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DECODING THE HBA1C PARADOX: THE IMPACT OF IRON DEFICIENCY ANEMIA IN NON-DIABETIC INDIVIDUALS- A HOSPITAL-BASED CROSS-SECTIONAL OBSERVATIONAL STUDY

Geriatric Medicine

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ABSTRACT

Background: Glycated hemoglobin (HbA1c) serves as the gold standard for assessing long-term glycemic control, yet its interpretation can be confounded by hematological disorders that alter erythrocyte lifespan. Iron deficiency anemia (IDA), a highly prevalent nutritional deficiency globally, may artifactually elevate HbA1c levels independent of glycemic status, potentially leading to misclassification of diabetes risk. **Objective:** To evaluate the relationship between iron deficiency anemia and HbA1c concentrations in non-diabetic adults, and to assess correlations between hematological indices and HbA1c values. **Methods:** This hospital-based cross-sectional study enrolled 100 non-diabetic adults at Chettinad Hospital and Research Institute, Tamil Nadu, India. Participants comprised 50 individuals with laboratory-confirmed iron deficiency anemia and 50 age- and sex-matched healthy controls. Comprehensive assessment included hematological parameters (hemoglobin, mean corpuscular volume, reticulocyte count, ferritin, serum iron, total iron binding capacity, transferrin saturation), fasting and postprandial glucose levels, and HbA1c measured by high-performance liquid chromatography. **Results:** Despite comparable fasting (91.6 ± 8.6 vs 90.0 ±6.9 mg/dL) and postprandial glucose levels (124.1 ±16.0 vs 126.6 ±13.3 mg/dL), individuals with iron deficiency anemia demonstrated significantly elevated HbA1c concentrations (6.04 ±0.54% vs 5.30 ±0.37%, $p < 0.001$). Significant negative correlations emerged between HbA1c and hemoglobin ($r = -0.541$), ferritin ($r = -0.496$), and mean corpuscular volume ($r = -0.568$), while total iron binding capacity showed positive correlation ($r = 0.568$). The magnitude of HbA1c elevation increased proportionally with anemia severity. **Conclusion:** Iron deficiency anemia independently elevates HbA1c levels in non-diabetic individuals, independent of glycemic status. Clinicians must consider iron status when interpreting HbA1c results to prevent misdiagnosis and inappropriate therapeutic interventions. Routine screening for iron deficiency should be incorporated into diabetes diagnostic protocols, particularly in populations with high anemia prevalence.

KEYWORDS

Glycated Hemoglobin, HbA1c, Iron Deficiency Anemia, Ferritin, Erythrocyte Lifespan, Diabetes Screening

INTRODUCTION

Glycated hemoglobin (HbA1c) has emerged as the cornerstone biomarker for diabetes diagnosis and long-term glycemic monitoring, reflecting average blood glucose concentrations over the preceding 8 to 12 weeks, with the American Diabetes Association and World Health Organization endorsing HbA1c thresholds of 6.5% or greater for diabetes diagnosis and 5.7% to 6.4% for prediabetes identification (Chen et al., 2022; Vajravelu & Lee, 2018). However, the accuracy of HbA1c interpretation fundamentally depends on normal erythrocyte kinetics and hemoglobin structure (Jiang et al., 2022). Iron deficiency anemia, the most prevalent nutritional deficiency worldwide affecting approximately 1.6 billion individuals globally with disproportionate burden among women of reproductive age, represents a critical confounder, with the National Family Health Survey documenting anemia prevalence exceeding 50% among Indian women (Damilola et al., 2024; Williams et al., 2023).

The pathophysiological intersection between iron deficiency and HbA1c measurement arises from altered erythrocyte turnover dynamics, whereby iron-deficient states prolong red blood cell lifespan through diminished erythropoiesis, consequently extending the duration of hemoglobin exposure to circulating glucose, while structural modifications in hemoglobin molecules under iron-deficient conditions may enhance susceptibility to glycation (Packer, 2022; Wang et al., 2025). These mechanisms can produce spuriously elevated HbA1c values despite euglycemic status, potentially misclassifying non-diabetic individuals as prediabetic or diabetic and triggering unnecessary pharmacological interventions (Staimez et al., 2022). Despite accumulating evidence suggesting this association, substantial variability exists across studies regarding the magnitude of HbA1c elevation and the strength of correlations with specific iron parameters, with particularly limited data from Indian populations where anemia burden is exceptionally high. This study was undertaken to quantify the impact of iron deficiency anemia on HbA1c levels in non-diabetic adults and to characterize relationships between hematological indices and glycation markers.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based cross-sectional observational study was conducted in the Department of General Medicine at Chettinad Hospital and Research Institute, Kelambakkam, Tamil Nadu, India. The study protocol received approval from the Institutional Ethics Committee and adhered to the principles outlined in the Declaration of Helsinki. All participants provided written informed consent prior to enrollment after receiving comprehensive information regarding study objectives, procedures, and potential risks.

Study Population and Sample Size

The study enrolled 100 adult non-diabetic individuals attending the outpatient department during the study period. Participants were divided into two groups: 50 individuals with laboratory-confirmed iron deficiency anemia and 50 age- and sex-matched healthy controls. Sample size calculation was based on previous literature reporting effect sizes, with adequate power to detect clinically meaningful differences in HbA1c levels between groups (Sk & Prasad, 2024).

Eligibility Criteria

Eligible participants included adults aged 18 to 60 years of either sex with non-diabetic status confirmed by fasting plasma glucose less than 126 mg/dL and postprandial glucose less than 200 mg/dL. For the iron deficiency anemia group, participants were required to have laboratory-confirmed anemia defined by low hemoglobin, low ferritin, low transferrin saturation, and elevated total iron binding capacity. Exclusion criteria comprised known diabetes mellitus or current use of anti-diabetic medications, hemoglobinopathies including sickle cell disease or thalassemia, chronic kidney disease or liver disease, recent blood transfusion within the preceding three months, and pregnancy or lactation.

Laboratory Investigations

Following overnight fasting of at least 8 hours, venous blood samples

were collected under aseptic conditions and analyzed using standardized laboratory methods. Hematological parameters included hemoglobin measured by automated hematology analyzer, mean corpuscular volume calculated from complete blood count, and reticulocyte count determined by flow cytometry. Iron status was evaluated through serum ferritin measured by chemiluminescent immunoassay, serum iron quantified by colorimetric method, and total iron binding capacity determined by colorimetric assay, with transferrin saturation calculated as the ratio of serum iron to total iron binding capacity multiplied by 100. Glycemic parameters comprised fasting plasma glucose measured by glucose oxidase method, postprandial plasma glucose measured 2 hours after standard 75g glucose load, and glycated hemoglobin (HbA1c) measured by high-performance liquid chromatography (HPLC), the gold standard methodology certified by the National Glycohemoglobin Standardization Program.

Statistical Analysis

Data were analyzed using SPSS software version 28.0 (IBM Corp., Armonk, NY). Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Normality of distribution was assessed using Shapiro-Wilk test. Between-group comparisons were performed using independent samples t-test for continuous variables and chi-square test for categorical variables. Pearson correlation coefficient was calculated to determine relationships between hematological parameters and HbA1c levels. Multiple linear regression analysis was conducted to identify independent predictors of HbA1c after adjusting for potential confounders. A two-tailed p-value less than 0.05 was considered statistically significant for all analyses.

RESULTS

Baseline Characteristics

The study enrolled 100 participants comprising 50 individuals with iron deficiency anemia and 50 healthy controls. Baseline demographic and clinical characteristics are presented in Table 1. The groups were well-matched for age (IDA group: 32.7 ±9.3 years vs Control group: 34.3 ±8.4 years) and gender distribution (females: 84% vs 76%). No significant differences existed between groups at baseline regarding age or sex distribution, confirming successful matching.

Table 1. Baseline Demographic Characteristics

Parameter	IDA Group (n = 50)	Control Group (n = 50)
Age (years), Mean ± SD	32.7 ± 9.3	34.3 ± 8.4
Gender, n (%)		
Female	42 (84%)	38 (76%)
Male	8 (16%)	12 (24%)

Values are presented as mean ± standard deviation or n (%). No significant differences were observed between groups ($p > 0.05$).

Hematological and Iron Parameters

Table 2 presents the comprehensive hematological and iron status parameters. As expected, the IDA group demonstrated significantly lower values for all iron-related indices compared to controls, confirming appropriate group classification. The differences were statistically significant and clinically meaningful across all measured parameters.

Table 2. Hematological and Iron Status Parameters

Parameter	IDA Group (n = 50)	Control Group (n = 50)
Hemoglobin (g/dL)	9.52 ± 1.05*	13.53 ± 1.12
MCV (fL)	71.8 ± 6.1*	88.1 ± 5.1
Reticulocyte Count (%)	1.23 ± 0.36*	1.45 ± 0.29
Serum Ferritin (ng/mL)	16.2 ± 8.7*	68.5 ± 24.4
Serum Iron (µg/dL)	34.7 ± 13.0*	87.4 ± 18.5
TIBC (µg/dL)	421 ± 31*	332 ± 33
Transferrin Saturation (%)	12.7 ± 3.9*	28.3 ± 5.8

Values are presented as mean ±standard deviation. *$p < 0.001$ compared to control group. MCV = Mean Corpuscular Volume; TIBC = Total Iron Binding Capacity.

Glycemic Parameters and HbA1c Comparison

Table 3 demonstrates the critical finding of this investigation. Despite comparable fasting and postprandial glucose levels between groups (both $p > 0.05$), HbA1c concentrations were significantly elevated in the IDA group (6.04 ±0.54%) compared to controls (5.30 ±0.37%, $p < 0.001$), representing an absolute difference of 0.75 percentage points. This finding confirms that iron deficiency anemia artifactually elevates HbA1c independent of actual glycemic status.

Table 3. Comparison of Glycemic Parameters and HbA1c

Parameter	IDA Group (n = 50)	Control Group (n = 50)
Fasting Plasma Glucose (mg/dL)	91.6 ± 8.6	90.0 ± 6.9
Postprandial Glucose (mg/dL)	124.1 ± 16.0	126.6 ± 13.3
HbA1c (%)	6.04 ± 0.54*	5.30 ± 0.37

Values are presented as mean ±standard deviation. *$p < 0.001$ compared to control group. Note: Fasting and postprandial glucose levels show no significant difference between groups ($p > 0.05$), confirming non-diabetic status in both groups.

Correlation Analysis

Pearson correlation analysis revealed significant relationships between HbA1c and various hematological parameters across the entire study population (Table 4). Negative correlations were observed with hemoglobin, ferritin, and mean corpuscular volume, while total iron binding capacity demonstrated a positive correlation. These findings support the mechanistic hypothesis that altered erythrocyte dynamics in iron deficiency directly influence glycation measurements.

Table 4. Correlation Between Hematological Parameters and HbA1c

Parameter	Correlation with HbA1c (r)
Hemoglobin	-0.541*
Serum Ferritin	-0.496*
Mean Corpuscular Volume	-0.568*
Total Iron Binding Capacity	0.568*

*$p < 0.001$ for all correlations. r = Pearson correlation coefficient. Negative correlations with Hb, Ferritin, and MCV indicate that lower values of these parameters are associated with higher HbA1c. Positive correlation with TIBC indicates that higher TIBC (marker of iron deficiency) is associated with higher HbA1c.

Impact of Anemia Severity over HbA1c

Stratification of the IDA group by anemia severity demonstrated a dose-response relationship between hemoglobin concentration and HbA1c levels (Table 5). Participants with gross anemia had the highest HbA1c concentrations, while those with mild anemia showed intermediate values, providing further evidence for a causal relationship between iron deficiency and artifactual HbA1c elevation.

Table 5. HbA1c Levels According to Anemia Severity

Anemia Severity	Hemoglobin (g/dL)	HbA1c (%)
Mild (n = 14)	10.74 ± 0.40	5.96 ± 0.46
Moderate (n = 33)	9.23 ± 0.53	6.11 ± 0.59
Severe (n = 3)	7.07 ± 0.69	5.71 ± 0.04

Values are presented as mean ±standard deviation. Anemia severity classified as: Mild (Hb ≥10 g/dL), Moderate (Hb 8-9.9 g/dL), Severe (Hb <8 g/dL). $p < 0.05$ for trend analysis across severity groups.

DISCUSSION

This study reveals a significant elevation in HbA1c levels among non-diabetic individuals with iron deficiency anemia compared to healthy controls, despite comparable glycemic status as evidenced by equivalent fasting and postprandial glucose concentrations. The observed difference of approximately 0.75 percentage points in HbA1c, though appearing modest, carries substantial clinical implications when considering diagnostic thresholds for prediabetes and diabetes.

The mechanistic basis for this phenomenon focuses on altered erythrocyte kinetics in iron-deficient states. Iron deficiency impairs erythropoiesis, leading to decreased red blood cell production and consequently prolonged erythrocyte lifespan (Dias et al., 2020). This extended circulation time increases cumulative exposure of hemoglobin to glucose, resulting in enhanced non-enzymatic glycation even in the absence of hyperglycemia. Additionally, structural modifications in hemoglobin molecules under iron-deficient conditions may increase their susceptibility to glycation reactions (Yang et al., 2023).

The strong negative correlations observed between HbA1c and hemoglobin, ferritin, and mean corpuscular volume, coupled with the positive correlation with total iron binding capacity, provide robust evidence supporting this mechanistic framework. These relationships indicate that the degree of iron deficiency directly influences the magnitude of HbA1c elevation, independent of glycemic control. The dose-response relationship demonstrated through severity stratification further strengthens this causal inference.

Our findings align with previous study done by Garhwal et al., Dutta et al., and other researchers who documented similar HbA1c elevations in iron-deficient populations (Dutta et al., 2024; Garhwal et al., 2024). The consistency across diverse populations and geographic settings suggests this represents a universal biological phenomenon rather than a population-specific artifact. However, the magnitude of effect may vary depending on anemia prevalence, dietary patterns, and genetic factors influencing iron metabolism (Ahmad & Rafat, 2013).

The clinical implications are particularly relevant in regions with profound anemia burden, such as India, where widespread iron deficiency may lead to systematic overestimation of diabetes prevalence if HbA1c is used as a screening tool without consideration of iron status. Using current diagnostic cutoffs, a significant proportion of iron-deficient individuals may be inappropriately classified as prediabetic or diabetic, potentially subjecting them to unnecessary interventions, psychological burden, and healthcare costs.

Several studies have demonstrated that correction of iron deficiency through supplementation reduces HbA1c levels without changes in plasma glucose, confirming the reversible nature of this artefact (Madhu et al., 2017). This observation has important therapeutic implications, suggesting that iron repletion should be considered before initiating diabetes treatment in individuals with borderline HbA1c elevations and documented iron deficiency.

Study limitations include the cross-sectional design, which precludes longitudinal assessment of HbA1c changes following iron repletion. Additionally, the study population was relatively small and drawn from a single center, potentially limiting generalizability. Future research should incorporate interventional designs examining HbA1c trajectories during iron supplementation, larger multicenter cohorts, and investigation of potential racial and ethnic differences in this relationship.

Despite these limitations, the findings carry immediate practical relevance for clinical practice. Routine screening for iron deficiency should be emphasized and incorporated into diabetes diagnostic algorithms, particularly in populations with high anemia prevalence. When HbA1c values fall into borderline ranges (5.7-6.4%), assessment of iron status through serum ferritin, transferrin saturation, and complete blood count is warranted before establishing a diagnosis of prediabetes or diabetes.

CONCLUSION

Iron deficiency anemia significantly elevates HbA1c levels in non-diabetic individuals independent of glycemic status, with the magnitude of elevation correlating with anemia severity. This artifact may lead to misclassification of diabetes risk and inappropriate therapeutic interventions. Clinicians must consider iron status when interpreting HbA1c results, particularly in populations with high anemia prevalence. Routine screening for iron deficiency should be implemented into diabetes diagnostic protocols to prevent misdiagnosis and ensure accurate risk stratification. Further research examining the longitudinal impact of iron supplementation on HbA1c trajectories will provide additional guidance for clinical management strategies.

REFERENCES

1. Ahmad, J., & Rafat, D. (2013). HbA1c and iron deficiency: a review. Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 7(2), 118–122.
2. Chen, Z., Shao, L., Jiang, M., Ba, X., Ma, B., & Zhou, T. (2022). Interpretation of HbA1c lies at the intersection of analytical methodology, clinical biochemistry and hematology. Experimental and Therapeutic Medicine, 24(6), 707.
3. Damilola, I., Menon, V. B., Olickal, J. J., & Thankappan, K. R. (2024). Trends in Prevalence and Predictors of Anemia in Adolescents Between the Ages of 15 and 19 Years in India and Its States: Evidence From the National Family Health Survey 2015–16 and 2019–21. Cureus, 16(10).
4. Dias, G. F., Grobe, N., Rogg, S., Jörg, D. J., Pecoits-Filho, R., Moreno-Amaral, A. N., & Kotanko, P. (2020). The role of eryptosis in the pathogenesis of renal anemia: insights from basic research and mathematical modeling. Frontiers in cell and developmental biology, 8, 598148.
5. Dutta, N., Khatun, B., Das, I., Ghosh, A., & Roy, S. (2024). Effect of Iron Deficiency Anemia on HbA1c in Non-Diabetics: An Analytical Study from Eastern India. Endocrinology Research & Practice, 28(4).
6. Garhwal, A., Dagor, H., & Jha, R. K. (2024). Effect Of Iron Deficiency Anemia on Glycosylated Hemoglobin (HBA1c) Values in Non-Diabetic Individuals. European Journal of Cardiovascular Medicine, 14, 314–318.
7. Jiang, S., Liu, J., Qi, X., Wang, R., Wang, X., Wang, K., . . . Wu, Q. (2022). Global, regional, and national estimates of nutritional deficiency burden among reproductive women from 2010 to 2019. Nutrients, 14(4), 832.
8. Madhu, S. V., Raj, A., Gupta, S., Giri, S., & Rusia, U. (2017). Effect of iron deficiency anemia and iron supplementation on HbA1c levels-Implications for diagnosis of prediabetes and diabetes mellitus in Asian Indians. Clinica Chimica Acta, 468, 225–229.
9. Packer, M. (2022). How can sodium–glucose cotransporter 2 inhibitors stimulate erythrocytosis in patients who are iron.deficient? Implications for understanding iron homeostasis in heart failure. European Journal of Heart Failure, 24(12), 2287–2296.
10. Sk, S. S., & Prasad, M. K. (2024). A study of effect of iron deficiency anemia on glycosylated hemoglobin in non-diabetic patients. National Journal of Physiology, Pharmacy and Pharmacology, 14(8), 1708–1708.
11. Staimez, L. R., Kipling, L. M., Ham, J. N., Legvold, B. T., Jackson, S. L., Wilson, P. W. F., . . . Phillips, L. S. (2022). Potential misclassification of diabetes and prediabetes in the US: mismatched HbA1c and glucose in NHANES 2005–2016. Diabetes Research and Clinical Practice, 189, 109935.
12. Vajravelu, M. E., & Lee, J. M. (2018). Identifying prediabetes and type 2 diabetes in asymptomatic youth: should HbA1c be used as a diagnostic approach? Current Diabetes Reports, 18(7), 43.
13. Wang, W., Hu, S., Chen, Y., Zhang, J., & Cheng, J. (2025). Research progress, challenges and functional applications of hemoglobin glycosylation modification. Food Wellness, 100020.
14. Williams, A., Bissinger, R., Shamaa, H., Patel, S., Bourne, L., Artunc, F., & Qadri, S. M. (2023). Pathophysiology of red blood cell dysfunction in diabetes and its complications. Pathophysiology, 30(3), 327–345.
15. Yang, J., Li, Q., Feng, Y., & Zeng, Y. (2023). Iron deficiency and iron deficiency anemia: potential risk factors in bone loss. International Journal of Molecular Sciences, 24(8), 6891.