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ORIGINAL RESEARCH PAPER

General Medicine

A STUDY ON EFFECT OF IRON DEFICIENCY ANEMIA ON GLYCATED HEMOGLOBIN (HBA1C) LEVELS

KEY WORDS: Anemia, Glycated Hemoglobin, Iron deficiency, Diabetes mellitus, serum ferritin

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ABSTRACT

Background: Diabetes is one of the most widespread illnesses in the world, causing substantial mortality and morbidity. HbA1c is still one of the most crucial tests for identifying and tracking the progression of the illness. The HbA1c readings typically reflect the glycemic control status of diabetes individuals during the previous three months. Measurements of HbA1c can be affected by variables altering hemoglobin (Hb) and the half-life of red blood cells since HbA1c is a reflection of the glucose linked to red blood cells. Low Hb concentration and high glycated hemoglobin (HbA1c) have been linked in studies of people with iron deficiency anemia (IDA). **Aim:** The present study aimed to study the levels of HbA1c in iron deficiency anemia patients. **Materials and Method:** The present study was a cross sectional study conducted for a period of is a retrospective study conducted for a period of 12 months from August 2022 to July 2023. The study comprises 100 patients with iron deficiency anemia, and 100 healthy volunteers as a control group. Complete blood count, anemia profile including serum ferritin and HbA1c levels were measured at baseline and after treatment of anemia. These values were compared with those in the control population. Results were analysed using SPSS 20.0 version and the association was tested using Chi square test. **Results:** The hematological parameters (Hb, MCV, hematocrit), Serum ferritin and HbA1c levels were lower in IDA group when compared with control group. The mean HbA1c level was significantly lower in the group with IDA (5.3±0.8%) than in the healthy control group (5.9±1.5%; $p< 0.05$). When the patients were divided into three groups according to the severity of anemia through Hb levels, HbA1c levels were observed to decrease as the severity of the anemia increased ($p< 0.05$). The HbA1c levels of the patients with IDA were higher after iron therapy (from 5.3±0.8 to 5.5±2.5; p=<0.001). The mean Hb, hematocrit, mean cell volume (MCV), ferritin values and HbA1c also increased after iron therapy ($p< 0.05$). **Conclusion:** Patients with iron deficiency anemia have decreased HbA1c values, which rise after receiving iron supplementation. Therefore, it is important to consider iron deficiency anemia before utilizing the HbA1c to diagnose diabetes.

INTRODUCTION:

Iron deficiency anemia (IDA), one of the several types of anemia that are known to exist in India, is more frequently observed in both urban and rural areas of our culture. The most frequent cause of this, particularly in girls, is undernutrition. The cause of 50% of anemia worldwide is iron deficiency.[1] The amounts of ferritin (iron storage form) provide a precise and reliable prediction of the iron status of the body.[2]

A ketamine interaction between glucose as well as the N-terminal valine of both the ß-chains of the Hb molecule results in glycated Hb. When Hb, a protein found in red blood cells(RBCs) that transports oxygen through the human body, combines with blood glucose and becomes "glycated," it develops.[3]

The main fraction of hemoglobin A is known as hemoglobin A1c (HbA1c), also known as glycated hemoglobin (Hb). HbA1c is primarily generated by the chemical reaction of glucose with the N-terminal valine domains of both beta chains, resulting in the formation of an aldimine linkage that eventually realigns to create the stable ketamine link of HbA1.[4] Clinicians can obtain a general overview of the mean blood sugar levels over a three-month period using the HbA1c. This is crucial for diabetics because a higher HbA1c indicates a higher risk of complications from the disease.[5]

The formation of HbA1c for the purpose of assessing glycemic status in clinical practice depends on a number of variables, including the rate of HbA1c synthesis, the mean age of circulating erythrocytes, and the release of HbA1c in reticulocytes from the bone marrow. It serves as the gold standard method for evaluating glycemic control.[6]

According to the guidelines established by the American Diabetes Association, diabetic patients with HbA1c values below 7% are said to have good control, which prevents them from developing a variety of potentially fatal micro vascular problems related to diabetes.[7] The amount of HbA1c can possibly be incorrectly affected by anomalies in Hb because HbA1c measures the sugar that is connected to a form of Hb.

Initial studies pointed to a connection between HbA1c levels as well as iron deficient anemia. They made an effort to justify this by pointing to structural changes and variations in HbA1c levels in both old and young RBCs. The HbA1c levels of anemic patients were not different from those of healthy controls, according to a small number of studies. Only a few studies reported that IDA patients had increased HbA1c values, which considerably decreased after therapy. The findings of numerous investigations on the connection between IDA and HbA1c were contradictory.

The mechanism underlying this relationship, however, is still unknown. It is hypothesised that IDA predisposes the molecule to a higher rate of glycation due to changes in the Hb backbone, delayed turnover, and the extended lifespan of RBCs.8 Only a few research on this subject have been done in the Indian community. The aim of the present study was to study the levels of HbA1c in iron deficiency anemia patients and to evaluate the changes in HbA1c level after the correction of iron deficiency anemia.

MATERIALS AND METHODS:

The present study was a cross sectional study conducted for a period of is a retrospective study conducted for a period of 12 months from August 2022 to July 2023 in Department of General Medicine, Sree Mookambika Institute of Medical

Sciences, Kulasekharam. The study comprises 100 patients with iron deficiency anemia, and 100 healthy volunteers as a control group.

All patients above the age of 18 years having IDA and willing to participate in the study were included in the present study. Patient below the age of 18, patient with diabetes, chronic renal failure, hemolytic anemia, liver disease, pregnant women, chronic alcoholism, know case of malignancy, patients on iron therapy and those who were not willing to participate in the present study were excluded.

A detailed history was recorded along with a complete clinical examination. Hb, hematocrit, mean cell volume (MCV), ferritin, and HbA1c were measured before iron therapy. Elemental iron was administered to all IDA patients for a median duration of 3 months at a dose of 100 mg/day. Following that, the anemic patients were separated into three groups based on the total Hb levels: There are three types of anemia: mild (Hb ≥11g/dL and <12g/dL for females and ≥11g/dL and <13g/dL for males), moderate (Hb ≥8g/dL and <11g/dL, for both gender), and severe (Hb <8g/dL, for both gender). Testing was done again after receiving iron therapy. The HbA1c values in of IDA groups was compared to the control group without anemia.

Data entered in Excel sheet. Results were analysed using SPSS 20.0 version. Categorical variables are expressed in numbers and percentages, whereas continuous variables are expressed in mean and standard deviation (SD) where appropriate. The chi-square -test was used to compare categorical variables between the groups. Student's t-test was used to compare continuous variables between the two groups. A p value less than 0.05 was considered statistically significant.

OBSERVATION AND RESULTS:

Of the total 200 patients, the 100 patients were in IDA group and 100 patients were in control group. The mean age of patients in IDA group was 43±12.5 years with age ranged from 28 to 63 years and in control group the mean age was 40±10.6 years with age ranged from 30 to 54 years. The hematological parameters and HbA1c levels were lower in IDA group when compared with control group. Comparison between the two groups had significant differences. ($p < 0.05$). (Table 1)

Table 1: Comparison of demographic and Laboratory parameters among both groups.

	IDA group (n=100)	Control group (n=100)	p value
Age (years)	43±12.5	40±10.6	0.52
Hb (g/dl)	10.16±1.8	13.3±0.8	0.001
Hematocrit (%)	35±4.65	39±4.3	0.021
MCV (fL)	70±2.5	86±4.5	0.032
Ferritin (μg/ml)	9.8±6.89	38±5.2	<0.001
HbA1c (%)	5.3±0.8	5.9±1.5	<0.001

Based on the severity of anemia the mean Hb and HbA1c values, a decline in HbA1c levels was observed as the Hb levels decreased and the comparison showed statistical significance (Table 2)

Table 2: Mean Hb and Hb A1c value based on severity of anemia

	Case group (IDA)			Control group	p value
	Mild	Moderate	Severe		
Hb (g/dl)	11.7±1.3	9.6±0.8	6.5±0.5	13.3±0.8	0.021
HbA1c	5.5±0.5	5.3±0.8	5.1±0.6	5.9±1.5	0.005

The Hb, Hematocrit, MCV, Ferritin and HbA1c levels of the patients with IDA were higher after iron therapy. The comparison between pre and post therapy in IDA group, mean difference in pre & post correction for Hb & HbA1c values showed statistically significant correlation as the p values were <0.05. (Table.3,4)

Table 3: Comparison of Laboratory parameters in IDA group before and after treatment

	Before treatment	After treatment	p value
Hb (g/dl)	10.16±1.8	12.4±1.1	<0.001
Hematocrit (%)	35±4.65	38±7.2	0.042
MCV (fL)	70±2.5	82±3.7	0.004
Ferritin (μg/ml)	9.8±6.89	27±7.9	0.001
HbA1c (%)	5.3±0.8	5.5±2.5	<0.001

Table 4: Mean Difference in pre and post correction for Hb & HbA1c values in IDA group

Parameters	Mean difference	p value
Hb (g/dl)	4.86	0.0001
HbA1c	1.28	0.0001

DISCUSSION:

The measurement of HbA1c is used to determine how much hemoglobin has been glycosylated in the blood over the previous three months. It is primarily used to identify individuals with diabetes and to track those who have been identified to gauge how well they are responding to treatment.[9] The American Diabetes Association states that diabetes is identified when the HbA1c level is ≥6.5%. Prediabetes is defined as levels between 5.7 and 6.4%, while a normal HbA1c is less than 5.7%.[7]

Blood levels of HbA1c might be impacted by illnesses such various anemias. The extended half-life of red blood cells in general causes disorders linked with reduced erythropoiesis (such IDA) to artificially elevate HbA1c. On the other hand, a rise in erythropoiesis that causes a rapid turnover of RBCs can erroneously lower HbA1c.[10] Numerous earlier investigations in this area produced conclusions that were incredibly ambiguous.

In the present study the hematological parameters (Hb, MCV, hematocrit), Serum ferritin and HbA1c levels were lower in IDA group when compared with control group. Based on the severity of anemia the mean Hb and HbA1c values, a decline in HbA1C levels was observed as the observed as the Hb decreased. The Hb, Hematocrit, MCV, Ferritin and HbA1c levels of the patients with IDA were higher after iron therapy. The comparison between pre and post therapy in IDA group, mean difference in pre & post correction for Hb & HbA1c values showed statistically significant correlation as the p values were <0.05.

Etinkaya Altuntaş S et al.11 observed that the mean HbA1c level in the IDA group was considerably lower (5.4%) than in the control group with no disease (5.9%; p <0.05) than in the control group. Following iron therapy, the mean hemoglobin, hematocrit, mean corpuscular hemoglobin (MCH), and ferritin readings all rose (p <0.05).

Similar to this, Jeyaprakash N et al.12 found that the mean HbA1c level in patients with IDA was considerably lower than the control group (4.619 ± 0.308%) and (5.446 ± 0.281%) respectively. After therapy, there was a substantial rise in the mean HbA1c of the anemia group (5.816 ± 0.323%). Additionally, Sinha N et al.13 observed that the mean baseline HbA1c level in anemic patients (4.6%) was considerably lower than that in the control group (5.5%, p <0.05) than that of the control group. At two months following treatment, there was a discernible rise in the patients HbA1c levels (0.29 g/dL vs. 0.73 g/dL, p<0.01). The baseline values of patients and controls were significantly different.

In contrast to the current study, Sumathi K et al.14 reported that iron-deficient diabetic patients' HbA1c levels were increased (7.3±0.9) in comparison to the usual level (5.4±0.6) in controls. According to the study, there is a link between the presence of IDA and higher HbA1c values in the community of people with managed diabetes. Similar to this, Alzahrani BA et al.15 found that the mean HbA1c values in IDA were substantially higher than those in the control group, at 5.75% (95% CI = 5.68-5.82), in their study. HbA1c in the iron-deficient group reduced from 5.75 to 5.44% after treatment, with a p-value less than 0.001.

HbA1c did not substantially differ across the groups, but absolute HbA1c levels were significantly lower in the groups with mild and moderate-severe anemia than in the non-anemic group, and they were positively correlated with Hb, ferritin, and RBC count. This finding was made by Bindayel IA et al.[16] Additionally, there was an inverse relationship between the Hb concentration and the HbA1c level.

CONCLUSION:

The findings of the study demonstrated a correlation between IDA and low HbA1c levels, which then increased following iron therapy. Therefore, before deciding on any course of treatment, doctors should take this into account. Large-scale studies with extended follow-up times may provide reliable data on the impact of iron deficient anemia on HbA1c levels. As a result, HbA1c will be more accurate in identifying diabetes. To determine the utility of alternative glycemic control markers in individuals with iron deficient anemia, more research can be done on glycated albumin and fructosamine.

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Conflicts Of Interest:
There are no conflicts of interest

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