ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 05 | May - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

THE CORRELATION BETWEEN THE RBC INDEX AND THE HBA1C LEVEL IN NON-DIABETICS IN JAZAN, SAUDI ARABIA

Hematology

Dr. Ogail Yousif Dawod*	Lecturer *Corresponding Author
Dr. Monami Mukherjee Mondal	Assistant Professor
Ms. Rasha Mohamed Alamin	Lecturer
Dr. Omer Ahmed Elrhima	Assistant Professor

ABSTRACT

Objectives: To investigate the relationship between HbA1C and red cell indices in non-diabetics. **Methods:** This is a cross-sectional descriptive study conducted at Abu Arish General Hospital and College of Applied Medical Sciences, Jazan University, Jazan, Saudi Arabia. 5ml of anticoagulated venous blood samples from non-diabetic subjects were collected and analyzed to estimate the CBC, RBC indices, and HbA1c by Abbott and Sysmix Coulters. SPSS was used to perform statistical analysis on the data, and linear regression was used to determine the correlation. The t-test and P value were calculated to determine the significance of the results. **Results:** HbA1c and RBC indices were found to have a significant relationship**. Conclusion:** There is a relationship between HbA1c levels and RBC indices. The modulation of HbA1c levels in our bodies affects RBC indices. In diabetic cases, it is prudent to consider changes in RBC indices when interpreting HbA1c concentrations. So, when diagnosing diabetes, it is also advisable to consider HbA1c, anemia, hemoglobinopathy, and people who are at risk of having their red cells live less than normal.

KEYWORDS

non-diabetic, anemia, HbA1c, RBC indices

INTRODUCTION

Hemoglobin A1c(HbA1c), a glycated form of hemoglobin (Hb) produced by non-enzymatic catalysis of the globin chain in mature Hb (1). The reaction between Hb and glucose is slow and irreversible (2). HbA1c is the main glycated Hb found in HbA1 fractions and is present for the entire 120-day lifecycle of red blood cells (RBCs) (3). The percentage value of HbA1c is directly proportional to the blood glucose concentration level. A rise in glucose levels will also imply an increase in HbA1c levels (2). Other than hyperglycemia, several clinical disorders can interfere with HbA1c readings (4).

Irrespective of the testing method used, a low level of HbA1c can be found when the lifespan of RBCs is reduced (2). Anemia is a widespread disease around the world, and a higher prevalence is observed among pregnant women which are estimated to be around 38% of the population, compared to 29% of non-pregnant women (5).

In cases of blood loss, hemolysis, hemoglobinopathies, red cell diseases, and myelodysplastic disease, anemia increases RBC turnover lowering HbA1c readings. Again, a reduction in the RBC count is accompanied by an increase in the rate of glycation of Hb and a high value of HbA1c (6).

Fundamentally, RBC survival and exposure to blood glucose are determinants of glycated hemoglobin synthesis. Based on this, HbA1c cannot be considered an adequate metric for the diagnosis of diabetes in those who have anemia, hemoglobinopathy, or are at risk of having altered red cell survival (7). Furthermore, the age of red blood cells is directly related to mean corpuscular hemoglobin concentration (MCHC) and is negatively correlated with mean corpuscular volume (MCV) and hemoglobin content (mean corpuscular hemoglobin; MCH), owing to significant water loss compared to hemoglobin during their existence. MCV is a measure of the volume of RBCs, whereas MCH is the quantity of hemoglobin content in RBCs (8).

Another crucial indicator is the red cell distribution width (RDW), which assesses the heterogeneity of the volume of RBCs (change in cell size) and aids in the differentiation of anemia types (9).

Current studies established strong links between an increased RDW and many medical conditions (10). A high RDW (11) has also been linked to atrial fibrillation, heart failure, and a poor prognosis in people suffering from heart failure or coronary heart disease (12). A connection was affirmed between HbA1c and RDW in a study with healthy non-diabetic National Health and Nutritional Examination Survey (NHANES) subjects. Furthermore, they hypothesized chronic hyperglycemia results in a raised RDW level and cardiovascular illness (13).

Research also revealed hyperglycemia alters RBC count. When compared to normal glucose homeostasis, it is seen to increase in pre-diabetes cases and decrease in cases of developed diabetes mellitus (14). The effects are prolonged to encompass Hb glycation, lower RBC deformability (15), and decreased life expectancy (16).

Iron is crucial for the body's metabolic processes. It is physiologically important in the tricarboxylic acid cycle and its deficiency is the most common cause of anemia worldwide, but its usefulness in diagnosis and therapy is limited because it is a known source of potential intervention (17).

According to the World Health Organization (WHO), the global prevalence of anemia is estimated to be roughly 1.62 billion people (18), with students accounting for 25.4% and preschool-age children accounting for 47.7%. Iron deficiency anemia accounts for 75% of all instances of anemia (19), affecting around 30% of the world's population (20). The prevalence of iron deficiency anemia in underdeveloped countries ranges from 16.5% to 62.6% (21). Several reports stated the total prevalence of iron deficiency anemia in Saudi Arabia ranges from 30 to 56% (22). A prevalence of 40.5% was found in a cross-sectional survey of schoolgirls in Riyadh, Saudi Arabia (23).

A study from Taibah University in Almadinah Almunawwarah, Saudi Arabia, found that the prevalence of overall mild, moderate, and severe anemia was 45%, 49%, and 6%, respectively, in female university students (24). A recent study on both female and male students at Jazan University's Faculty of Applied Medical Sciences revealed that iron deficiency anemia is remarkably common among female students, while one-third of male students are projected to be carriers of alpha or beta-thalassemia (25).

Many linked studies focused on the impact of iron deficiency on HbA1c in the diagnosis of diabetes and prediabetes. Even if a person doesn't have anemia, these studies found that a lack of iron causes HbA1c levels to rise without a corresponding rise in glucose indices.

 PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr

A reduced MCV in anemic patients implies that the anemia is mostly caused by an iron shortage. However, the anemic individuals in our study included a mix of those with iron-deficiency anemia with or without therapy and those with other kinds of anemia.

Previous research concentrated on specific types of anemia, such as dietary deficiencies or menstruation.

So, the present study was conducted to detect the relation between HbA1c and red cell indices in non-diabetes individuals. Hence, when interpreting HbA1c concentrations in diabetes mellitus, anemia should be considered.

MATERIALS AND METHODS

Study Settings:

This was conducted at Jazan University and Abu Arish General Hospital.

Study Design:

This is a cross-sectional and descriptive study.

Study Participants:

Fifty non-diabetics from Abu Arish general hospital and the students at the College of Applied Medical Sciences, Jazan University were included in this study.

Inclusion Criteria:

Nondiabetics, normal or anemic people.

Exclusion Criteria:

Diabetic cases.

Study Period:

October 2018 to March 2019

Data Collection Technique:

Before the collection of samples, the participants were asked to read, understand, and sign consent forms.

Venous blood (5 mL) was collected and immediately analyzed by Ruby's automatic blood cell counter. RBC indices and glycosylated hemoglobin (HbA1c) were calculated by enzymatic digestion (Abbott Chemistry) using a colorimetric reaction at Abu Arish general hospital.

Statistical Analysis:

SPSS was used to evaluate the results, and linear regression was utilized to correlate them. The T-test and P value were used to determine the significance of the results.

RESULTS:

45% of the individuals were anemic, whereas 55% were normal Figure 1. Among the anemic cases, 37% were microcytic anemic (low MCV) cases and 63 were normocytic (normal MCV) Figure 2. According to hemoglobin concentration, 24% of the cases had hypochromic anemia (low MCH), whereas the remaining 76% had normochromic anemia (normal MCH) Figure 3.

To compare MCHC with HbA1c, a two-sample t-test was used. MCHC (M = 32.27, SD = 0.851) and HbA1c (M = 5.47, SD = 0.622) were significantly different; t (22) = 98.69, p = 0.00001, Table 1.

Similarly, a two-sample t-test was used to compare MCH and HbA1c. MCH (M = 24.77, SD = 2.144) and HbA1c (M = 5.47, SD = 0.622) showed a significant difference; t (43) = 24.6, p = 0.00001, Table 2.

Again, for MCV and HbA1c, a two-sample t-test was used. MCV (M = 76.5, SD = 9.053) and HbA1c (M = 5.47, SD = 0.622) were significantly different; t (37) = 24.6, p = 0.00001, Table 3.

A two-sample t-test showed Hb g/dl (M = 4.9, SD 0.786) and HbA1c (M = 5.47, SD = 0.622) showed a significant difference; t (13) = 4.01, p = 0.00001, Table 4.

Furthermore, a two-sample t-test also revealed RBC x 1012/L (M = 12, SD = 1.762) and HbA1c (M = 5.47, SD = 0.622) were significantly different; t (33) = 61.07, p 0.00006, Table 5.

Table 1. Descriptive statistics of HbA1c and MCHC

Parameter (normal range)	Mean	SD
MCHC (32% – 36%)	32.27	0.851
HbA1c (4% – 6%)	5.47	0.622
T-test	98.69	
P value	0.00001	

Table 2. Descriptive statistics of HbA1c and MCH

Parameter (normal range)	Mean	SD
MCH (27 – 32 pg)	24.77	2.144
HbA1c	5.47	0.622
T-test	24.6	
P value	0.00001	

Table 3. Descriptive statistics of HbA1c and MCV

Parameter (normal range)	Mean	SD
MCV (80 – 100 fl)	76.5	9.053
HbA1c	5.47	0.622
T-test	61.07	
P value	0.00001	

Table 4. Descriptive statistics of HbA1c and Hb

Parameter (normal range)	Mean	SD
Hb g/dl (12 – 16F, 13 – 17M)	12	1.762
HbA1c	5.47	0.622
T-test	24.6	
P value	0.00001	

Table 5. Descriptive statistics of HbA1c and RBC

Parameter (normal range)	Mean	SD
RBC x 1012/L (3.8 – 4.8 F, 4.5 – 5.5 M)	4.9	0.786
HbA1c	5.47	0.622
T-test	4.01	
P value	0.00006	

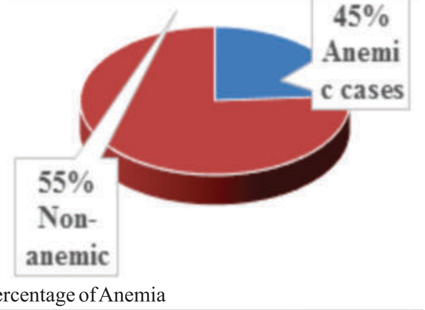

Fig. 1 - Percentage of Anemia

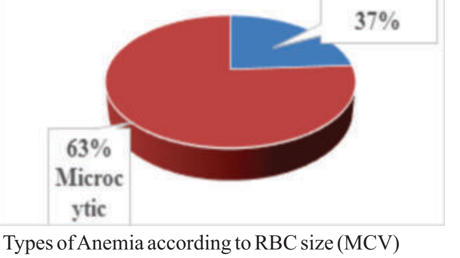

Fig. 2 - Types of Anemia according to RBC size (MCV)

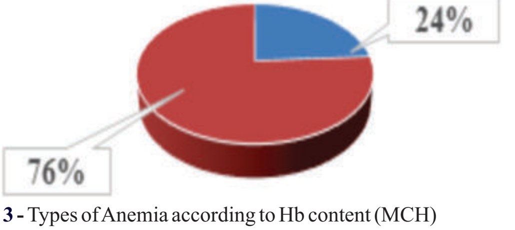

Fig. 3 - Types of Anemia according to Hb content (MCH)

DISCUSSION:

In this study, 45% of the individuals were anemic, whereas 55% were normal. There were 37% microcytic anemic (low MCV) cases and 63 normocytic (normal MCV) cases among the anemic patients. According to hemoglobin concentration, 24% of the cases had hypochromic anemia (low MCH), whereas the remaining 76% had normochromic anemia (normal MCH). This suggests that the types of anemia seen in Jazan include iron deficiency anemia with low MCV, sickle cell anemia with normal MCV, or thalassemia (low MCV).

Regardless of the type of anemia, the t-test and p-value showed that the RBC count, Hb values, and RBC indices all changed significantly with HbA1c.

The level is increased or decreased with a change in the MCV, MCH, or MHCH. Patients with low red blood cell indices had higher HbA1c levels. This demonstrates the unreliability of HbA1C in the diagnosis or follow-up of diabetes and the need to diagnose and treat anemia in diabetic patients.

In a previous study, Segade et al. (2016) found that the hematological parameters MCH and MCV had the most impact on HbA1c values regardless of the glycemic environment (26).

According to Takeuchi and Kawakami, the influence of anemia on HbA1c concentration varies depending on the cause; iron deficiency anemia may modestly raise HbA1c, whereas other forms of anemia or the recovery phase after iron deficiency anemia are related to a decrease in HbA1c (27).

The suggested mechanism could be related to iron's critical role in the tricarboxylic acid (TCA) cycle. Elevated iron levels limit glucose metabolism, increasing blood glucose levels (28)

Hence, the current study establishes a relationship between RBC indices and HbA1c levels.

CONCLUSIONS

This study aims to detect the effect on HbA1c levels due to changes in RBC indices.

We may conclude that changes in RBC indices have an impact on HbA1c levels. So, when interpreting HbA1c concentrations in diabetes mellitus, anemia should be deemed. It is advisable not to use HbA1c alone to diagnose diabetes without considering anemia, hemoglobinopathies, and people who are at risk.

Funding: Not required

Conflicts of interest: The authors state that they do not have any conflicts of interest.

Ethical Approval: Ethical approval was obtained from the Standing Committee for Scientific Research - Jazan University (HAPO-10-Z-001).

REFERENCES:

1. Konnert A, Arends S, Schubert S, et al. Uncertainty calculation for calibrators of the IFCC HbA1c standardization network. Accredit Qual Assur 2006; 11:319-28.
2. Cohen Robert M, Franco Robert S, Khera Paramjit K, et al. Red cell life span heterogeneity in hematologically normal people is sufficient to alter HbA1c. Blood 2008;112:4284-91.
3. Nitin S. HbA1c and factors other than diabetes mellitus affecting it. Singapore Med J 2010; 51:616-22.
4. WHO. WHO - Use of glycated hemoglobin (HbA1c) in the diagnosis of diabetes mellitus. Abbrev Rep WHO Consult 2011;1-25.
5. Stevens Gretchen A, Finucane Mariel M, De-Regil Luz M, et al. Global, regional, and national trends in hemoglobin concentration and prevalence of total and severe anemia in children and pregnant and non-pregnant women for 1995-2011: a systematic analysis of population-representative data. Lancet Glob Heal 2013; 1:16-2
6. Franco Robert S. The measurement and importance of red cell survival. Am J Hematol 2009;109-14.
7. Church D, Simmons D. More evidence of the problems of using HbA1c for diagnosing diabetes? The known knowns, the known unknowns, and the unknown unknowns. J Intern Med 2014; 276:171-3.
8. Bosch FH, Werre JM, Roerdinkholder- Stoelwinder B, et al. Characteristics of red blood cell populations fractionated with a combination of counterflow centrifugation and Percoll separation. Blood 1992; 79:254-60.
9. Montagnana M, Cervellin G, Meschi T, Lippi G. The role of red blood cell distribution width in cardiovascular and thrombotic disorders. Clin Chem Lab Med 2012; 50:635-41.
10. Perlstein TS, Weuve J, Pfeffer MA, Beckman JA. Red blood cell distribution width and mortality risk in a community-based prospective cohort. Arch Intern Med 2009; 169:588-94.
11. Adamsson ES, Borné Y, Melander O, et al. Red blood cell distribution width is associated with the incidence of atrial fibrillation. J Intern Med 2014; 275:84-92
12. Tonelli M, Sacks F, Arnold M, et al. Relation between red blood cell distribution width and cardiovascular event rate in people with coronary disease. Circulation 2008; 117:163-8.
13. Veeranna V Zalawadiya SK Panaich SS, et al The association of red cell distribution width with glycated hemoglobin among healthy adults without diabetes mellitus. Cardiology 2012; 122:129-32]
14. Simmons D. Increased red cell count in diabetes and pre-diabetes. Diabetes Res Clin Pract 2010; 90:3.
15. Singh DK, Winocour P, Farrington K. Erythropoietic stress and anemia in diabetes mellitus. Nat Rev Endocrinol 2009; 5:204-10.
16. Virtue Mark A, Furne Julie K, Nuttall Frank Q, Levitt Michael D. Relationship between GHb concentration and erythrocyte survival determined from breath carbon monoxide concentration. Diabetes Care 2004; 27:931-5.
17. Akşit M, Aksit M Z and Bozkaya G How is Effect of Iron Deficiency Anemia on Hemoglobin A1c Levels in Normoglycemic Individuals? Turkiye Klinikleri J Intern Med 2018;3(2):43-9 DOI: 10.5336/intermed.2018-59979
18. McLean E, Cogswell M, Egli I, Wojdyla D, de Benoist B. Worldwide prevalence of anemia, WHO Vitamin and Mineral Nutrition Information System, 1993-2005. Public Health Nutr. 2009 Apr;12(4):444-54. DOI: 10.1017/S1368980008002401. Epub 2008 May 23. PMID: 18498676.
19. B. Benoist, E. McLean, I. Egll, M. Cogswell, Worldwide prevalence of anemia 1993–2005: WHO global database on anemia World Health Organization (2008)
20. N. Soleimani, Relationship between anemia, caused from the iron deficiency, and academic achievement among third-grade high school female students, Procedia: Soc Behav Sci, 29 (2011), pp. 1877-1884
21. Abidoye RO, Akande PA. Nutritional status of public primary school children: a comparison between an upland and riverine area of Ojo LGA, Lagos State Nigeria. Nutrition and health. 2000 Jul;14(4):225-40.
22. A. Verster, J.C. van der Pols Anaemia in the Eastern Mediterranean region East Mediterr Health J, 1 (1) (1995), pp. 64-79.
23. Musaiger AO. Iron deficiency anemia among children and pregnant women in the Arab Gulf countries: the need for action. Nutrition and Health. 2002 Jul;16(3):161-71.
24. Nora Nasir Al Hassan, The prevalence of iron deficiency anemia in a Saudi University female students, Journal of Microscopy and Ultrastructure, Volume 3, Issue 1,2015, Pages 25-28, ISSN 2213-879X,https://doi.org/10.1016/j.jmau.2014.11.003.
25. Hamali HA, Mobarki AA, Saboor M, Alfeel A, Madkhali AM, Akhter MS, Dobie G. Prevalence of Anemia Among Jazan University Students. Int J Gen Med. 2020 Oct 5; 13:765-770. doi: 10.2147/IJGM.S275702. PMID: 33116767; PMCID: PMC7547133.
26. Segade, S R: Garcia, J R; Garcı´J M; Gude F; Casanueva F; Alonso S R; and Camin˜ F L; Impact of Mean Cell Hemoglobin on Hb A1c–Defined Glycemia Status Clinical Chemistry 62:12 1570–1578 (2016).
27. Takeuchi M and Kawakami, K. Association between Hemoglobin and Hemoglobin A1c: A Data-Driven Analysis of Health Checkup Data in Japan J. Clin. Med. 2018, 7, 539; doi:10.3390/jcm7120539
28. Nasli-Esfahani F, Larijani B, Amini P, Ghodssi-Ghassemabadi R, Razmandeh R Effect of treatment of iron deficiency anemia on hemoglobin A1c in type 2 diabetic patients Turk J Med Sci (2017) 47: 1441-1446