

## Effect of Iron Deficiency Anemia on HbA1c in Diabetic Patients in Salah al-Din Hospital, Iraq

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### Abstract

Hemoglobin A1C (HbA1c) is the main hemoglobin detected in HbA1 components. A1C test is the approved assay for assessing diabetes. Iron deficiency anemia (IDA), on the other hand, has been discovered to have an effect on HbA1C level; however, the effects are still being investigated. The present study was designed to examine the association between Iron Deficiency Anemia (IDA) and HbA1c in diabetic patients presenting at Salah al-Din Hospital, Iraq. From September 2021 to August 2022, 120 diabetic patients (60 with IDA and 60 without IDA) were included in a healthcare comparative cross-sectional research. A structured questionnaire was used to gather sociodemographic information as well as clinical circumstances. Venous blood was obtained for hematological tests and HbA1c test. SPSS version 21 was used to analyse the data. Pearson's correlation, and the one sample t-test were computed. The information was reported as mean  $\pm$  SD. P-value of less than 0.05 was considered statistically significant. In the IDA group, mean hemoglobin (Hgb), Red Blood Cell count (RBC), HbA1C, hematocrit (HCT), mean cell volume (MCV), mean cell hemoglobin (MCHC) and mean cell hemoglobin (MCH) levels were lower than in the non-IDA diabetic individuals. HbA1c (%) levels were substantially lower in the IDA group ( $6.78 \pm 7.0$ ) than in non-IDA diabetic individuals ( $7.04 \pm 0.46$ ) with statistically significant p-value.

The level of HbA1c in patients of diabetic with IDA are considerably lower than in diabetic patients without IDA. As a result, it is suggested that only HbA1C screening in these patients may be deceptive, so the doctors and clinicians should consider this before making any treatment decisions. A thorough assessment with a large number of subjects using sophisticated laboratory methods is advised.

**Keywords:** Hemoglobin A1C (HbA1c), Iron Deficiency Anemia, and Diabetes.

### Introduction

A total of 1.62 billion people worldwide—or 24.8% of the world's population—have anemia [1]. India is one of the nations having the highest overall incidence of iron deficiency anemia among the underdeveloped nations (IDA) If there is an ongoing military conflict with Iraq, however, the situation is much worse [2]. The incidence of various types of anemia ranges from 70% to 80% in toddlers, 70% in expectant mothers, and 24% in middle-aged males, according to data from the National Survey of Family Health (NFHS) [3]. The incidence of diabetes mellitus often known as type 2 diabetes, has been steadily rising across the world, with the rise being

particularly dramatic in under developing nations [4]. It is observed that there are 63 million individuals diagnosed with diabetes in India at the current time, and it is anticipated that this figure would climb to about 87 million people by the year 2030 [5-7].

### Problem Statement

It is crucial to assess the association between iron deficiency anemia and HbA1C since many poor income countries have a high incidence of two health disorders, namely iron deficiency anaemia and diabetes mellitus. Both of these conditions may lead to complications such as heart disease and stroke. As a result of the recent guidelines

made by American Diabetes Association (ADA), in which HbA1c was listed as the single diagnostic test for diabetes mellitus, this research has taken on an especially significant role [8]. It is recommended that the diagnostic threshold for diabetes mellitus be set at lesser than 6.5% of HBA1C for diabetic patients. The World Health Organization (WHO), among other organizations, acknowledges the reliability of this approach for diabetes diagnosis. If a person's HbA1c level falls between 5.7% and 6.5%, the American Diabetes Association (ADA) classifies them as having prediabetes. Previous study has shown that iron deficiency anemia, often known as IDA, has the ability to alter HbA1c levels [9, 10].

### Research Objectives

1. To determine whether there is a correlation between anemia caused by a lack of iron and high levels of HBA1C in diabetic patients.
2. To determine the impact that iron deficiency anemia on HBA1C levels in diabetic patients.

### Research Questions

1. Is there any evidence to suggest a connection between iron deficiency anemia and HBA1C levels in diabetic patients?
2. To investigate the relationship between iron deficiency anemia and HBA1C levels in diabetic participants.

### Significance of Study

As a result of a lack of awareness of diabetic anemia in Iraq, diabetic patients frequently do not get treatment for the ailment. There has only been a little amount of study conducted in Iraq to determine how the presentation of

IDA affects the HbA1c levels of diabetic individuals. As a consequence of this, we would want to perform a study on the effect that IDA has on the levels of HbA1c in the diabetic patients who presented themselves at the Salah al-Din Hospital in Iraq.

### Literature Review

Hemoglobin A1C, is the main hemoglobin that is found in HbA1 fractions. In healthy persons, HbA1c makes up 5% of the total hemoglobin, but it may make up as much as 15% of the total hemoglobin in diabetic patients [11]. The conversion of Hgb A to HbA1c occurs throughout the lifetime of erythrocyte. The pace at which this reaction takes place is accelerated in individuals diagnosed with diabetes, due to the higher glucose concentration, which ultimately results in elevated HbA1c concentration [12]. Hemoglobin is virtually subjected to the same concentration of glucose as plasma because erythrocytes are readily permeable to the glucose molecules in plasma [10]. As a result, the quantity of HbA1c is directly related to the average blood glucose level throughout the red blood cell's typical lifespan [13].

HbA1c may be altered by a wide range of hematological, genetic, physiological and certain other comorbidities [8]. Despite its benefits, HbA1c can be difficult to predict. Delayed red blood cell clearance or diminished reticulocyte synthesis may result in erroneously high levels of HbA1c. However, a falsely low level of HbA1c may be identified under conditions that result in early red blood cell clearance or increased production of reticulocytes in the body [14]. Iron deficiency anemia is the most widespread nutrition-related deficit in the

world, accounting for fifty percent of all instances of anemia. It is the diminished capacity of the organism to manufacture red blood cells. Insufficient iron intake with increasing iron demand, poor iron absorption, and excessive iron loss may all contribute to iron deficiency anemia [2, 15]. Patients who suffer from diabetes may have a greater susceptibility to the consequences of anaemia. Aspiration of bone marrow is the test that is considered to be the gold standard for diagnosing IDA. However, given the technique is intrusive, challenging, and costly, serum ferritin has been demonstrated to be an alternate test for discriminating between people who have iron deficiency anaemia and those who do not have iron deficiency [16].

There are 1.62 billion individuals throughout the globe who suffer from anaemia, which is equivalent to 24.8% of the total population [17]. There is a lack of clarity on the scope and trajectory of the diabetes misclassification that is brought on by IDA and rest of the anemia. However, most epidemiologic research imply that iron-deficiency anemia (IDA) may result in spuriously high HbA1c levels, however others suggest that there is lower HbA1c among patients with IDA or anemia. The mechanism via which IDA and anemia effect HbA1c has yet to be thoroughly explained. These distinctions could have something to do with the numerous causes of anemia, which might include iron deficiency anemia (IDA), a lack of folic acid, sickle cell disease, or a lack of vitamin B12 [2].

## **Methodology**

### **Patient Recruitment**

Patients were divided into two groups and enrolled in the trial from September 2021 to August 2022 at the Salah al-Din hospital based on their laboratory test results. All patients who met the inclusion criteria for this study during the research period and had a diagnosis of diabetes mellitus, either with or without IDA, were enrolled.

### **Study Grouping**

Patients were divided into 2 group bases on the presence or absence of Iron Deficiency Anemia [2]. Patients in Group 1 had IDA, as they had serum ferritin levels less than 15 g/mL, while patients in Group 2 had serum ferritin levels more than 15 g/mL; nonetheless, both groups were confirmed diabetic patients. All other factors that may alter the interpretation of HbA1c levels were ignored.

### **Clinical Investigations**

Using structured questionnaires, socio-demographic information was gathered. Every patient was required to submit a thorough medical history. We assessed the concentrations of hemoglobin, HbA1C, MCV, MCH, hematocrit, MCHC and RBC count. Each participant in the trial donated five milliliters of venous blood using the needle-and-syringe procedure [10].

### **Data analysis**

Version 21 of SPSS was used to perform analysis. The distribution of gender and age groups in the IDA and non-IDA cohort was described using frequency and summary statistics. The association between hematological markers and level of HbA1c

was analyzed by Pearson's correlation test. The hematological attributes and mean of HbA1c level in IDA and non-IDA diabetic individuals were compared using one sample t-test. Considered significant value of p was <0.05.

## Results

A total of 120 diabetic patients were studied, including 60 with IDA and 60 without IDA. In the IDA group, 29 (48%) men and 31 (51.7%) women were present, while in the non-IDA group, 28 (46.7%) men and 32 (53.3%) women were present. Ages for the IDA and non-IDA groups varied from 15 to 87 years and 15 to 70 years, respectively (Table 1).

**Table 1: Frequency Distribution of Demographic Attributes**

	IDA GROUP		NON-IDA GROUP	
	(n=60)		(n=60)	
	Frequency	Percentage (%)	Frequency	Percentage (%)
<b>GENDER</b>	Male	29	28	46.7
	Female	31	32	53.3
<b>AGE</b>	15 - 35 Years	28	33	55.0
	35 - 55 Years	24	25	41.7
	>55 Years	8	2	3.3

Table 1: Categorical variables were computed in frequency and percentage.

Iron Deficiency Anemia (IDA), Non-Iron Deficiency Anemia (Non-IDA)

Both groups' HbA1c levels and all other hematological parameters, were analyzed. The mean values of RBC, HBA1C, HCT, Hb, MCHC, MCH and MCV were compared between the IDA group and the non-IDA group using one sample t-test. The mean values were

determined using mean  $\pm$  standard deviation. When compared with the non-IDA group, the IDA group had reduced levels of RBC, HBA1C, HCT, Hb, MCHC, MCH and MCV and computed value was statistically significant i.e.  $P < 0.05$  (Table 2).

**Table 2: Descriptive Table for Red Blood Cell Indices**

	IDA GROUP	NON-IDA GROUP	T-TEST (95% CI)
			p-Value
<b>AGE (YEARS)</b>	38.45 + 15.06	34.13 + 10.5	<0.05
<b>RBC (10*12L)</b>	3.13 + 0.27	4.4 + 0.28	

<b>HB (G/DL)</b>	9.73 + 1.13	13.58 + 1.39
<b>HBA1C (%)</b>	6.78 + 7.0	7.04 + 0.46
<b>HCT (%)</b>	30.03 + 3.47	43.80 + 2.35
<b>MCV (FL)</b>	85.32 + 5.67	90.88 + 2.49
<b>MCH (PG/CELL)</b>	28.11 + 2.26	30.87 + 1.22
<b>MCHC (G/DL)</b>	31.34 + 0.95	32.39 + 1.02

Table 2: Age and hematological parameters of IDA and non-IDA group were presented as mean  $\pm$  SD. One sample t-test was performed to calculate the p-value. P-value  $>0.05$  was considered statistically significant.

Iron Deficiency Anemia (IDA), Non-Iron Deficiency Anemia (Non-IDA), Standard Deviation (SD), Red Blood Cell (RBC), Hemoglobin (Hb), Hemoglobin A1C (HBA1C), Hematocrit (HCT), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCV) and Mean Corpuscular Hemoglobin Concentration (MCHC)

Age, RBC, Hb, HCT, MCV, MCH, and MCHC had respective mean values of 38.45 + 15.06, 3.13 + 0.27, 9.73 + 1.13, 30.03 + 3.47, 85.32 + 5.67, 28.11 + 2.25, and 31.34 + 0.95. In the IDA patients, a Pearson correlation test was performed to evaluate whether there was any association between HbA1C and the hematological indicators. No statistically significant association was detected between HbA1C and age, RBC, HBA1C, HCT, Hb, MCHC, MCH and MCV (Table 3).

**Table 3: Correlation between Red Blood Cell Indices and HBA1C Level**

	MEAN + SD	CORRELATION VALUE (R)	P-VALUE
AGE (YEARS)	38.45 + 15.06	-0.001	0.996
RBC (10*12L)	3.13 + 0.27	0.152	0.246
HB (G/DL)	9.73 + 1.13	0.091	0.49
HCT (%)	30.03 + 3.47	0.2	0.126

MCV (FL)	85.32 + 5.67	-0.017	0.897
MCH (PG/CELL)	28.11 + 2.26	0.059	0.652
MCHC (G/DL)	31.34 + 0.95	0.041	0.757

Table 3: Age and hematological parameters of IDA group was correlated with HbA1C using Pearson Correlation test. P-value less than 0.05 was considered statistically significant.

Iron Deficiency Anemia (IDA), Standard Deviation (SD), Red Blood Cell (RBC), Hemoglobin (Hb), Hemoglobin A1C (HbA1C), Hematocrit (HCT), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCV) and Mean Corpuscular Hemoglobin Concentration (MCHC)

### Discussion

HbA1c has become more popular as a screening test for the diagnosis of diabetes and measure of glycemic control, along with the risk of elevated glycemic levels, and also predispose pre-diabetic complications [18]. Changes in the RBC half-life may cause anaemia to either raise or lower HbA1c readings. This can happen in either direction. There have been a lot of studies done on the impact of iron deficiency anemia on the level of HbA1c in individuals with or without diabetes and contradictory findings have been observed. However, researchers have not yet been successful in elucidating the mechanism that underlies these observations [4].

The outcomes of the present study indicate that the HbA1c % in the IDA group was discovered to be significantly lower (6.78 +

7.0) than that observed in the non-IDA group (7.704 + 0.46), with a p-value that was less than 0.05. This assumption is backed up by research that was carried out by Sinha, Kalasker, and Cavagnoli with the assistance of their respective coworkers in the years 2012, 2014, and 2015 respectively [2, 10, 19]. They were all of the same findings when they came to the conclusion that having iron deficiency anemia is related with an overall lower concentration of HbA1c. It's likely that the participants in the study had a higher degree of anemia than average, which might be the reason why their HbA1c levels were much lower than average. On the other hand, a different research that was carried out between the years 2011 and 2015 discovered that IDA influences the level of HbA1C by dramatically increasing pattern [20, 21]. Shekhae and Chhabra, along with their colleagues, found that IDA patients had an increased level of HbA1C [22, 23].

In current study, we performed correlation test in IDA group in order to assess whether or not there was a relationship between HbA1C levels and different indices of Red Blood Cells; the result was not statistically significant. Similarly, a research that was carried out in India in the year 2014 found that there was no statistically significant connection between MCH and HbA1c levels in individuals of IDA group [24]. RBC, Hgb, MCV, and MCH were the hematological indicators that demonstrated a significant

difference in mean value between the two study cohorts i.e. IDA and non-IDA group. This study is consistent with the findings of a research that was carried out in 2016 [25].

The outcomes of the present study indicated that there was no significant link between HbA1c levels and age in the IDA group. These findings are consistent with the findings of a study that was carried out in a manner that was quite similar in India [24].

Depending on the methods employed to determine HbA1c, numerous variables might alter or interfere with the HbA1c findings [2, 26]. Historically, several illnesses and pathological conditions, such as anemia and haemoglobinopathies, have been regarded as possible variables that might considerably affect HbA1c readings [27].

IDA is the most prevalent nutritional deficiency in the world, although its incidence is greater in poor nations. Women, children, and adolescents are the most at risk for acquiring IDA. As a result, the assessment of a patient's HbA1c values has become more commonplace in diabetes screening and diagnosis. Clinicians have a responsibility to conduct an analysis of the non-glycemic variables that may have an effect on a patient's HbA1c levels. Various forms of anemia are capable of having a detrimental impact on HbA1c levels. While some researchers have shown that IDA causes a rise in HbA1c levels, other researchers have been able to refute these results. In either scenario, the clinical data are insufficient, and more research must be conducted in order to determine the function that erythrocyte indices play in the regulation of HbA1c levels. In order to analyze the difference between the severity of IDA and

its impact on HbA1c readings, studies involving large populations are need to be carried out.

### **Conclusion**

In conclusion, this research revealed that individuals with IDA had a much lower HbA1c than diabetic patients without IDA. Considering the levels of HbA1C in these patients may be deceptive, since the correct level of HbA1c might be decreased when compare with the true number. Before making any treatment decisions, doctors and other medical professionals should take this into consideration. Prior to use HbA1c to diagnose diabetes, they should also consider treating iron-deficiency anaemia.

### **Study Limitations**

This work has a few shortcomings to its credit as well. Because it was a cross-sectional study, the researchers were unable to determine the exact mechanism by which anaemia impacts HbA1c. It is important to take notice of the many restrictions; it is possible that the findings of the current research cannot be properly generalized to persons who have severe degrees of IDA or who do not have IDA at all. Second, despite the breadth of the research's sample, there were only a small number of individuals who had IDA. This is despite the fact that the study had enough sample size. In light of this, it would be beneficial to conduct more studies in IDA individuals but with more sample in order to investigate the effect that IDA has on HbA1c levels.

### **Future Recommendations**

The foregoing research make apparent that it is still unknown exactly how iron deficiency anemia impacts the levels of HbA1c. The

reasons offered above are just contemplations, necessitating more research to corroborate and clarify the functions of these components. Future, large-scale studies are needed to thoroughly examine the HbA1c-reducing impact of iron deficiency anemia along with the possible mechanism that facilitates reduced glycation of HbA in anemic conditions like iron deficiency anemia since there hasn't been much research done in this area.

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