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Kaziri et al

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The Effect of Iron Deficiency Anemia on HbA1C among Non-Diabetic Adults in Benghazi, Libya

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ABSTRACT

Iron Deficiency Anemia (IDA) is the most common hematological disorder that has an impact on various physiological processes in the body. This research aims to investigate the relation between IDA and HbA1c levels, a marker of long-term glycemic control. Data from 100 patients with IDA and 100 as a control group were collected from the First Medical Tech Laboratory in Benghazi, Libya, and analyzed using SPSS version 21. The distribution of age and sex among the groups was described using frequency and summary statistics. The statistical analysis showed that the data follows a normal distribution. However, it was not homogenous. Consequently, the non-parametric Mann-Whitney U test was employed. The results indicated no statistically significant correlation between IDA and HbA1c levels ($p = 0.08$), suggesting that IDA may not have a significant impact on long-term glycemic control. These findings contribute to the existing body of literature on the relationship between IDA and HbA1c levels, and many researchers suggest the fact that IDA increases HbA1c levels; others align with our results by showing no correlation; some even suggest that IDA decreases HBA1c levels. These conflicting results highlight the need for further research to shed light on the underlying mechanisms involved.

KEYWORDS: Anemia, Diabetes, Iron Deficiency Anemia, Libya, Benghazi, Young Adults, Hba1c, Hemoglobin.

1. INTRODUCTION

Anemia is a serious problem in developing countries, particularly among nutritionally compromised individuals. It impairs growth and increases the risk of mortality and morbidity [(1)]. One of the most prevalent causes of anemia is iron deficiency. Blood loss from gastrointestinal bleeding and blood loss during menstruation are the two primary causes of iron deficiency anemia [(2)].

IDA has a major negative influence on living quality and work abilities and may result in recurrent hospitalization, delayed discharge, and higher healthcare expenses [(3)]. Iron deficiency anemia affects 4-5 billion people worldwide, according to the World Health Organization. The primary component of hemoglobin, which distributes oxygen throughout the body, is iron. It contributes to the general function of cells by supporting the enzymatic system, brain development, and oxygen usage.

IDA symptoms include shortness of breath, dizziness, fatigue, recurrent infections, and poor appetite. They might be produced by hemolysis or a higher demand for iron [(4)]. Iron deficiency accounts for around 50% of all cases of anemia. Worldwide, iron deficiency is responsible for 35,057,000 DALYs lost and 841,000 deaths. The diagnosis of IDA is typically established by assessing iron levels, with values below 10 mmol/L, and ferritin levels, with values below 10 mg/L, indicating iron deficiency [(5)].

HbAlc, a glycated hemoglobin, is formed by the glycosylation of hemoglobin. HbA1c is formed by the binding of glucose to the N-terminal valine of both B-chains of the hemoglobin molecule. The result indicates a person's glycemic status over the past 2-3 months. This test is used to determine glycemic status in diabetics and people who have impaired glucose tolerance. The American Diabetes Association (ADA) suggests maintaining HbAlc levels below 7% for all diabetics (2007 guidelines) [(6)]. HbA1c levels can be impacted by several factors, including blood glucose, hemolytic anemias, hemoglobinopathies, acute and chronic blood loss, pregnancy, IDA, and uremia.

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A variety of theories have been brought out to explain why the presence of IDA causes an increase in HbA1c levels. One theory suggests that changes to hemoglobin's quaternary structure cause the globin chain to glycate more quickly [7]. Secondly, the lower hemoglobin levels associated with IDA, coupled with a constant glucose concentration, may lead to a higher proportion of glycated hemoglobin. As HbA1c is measured as a percentage of total hemoglobin, this relative increase in the glycated fraction could contribute to elevated HbA1c levels [8].

Moreover, the reduced generation of red blood cells in IDA patients increases the average age of circulating erythrocytes. This causes each red blood cell to be exposed to glucose for a longer time, perhaps contributing to greater HbA1c levels [9]. Previous research findings on the link between IDA and HbA1c levels were conflicting, requiring more investigation. Specifically, there is a need to investigate the effect of IDA on HbA1c levels in non-diabetic persons in Benghazi. Several studies examined the relationship between iron deficiency anemia (IDA) and glycated hemoglobin (HbA1c) levels.

Some research supports the hypothesis that IDA raises HbA1c levels, and the severity of iron deficiency anemia exacerbates this effect [10]. However, an investigation carried out at Cukurova University found that IDA decreases HbA1c levels [9]. Another study found that whereas IDA initially reduced HbA1c levels, HbA1c levels recovered to normal during a two-month iron supplementation period, indicating a strong correlation between IDA and HbA1c [11].

Moreover, while moderate forms of IDA may not significantly impact HbA1c levels, severe forms of IDA have been associated with increased HbA1c levels. The specific mechanism through which IDA influences HbA1c remains unclear. Given the divergent findings in the literature, further investigation is warranted to determine the relationship between IDA and HbA1c levels. The purpose of this study is to close this knowledge gap and offer valuable insights into the relationship between IDA and HbA1c levels in this particular cohort. The results have the potential to improve diabetes diagnostic accuracy, especially for this particular group in the Benghazi area.

2. METHODS AND MATERIALS

2.1. Study design and population

A case-control study with 200 subjects targeted for inclusion in the study.

2.2. Inclusion criteria:

Adults with iron deficiency anemia who are non-diabetic. The diagnosis of IDA is typically established by assessing iron levels, with values below 10 mmol/L and ferritin levels, with values below 10 mg/L indicating iron deficiency.

2.3. The exclusion criteria for this research:

- Patients who are diagnosed with diabetes or who have glucose intolerance.
- Patients who have abnormalities in their hemoglobin structure, liver problems, alcohol ingestion, renal impairment, or rheumatic diseases.

To determine the sample size, we used the Cochran formula. Since there is no specific data available on the number of adults with IDA in Benghazi, the population size was estimated at 54,000. This estimation is based on the total number of adults in Libya (400,000) and the fact that Benghazi accounts for approximately 14% of the Libyan population. Considering that around 25% of adults worldwide are diagnosed with anemia and approximately half of these cases are IDA, the estimated prevalence of IDA in the population was 12.5%.

3. DATA COLLECTION

Data on non-diabetic people newly diagnosed with IDA was requested from the First Medical Tech Laboratory in the Benghazi area. One hundred people in all will be selected to fulfill the study's inclusion requirements. Furthermore, a control group consisting of one hundred individuals who are neither anemic nor diabetic was chosen. Gender will not be taken into account when choosing participants. The collected data will include the participant's past medical history, complete blood count, ferritin level, random blood glucose, and glycated hemoglobin (HbA1c). The level of HbA1c considered to be raised will be defined as 5.7%, following the guidelines of the American Diabetes Association (ADA). All collected data was analyzed and statistically interpreted using statistical software, such as SPSS version 21 (Statistical Package for the Social Sciences). Appropriate statistical tests, such as t-tests or Mann-Whitney tests, were used to assess the relationship between iron deficiency anemia and HbA1c in non-diabetic individuals.

4. RESULTS

The sample size used was 200 samples from otherwise healthy adult non-pregnant females; 100 had IDA, while the other 100 had normal HB levels of about 12 g/dL. The age distribution ranges from 16 to 51, with an average age of 29 and a standard deviation (SD) of 8. The normal group had an age average of 29 with an SD of 9, while the IDA group had an average age of 30 and an SD of 6.

4.1. Age distribution:

The figure below shows the age distribution of the samples, clarifying the normal group and the IDA group.

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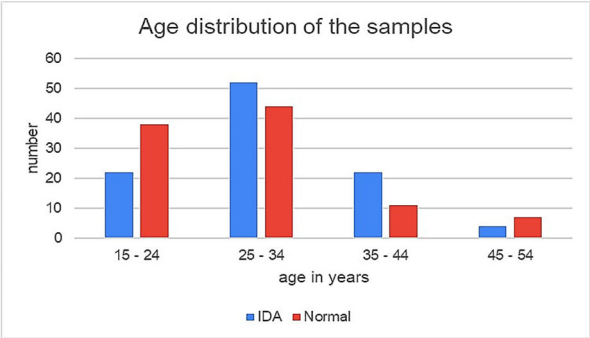

Fig. 1. Distribution of age of the IDA and normal groups.

4.2. Blood Parameters of Normal and IDA Groups

When the normal population results were compared to the IDA results of the obtained data, a statistically significant difference was found using a t-test with a two-tailed distribution and two samples with equal variance. All results for HB, HCT, RBC number, and serum ferritin had a P value < 0.05. These results revealed that data was collected accurately and that the statistical procedure was precise. Data shown in Table 1 is explained in Figure 2. (A, B, C, and D) stand for HB, HCT, RBC count, and serum ferritin, respectively.

Table 1: Blood Parameters of Normal and IDA Groups

Groups	HB (g/dl)	HCT (%)	RBC (no.)	S. Ferritin (ng/mL)	
IDA group	Average	7.6	21	3.5	19.4
	SD	0.98	2.16	0.48	6.16
Normal group	Average	12	32.3	3.9	39.6
	SD	1.23	3.11	0.57	9.97

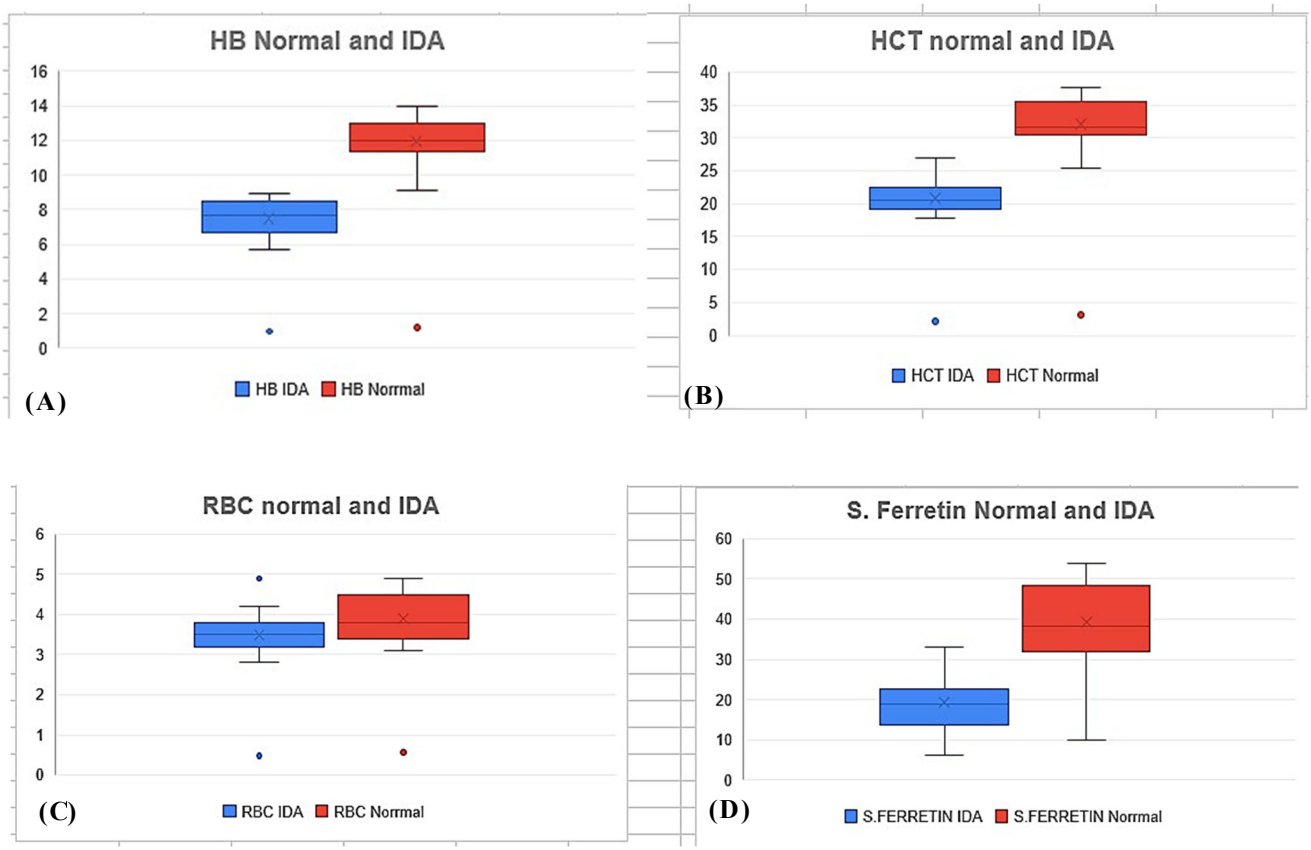

Fig. 2. shows the blood analysis of the normal and IDA groups for (A) HB, (B) HCT, (C) RBC numbers, and (D) serum ferritin.

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4.3. Blood sugar parameters of normal and IDA groups:

When comparing the HBA1C data of the normal population and the IDA group statistically, the p-value was more than 0.05, indicating that there was no significant difference between the two groups. However, Figure 3 and Table 2 showed that the IDA group had considerably higher fasting blood sugar levels than the normal group.

Table 2. Blood sugar parameters of normal and IDA groups.

Groups		FBS (mg/dL)	HbA1C (%)
IDA group	**Average**	90.5	4.96
	SD	11.4	0.96
Normal group	**Average**	81.7	4.86
	SD	10.1	0.52

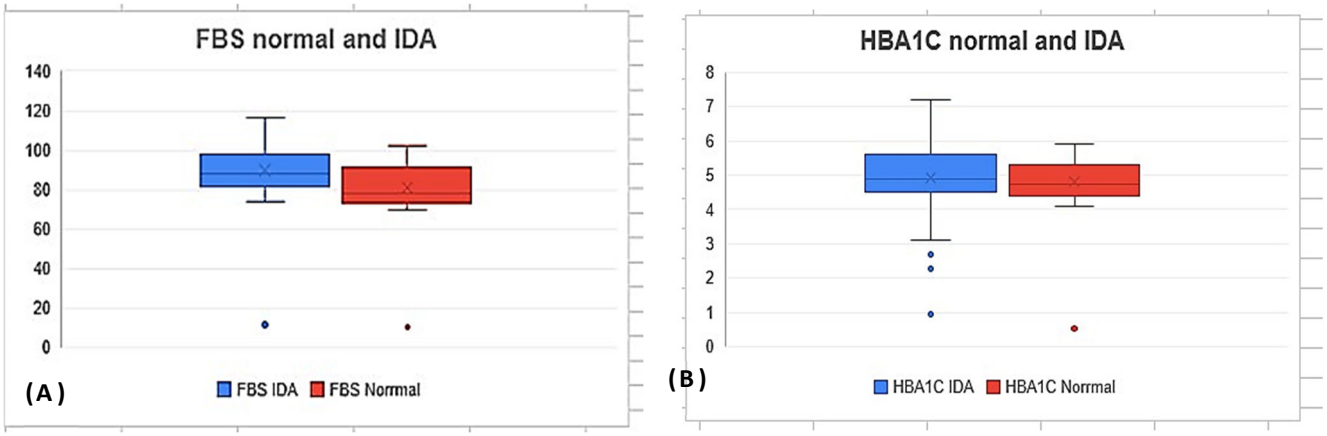

Fig. 3. Shows the blood analysis of the FBS (A) and the HBA1C (B).

5. DISCUSSION

IDA is the most prevalent cause of anemia and the most common nutritional deficiencies worldwide. The characteristic of IDA is a decrease in serum ferritin, which shows a depletion in the body's iron reserves. IDA also exhibits a decrease in hemoglobin and blood indicators such as MCV and MCH. A common method for evaluating glycemic control in diabetics during the last three months is glycated hemoglobin, or HbA1c. In addition to blood sugar levels, HbA1c can be influenced by illnesses such as uremia, hemoglobinopathies, acute and chronic blood loss, pregnancy, and hemolytic anemias [12]. This study aimed to evaluate the relationship between iron deficiency anemia (IDA) and HbA1c levels because there have been contradictory findings from previous studies on the relationship between IDA and HbA1c.

It has been shown that patients with IDA had considerably lower glycated hemoglobin levels than the healthy control group. Iron supplementation resulted in a subsequent elevation in HbA1c n two months after treatment started [12]. In contrast, it has documented higher levels of HbA1c in non-diabetic patients with IDA, which fell to near-normal levels following iron supplementation [13]. Our study used a two-independent sample t-test to examine the association between IDA and HbA1c levels. The normality assumption was met. However, the homogeneity of variance was not so; a non-parametric Mann-Whitney U test was employed, which resulted in a p-value of 0.08, indicating no statistical significance in the correlation between IDA and HbA1c levels.

Another study conducted by van Heyningen and Dalton R.G. found no difference in HbA1c levels between nondiabetic individuals with IDA before and after treatment with iron and healthy controls [14]. Further analysis revealed that women with severe anemia had considerably lower HbA1c levels than those with mild anemia. Low serum ferritin, Hb, MCV, MCH, and MCHC levels are indicators of IDA. Based on these data, we propose that HbA1c decreases with the severity of IDA. There is insufficient data on the link between HbA1c and anemia severity in non-diabetic patients [15].

Furthermore, the investigation was conducted on non-diabetic women with and without IDA. The IDA group of 21 women was then separated into two groups based on

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the severity of anemia: mild (n = 9) and moderate-severe (n = 12). The HbA1c readings were not different between the two severity groups. However, the absolute HbA1c concentrations showed a significant difference in mean values between the two groups [15].

Currently, the specific processes involved are not well understood. The IDA likely influences HbA1c levels through its effect on erythrocyte lifespan, changes in glucose metabolism, or other undiscovered mechanisms. Additional study is needed to validate these pathways and have a better understanding of the link between IDA and HbA1c levels [16]. In contrast to our work, the degree of anemia determines how IDA impacts HbA1c levels. When the total variability of the HbA1c test is taken into account, these increases may not be clinically important while being statistically significant [17]. Furthermore, in the non-diabetic population, IDA has been found to positively correlate with increased HbA1C levels [18]. It has been shown that there is a favorable relationship between hemoglobin, ferritin, and HbA1c [19]. The study emphasizes that individuals with IDA had lower HbA1c levels, which may rise if IDA is corrected [20].

6. CONCLUSION

Although the results of this study did not show a statistically significant association between IDA and HbA1c levels, the inconsistent findings in the literature and the limitations of our investigation suggest the need for more research. Future research should look at the severity of anemia and iron deficiency, as well as the underlying causes. More understanding of the link between IDA and HbA1c levels can help clinicians monitor and treat IDA as well as glycemic control.

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