Section: General Medicine

Original Research Article

STUDY OF HBA1C IN IRON DEFICIENCY ANEMIC NONDIABETIC PATIENTS: HOSPITAL BASED CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Diabetes Mellitus diagnosis increasingly relies on HbA1c (≥6.5%), a marker of long-term glycemia. However, non-glycemic factors such as iron deficiency anemia (IDA) may alter HbA1c values and lead to misclassification. Given the high prevalence of IDA in India, this study evaluated the impact of IDA on HbA1c levels in non-diabetic adults and assessed changes following iron therapy.

Materials and Methods: This prospective observational study was conducted over 1.5 years at a tertiary care hospital in North India. Ninety non-diabetic adults (18–65 years) with confirmed IDA were enrolled. Clinical evaluation and laboratory investigations including complete blood count, iron profile, fasting and post-prandial glucose, and HbA1c were performed. HbA1c levels were compared across iron status parameters and reassessed after iron supplementation. Statistical analyses included ANOVA, paired t-test, and correlation testing, with $p<0.05$ considered significant.

Results: The mean age was 41.76 ± 15.9 years; 66.7% were females. Mean ferritin (4.40 ± 1.37 ng/mL) and serum iron (22.6 ± 5.48 µg/dL) confirmed depleted iron stores. Mean HbA1c was 5.94 ± 0.78%. Participants with HbA1c>6.5% had significantly lower serum iron ($p = 0.03$) and ferritin ($p = 0.009$). HbA1c showed a significant decline after iron therapy (5.94 ± 0.78% to 5.18 ± 0.32%; $p<0.001$), while fasting and post-prandial glucose levels remained unchanged.

Conclusion: IDA was associated with falsely elevated HbA1c values independent of glycemia. Correction of iron deficiency significantly reduced HbA1c levels, underscoring IDA as an important confounder. Evaluation of iron status is essential before interpreting HbA1c in populations with high anemia prevalence.

Keywords: Anemia, HbA1c, Diabetes Mellitus, Iron.

INTRODUCTION

Diabetes Mellitus (DM) has emerged as a major global public health problem, with a rapidly increasing prevalence worldwide. Globally, approximately 10.5% of the adult population is affected, and India is projected to harbor nearly 80 million individuals with diabetes by 2030.[1-3] Maintenance of optimal glucose homeostasis is crucial to prevent long-term microvascular and macrovascular complications. Glycated hemoglobin (HbA1c) is an established biomarker for assessing chronic glycemic status and is widely used for both diagnosis and monitoring of DM.[4,5] As a measure of average blood glucose over the preceding 2–3 months, HbA1c reflects the non-enzymatic glycation of hemoglobin within erythrocytes during their lifespan.[6-10]

Although HbA1c is considered the gold standard for long-term glycemic assessment, several physiological and pathological conditions can influence its values independent of actual plasma

glucose levels.[6-8] Factors affecting erythrocyte survival, hemoglobin structure, or red blood cell (RBC) turnover may lead to falsely elevated or reduced HbA1c levels.[11] Among these, iron deficiency anemia (IDA)—the most common nutritional deficiency disorder globally and highly prevalent in India—has gained attention for its potential impact on HbA1c interpretation.[12]

Previous studies have demonstrated conflicting findings regarding the relationship between IDA and HbA1c levels. Some investigators have reported elevated HbA1c levels in patients with IDA that decreased following iron therapy,[13,14] whereas others have observed variable or even increased levels after treatment.[15-17] The precise mechanism underlying these variations remains unclear but may involve alterations inerythrocyte lifespan, changes in hemoglobin structure, or differences between younger and older RBC populations.[18,19]

Given the widespread prevalence of IDA and the increasing reliance on HbA1c as a diagnostic criterion for diabetes, understanding the interaction between iron status and HbA1c is of significant clinical importance. Misinterpretation of HbA1c in anemic individuals may result in inaccurate diagnosis or inappropriate management decisions.

Hypothesis: Iron deficiency anemia influences HbA1c levels in non-diabetic individuals independent of true glycemic status.

Purpose of the Study: This study aims to evaluate the effect of iron deficiency anemia on HbA1c levels in non-diabetic Indian individuals, to examine the correlation between iron parameters and erythrocyte indices with HbA1c, and to determine whether correction of iron deficiency alters HbA1c values. Establishing this relationship is essential to improve the accuracy of HbA1c interpretation and prevent potential misclassification of glycemic status in populations with a high burden of anemia.

AIM

To investigate the impact of iron deficiency anemia on HbA1c levels in non-diabetic patients.

Objectives

- To assess variations in HbA1c levels among subjects with iron deficiency anemia.
- To examine the correlation between iron status parameters and erythrocyte indices with HbA1c levels.
- To determine whether iron supplementation influences HbA1c levels in iron-deficient non-diabetic individuals.

MATERIALS AND METHODS

Study Duration: 1.5 years (April 2024 to September 2025).

Study Design: Hospital-based prospective observational Study.

Study Location: Department of General Medicine, SRMSIMS Hospital, Bareilly, India.

Subjects and Selection

Inclusion Criteria

- Patients giving written informed consent for the study
- Known cases of Iron Deficiency anemia of age 18-65 years Hb<13 (Male),Hb<12(Female).

Exclusion Criteria

- Patients non willing to participate,
- Known cases of Diabetes,
- Known cases of Hemoglobinopathy,
- Known cases of Chronic liver disease,
- Known cases of Chronic kidney disease,
- Known cases of Pregnancy and lactation,
- Known cases of Malignancies,
- Known cases of Chronic Alcoholics,
- Known cases of Hyper bilirubinemia,
- Known cases of Acute blood loss,
- Known cases of Vitamin B12 and folic acid deficiency,
- Known cases of Anemia due to causes other than Iron Deficiency.

Sample size: An a priori power analysis was conducted for the primary hypothesis test assesses the correlation between iron deficiency statusrelated parameters and HbA1c using a two-tailed point-biserial correlation framework. Hence, the required total sample size was 90.

Study tool.

Data Collection: The study was utilized a structured proforma for collecting the primary data. The study tool contains following details:

i. Detailed history, clinical examination
ii. Age at the time of admission
iii. Gender
iv. History (symptoms, dietary history, drug history, history of Blood Transfusion, any addiction)
v. Examination (Pallor, hepatosplenomegaly, icterus, lymphadenopathy etc.)
vi. Investigations:

- Complete Blood count (CBC)
- Peripheral Blood Smear with Reticulocyte count , Iron Profile , GGT
- Fasting and post prandial blood sugar
- Vitamin B 12, Folic acid, LDH, Uric acid
- S. Urea and S. Creatinine
- Stool for Occult Blood (if indicated)
- Bone Marrow Examination (if indicated)
- Upper and Lower Gastrointestinal Endoscopy (if indicated)

Statistical analysis: A pilot research including 9 patients was conducted to validate the methodology, with approval from the Institute's Ethics Committee. The data was collected and then evaluated using frequency and percentage for the categorical variable. The results were visually presented using charts and graphs.

RESULTS

A total of 90 non-diabetic adult patients with iron deficiency anemia who fulfilled the eligibility criteria were included in the final analysis.

Figure 1 shows the age distribution of the 90 non-diabetic patients with iron deficiency anemia included in the study. The participants' ages ranged from 18 to 65 years, with a mean ± SD of 41.76 ± 15.9 years, indicating that both younger and older adults were adequately represented.

The largest proportion of study subjects (32.2%) were in the 18–29 years age group, followed by 23.3% in the 60–65 years group. Middle-aged participants (30–59 years) collectively constituted about 44.5% of the study population. Since iron deficiency anemia (IDA) was present across all adult age groups, but it appeared more common among younger adults (18–29 years) and elderly individuals (60–65 years) in this cohort.

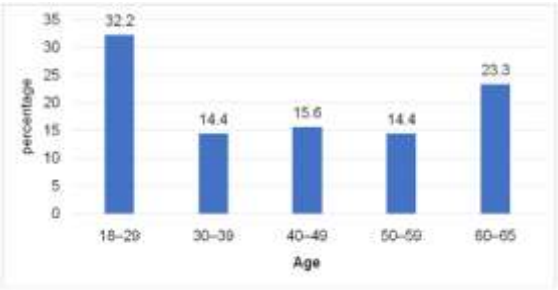

Figure 1: Age distribution of study participants

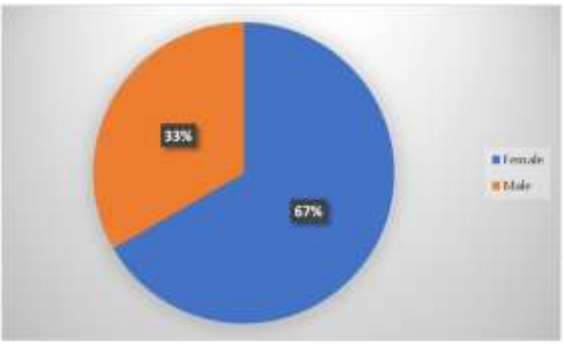

Figure 2: Gender distribution of study participants

[Figure 2] shows the gender distribution of the study participants. Out of the total 90 non-diabetic patients with iron deficiency anemia, 60 (66.7%) were females, and 30 (33.3%) were males. This indicates a female-to-male ratio of approximately 2:1. The predominance of females among study participants aligns with the well-documented higher prevalence of iron deficiency anemia (IDA) in women, particularly of reproductive age. This gender difference is primarily attributed to menstrual blood loss, inadequate dietary iron intake, and increased iron requirements during pregnancy and lactation.

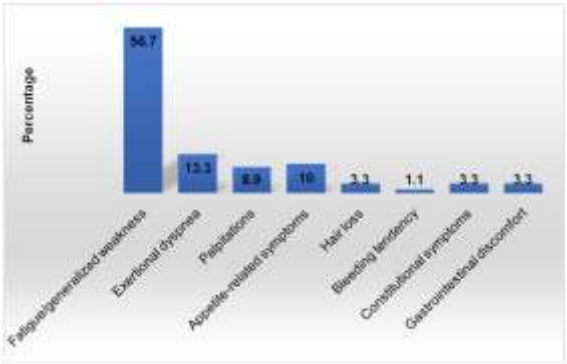

Figure 3: Presenting symptoms of study participants

[Figure 3] shows the distribution of presenting symptoms among the 90 non-diabetic patients with iron deficiency anemia. The most common symptom was fatigue or generalized weakness, reported by 51 participants (56.7%), followed by exertional dyspnea in 12 (13.3%), appetite-related symptoms in 9 (10.0%), and palpitations in 8 (8.9%). Less frequent complaints included hair loss (3.3%), constitutional symptoms such as malaise or low-grade fever (3.3%), gastrointestinal discomfort (3.3%), and bleeding tendency (1.1%).

[Table 1] represents the iron profile and associated biochemical parameters among the study participants (N = 90). The mean serum ferritin level was 4.40 ± 1.37 ng/mL, reflecting markedly depleted iron stores, consistent with iron deficiency anemia. The total iron-binding capacity (TIBC) was 412 ± 69.0 µg/dL, suggesting increased transferrin production and enhanced iron-binding potential as a compensatory mechanism for low circulating iron. The mean serum iron level was 22.6 ± 5.48 µg/dL, further confirming iron depletion and reduced bioavailability of iron for erythropoiesis. The transferrin saturation percentage averaged 8.9 ± 3.0%, indicating significant functional iron deficiency.

Meanwhile, vitamin B12 levels were within the normal reference range (438.61 ± 130.57 pg/mL), effectively ruling out megaloblastic anemia as a contributing factor. Lactate dehydrogenase (LDH) levels remained normal (171.62 ± 42.57 U/L), suggesting no evidence of hemolysis.

Table 1: Iron profile and related markers (N = 90)

Marker	Mean ± SD	Median	Min–Max
Serum ferritin (ng/mL)	4.40 ± 1.37	4.42	2.51 – 6.33
TIBC (µg/dL)	412 ± 69.0	400	329–515
Serum iron (µg/dL)	22.6 ± 5.48	23.1	15.5–29.4
Transferrin saturation (%)	8.9 ± 3.0	9.5	3.68-58.33
Vitamin B12 (pg/mL)	438.61 ± 130.57	439	208–840
LDH (U/L)	171.62 ± 42.57	165	18–321

This study demonstrates the mean HbA1c value was 5.94 ± 0.78% (range: 4.74–7.06%), which falls within the normal reference range for non-diabetic individuals (<5.7%), though few patients demonstrated mildly elevated values. The mean fasting blood sugar (FBS) was 99.08 ± 11.02 mg/dL (range: 77–126 mg/dL), and the mean post-prandial blood sugar (PPBS) was 138.16 ± 24.51 mg/dL (range: 28–198 mg/dL).

[Table 2] illustrates the comparison of iron profile parameters among different HbA1c categories in study participants. A statistically significant variation in serum iron and serum ferritin levels was observed across the HbA1c groups. Participants with higher HbA1c levels (>6.5%) had lower mean serum iron (19.34 ± 6.71 µg/dL) and serum ferritin (3.85 ± 1.25 ng/mL) compared to those with normal glycemic status (HbA1c 4–5.6%), whose mean values were 23.69 ± 6.37 µg/dL and 5.18 ± 1.53 ng/mL, respectively. The differences were statistically significant (p = 0.03 for serum iron; p = 0.009 for serum ferritin). In contrast, total iron-binding capacity (TIBC) showed a progressive but non-significant increase from the normal HbA1c group (393.61 ± 75.29 µg/dL) to the diabetic group (419.54 ± 94.51 µg/dL; p = 0.494).

Table 2: Comparison of iron profile parameters between HbA1c categories (N = 90)

Parameter	HbA1c Category			
	4 – 5.6 %	5.7 – 6.4 %	>6.5 %	p value#
Serum Iron (µg/dL)	23.69 ± 6.37	22.83 ± 6.70	19.34 ± 6.71	0.03
Serum Ferritin (ng/mL)	5.18 ± 1.53	4.63 ± 2.13	3.85 ± 1.25	0.009
TIBC (µg/dL)	393.61 ± 75.29	409.33 ± 84.24	419.54 ± 94.51	0.494

Data are presented as mean ± standard deviation (SD). #p-values obtained using one-way ANOVA.

The study reveals, 44 individuals had moderate anemia with a mean HbA1c of 5.9 ± 0.8%, while 46 individuals had severe anemia with a mean HbA1c of 6.0 ± 0.7%. The difference in HbA1c values between the two groups was not statistically significant (p = 0.329). This finding suggests that within this cohort, the severity of anemia, as defined by hemoglobin concentration, did not significantly influence HbA1c levels.

[Table 3] illustrates the changes in glycemic indices and HbA1c following iron therapy in the study participants. After treatment, the mean HbA1c significantly decreased from 5.94 ± 0.78 % to 5.28 ± 0.32% (p<0.001), demonstrating a clear effect of iron supplementation on lowering HbA1c levels. In contrast, fasting blood sugar (FBS) and post-prandial blood sugar (PPBS) showed minimal, non-significant changes, with FBS decreasing slightly from 99.08 ± 11.02 mg/dL to 98.8 ± 10.6 mg/dL (p = 0.41) and PPBS from 138.16 ± 24.51 mg/dL to 137.6 ± 24.0 mg/dL (p = 0.43). These findings indicate that the reduction in HbA1c was independent of changes in actual blood glucose, confirming that the elevated HbA1c observed in iron-deficient participants is primarily due to the iron deficiency itself rather than hyperglycemia.

Table 3: Pre–Post changes after iron therapy

Parameter	Pre mean ± SD	Post mean ± SD	p-value$
HbA1c (%)	5.94 ± 0.78	5.18 ± 0.32	<0.001
FBS (mg/dL)	99.08 ± 11.02	98.8 ± 10.6	0.41
PPBS (mg/dL)	138.16 ± 24.51	137.6 ± 24.0	0.43

$Paired t test.

DISCUSSION

Anemia affects over 30% of the global population, with iron deficiency accounting for nearly half of cases.19 As per WHO, iron deficiency anemia (IDA) is the most prevalent nutritional deficiency worldwide, including in India. IDA disproportionately affects women due to menstrual blood loss, pregnancy, and lactation.[3] In the present study, a female predominance (67%) with a 2:1 female-to-male ratio was observed, consistent with Dutta et al.[1] and Gharde et al.[2]

Fatigue (57%) was the most common symptom, followed by dyspnea (13%) and palpitations (8.9%), aligning with previous reports.[2] IDA was observed across adult age groups, with higher representation among younger (18–29 years) and elderly (60–65 years) individuals, reflecting known bimodal trends.

HbA1c is widely accepted as the diagnostic and monitoring standard for Diabetes mellitus (≥6.5%), yet it is influenced by non-glycemic factors such as anemia, hemoglobinopathies, renal disease, and vitamin deficiencies.20 In this study, a significant inverse association was observed between HbA1c and iron indices. Participants with HbA1c>6.5% had significantly lower serum iron and ferritin levels (p = 0.03 and p = 0.009, respectively), consistent with Dutta et al.[1]

Mean ferritin (4.40 ± 1.37 ng/mL), serum iron (22.6 ± 5.48 µg/dL), transferrin saturation (8.9 ± 3.0%), and elevated TIBC confirmed depleted iron stores. Mean HbA1c (5.94 ± 0.78%) remained within the non-diabetic range, though mildly elevated in some patients despite normal fasting and postprandial glucose values.

Mechanistically, prolonged erythrocyte lifespan in IDA increases glucose exposure, enhancing glycation.[2,3] Structural hemoglobin alterations and oxidative stress may further increase glycation

susceptibility.23 Following iron therapy, HbA1c levels declined significantly without changes in glucose levels, supporting earlier findings by El-Agouza et al,[3] Coban et al,[2] Tarim et al., and Rafat et al,[2] Rajagopal et al,[1] and Bansal et al,[2] similarly demonstrated higher HbA1c levels in IDA compared to controls.

However, some studies (Çetinkaya Altuntaş et al,[2] Krishna et al) reported lower HbA1c in IDA, possibly due to differences in anemia chronicity, erythrocyte turnover, and assay variability. In the present study, no significant correlation was found between HbA1c and hemoglobin or MCV, consistent with Christy et al.[3]

Collectively, the findings support that IDA can falsely elevate HbA1c in non-diabetic individuals, potentially leading to misclassification of glycemic status, particularly in populations with high anemia prevalence.

CONCLUSION

This study demonstrates a significant inverse relationship between HbA1c and iron status in non-diabetic individuals with IDA. HbA1c levels declined significantly after iron supplementation despite stable fasting and postprandial glucose values, confirming that elevated HbA1c in IDA reflects altered erythrocyte dynamics rather than true hyperglycemia. Even moderate iron deficiency may affect HbA1c interpretation.

IDA should therefore be recognized as an independent confounder of HbA1c measurement. Assessment and correction of iron deficiency are essential before diagnosing or monitoring diabetes based solely on HbA1c values.

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