10.3390/genes6010087.

Riset Kesehatan Dasar (2018). Laporan Nasional Riskesdas 2018. Lembaga Penerbit Badan Penelitian dan Pengembangan Kesehatan, 2019.

Rohrig G (2016). Anemia in the frail, elderly patient. Clin Interv Aging. 11: 319-326. DOI: 10.2147/CIA.S90727

Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, Colagiuri S., et al. (2019). Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract. 157: 107843. DOI: 10.1016/j.diabres.2020-.108086.

Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, Stein C., et al. (2022). IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 183: 109119. DOI: 10.1016/j.diabres.2021.109119.

Tsilingiris D, Makrilakis K, Barmpagianni A, Dalamaga M, Tentolouris A, Kosta O, Eleftheriadou I, et al. (2-21). The glycemic status determines the direction of the relationship between red cell distribution width and HbA1c. J Diabetes Complications. 35(10): 108-012. DOI: 10.1016/j.jdiacomp.2021.-108012

Wang J, Zhang Y, Wan Y, Fan Z, Xu R (2020). The Relationship between Red Blood Cell Distribution Width and Incident Diabetes in Chinese Adults: A Cohort Study. J Diabetes Res. 1623247. DOI: 10.1155/2020/-1623247.