

Effect of Iron Deficiency Anemia on HbA1c Levels in Nondiabetic Adults: A Prospective Interventional Study

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Abstract

Objective: To evaluate HbA1c levels in adults with iron deficiency anemia (IDA) without diabetes and to determine the change in HbA1c following correction of iron deficiency anemia. **Methods:** This prospective interventional study was conducted over 120 days in the Department of General Medicine, Doon Medical College, Dehradun. Adults aged 18–60 years with IDA fulfilling predefined inclusion and exclusion criteria were enrolled. Age- and sex-matched controls were included for baseline comparison. Clinical assessment and laboratory investigations included complete blood count, serum iron, ferritin, HbA1c and tests used to exclude relevant comorbid conditions. HbA1c was reassessed after correction of anemia with iron therapy. Continuous variables were summarized as mean $\pm$ standard deviation and categorical variables as frequency and percentage. Student's t test, paired t test and chi-square testing were used as appropriate. **Results:** The study included 120 participants with IDA and 120 matched controls. Mean age of the IDA group was 34.1 ± 8.4 years; 68.3% were female. Mean hemoglobin was 6.8 ± 1.1 g/dL at baseline and increased to 12.7 ± 0.4 g/dL after iron treatment ($p < 0.001$). Mean serum iron and ferritin were 21.257 ± 4.688 and 6.871 ± 1.5 , respectively, in the IDA group and increased significantly after treatment. Mean HbA1c was $4.619 \pm 0.308\%$ in the IDA group compared with $5.446 \pm 0.281\%$ in controls ($p < 0.001$). Following anemia correction, mean HbA1c increased to $5.816 \pm 0.323\%$ ($p < 0.001$). Baseline hemoglobin and HbA1c showed a weak positive correlation ($r = 0.26$, $p = 0.005$); the post-treatment correlation was weak and not statistically significant ($r = -0.15$, $p = 0.111$). **Conclusion:** In this study, HbA1c was significantly lower in adults with IDA than in matched controls and increased after correction of anemia. IDA should therefore be considered when interpreting HbA1c, particularly when results are near diagnostic thresholds.

Keywords: Senna auriculata; Alzheimer's disease; network pharmacology; molecular docking; acetylcholinesterase; butyrylcholinesterase; oxidative stress; rutin.

INTRODUCTION

Iron deficiency anemia is a common nutritional anemia and represents the advanced stage of iron deficiency, characterized by depleted iron stores together with reduced hemoglobin and circulating iron. The thesis underlying this manuscript notes that iron deficiency is substantially more common than overt anemia and that iron deficiency anemia has important clinical consequences. In India, anemia remains a major public-health problem.

HbA1c is widely used to estimate chronic glycemic exposure and has also been adopted as a diagnostic test for diabetes when measured by an appropriate standardized method. Because HbA1c depends on erythrocyte biology as well as glucose exposure, conditions that alter erythropoiesis, hemoglobin composition, or erythrocyte survival can influence the measured value. Iron deficiency has therefore been investigated as a potential non-glycemic determinant of HbA1c. The proposed study include changes in erythrocyte age distribution, altered hemoglobin structure or glycation, and increased production of young erythrocytes after iron therapy.

The present study was undertaken to determine HbA1c levels in adults with IDA without diabetes and to assess the change in HbA1c after correction of anemia.

METHODS

The present study is a prospective interventional study conducted over 120 days in the Department of General Medicine, Doon Medical College, Dehradun.

Participants. Consecutive consenting adults aged 18–60 years attending the medical outpatient department or medical wards and fulfilling the study criteria were enrolled. The thesis reports 120 participants in the IDA study group and an equal number of age- and sex-matched controls.

Eligibility. Inclusion criteria were consented patients with IDA attending the medical OPD or medical wards and age 18–60 years. Exclusion criteria were age below 18 or above 60 years, diabetes/impaired fasting glucose/impaired glucose tolerance, chronic renal failure or liver disease, hemolytic anemia, pregnancy, chronic alcoholism, and known

malignancy.

Clinical and laboratory assessment. A detailed history and clinical examination were performed. Laboratory investigations included complete blood count, blood urea, serum creatinine, serum electrolytes, fasting/postprandial blood glucose and/or glucose tolerance testing, urine examination, HbA1c, and an anemia profile including serum ferritin, vitamin B12 and folic acid. Serum iron, ferritin, TIBC and transferrin saturation were used as components of the iron assessment. The thesis records WHO hemoglobin cutoffs of <13 g/dL for men and <12 g/dL for women. Intervention and follow-up. Participants with IDA received iron supplementation for correction of anemia. HbA1c and hematological/iron parameters were reassessed after correction, with the protocol specifying follow-up at approximately three months.

Ethics. Ethical committee clearance was obtained and individual written informed consent was taken.

Statistical analysis. Quantitative variables were summarized as mean, standard deviation and range; qualitative variables were summarized as frequency and percentage. Student's t test was used for comparison of means, paired t test for within-group pre/post comparisons, and chi-square testing for categorical variables. Correlation between hemoglobin and HbA1c was assessed. Statistical analysis was performed using SPSS version 22.

RESULTS

A total of 120 adults with IDA and 120 age- and sex-matched controls were included. The mean age of the study population was 34.1 ± 8.4 years, with ages ranging from 19 to 49 years. Approximately 67% were aged 21–40 years and 28% were aged 41–60 years. Females constituted 68.3% and males 31.7% of the IDA group.

Table 1. Baseline hematological, iron-status and HbA1c findings reported in the thesis. Values are mean $\pm$ SD.

Parameter	IDA baseline	Matched control	p value
Hemoglobin (g/dL)	6.8 ± 1.1	—	<0.001
MCV (fL)	64.46 ± 6.674	91.316 ± 2.851	<0.001
MCH (pg)	19.615 ± 3.018	28.277 ± 0.836	<0.001
Serum iron	21.257 ± 4.688	117.167 ± 13.091	<0.001
Ferritin	6.871 ± 1.5	232.264 ± 28.394	<0.001
HbA1c (%)	4.619 ± 0.308	5.446 ± 0.281	<0.001

Mean hemoglobin concentration in the IDA group was 6.8 ± 1.1 g/dL; 85.8% had hemoglobin below 8 g/dL. After iron treatment, mean hemoglobin increased to 12.7 ± 0.4 g/dL ($p < 0.001$). Mean MCV and MCH increased from 64.46 ± 6.674 fL and 19.615 ± 3.018 pg at baseline to 91.349 ± 2.81 fL and 28.283 ± 0.833 pg, respectively. Mean serum iron increased from 21.257 ± 4.688 to 117.147 ± 12.661 , while ferritin increased from 6.871 ± 1.5 to 237.239 ± 25.267 after treatment; the thesis reports these changes as statistically significant.

Mean HbA1c was $4.619 \pm 0.308\%$ in the IDA group compared with $5.446 \pm 0.281\%$ among controls ($p < 0.001$). Before correction, 86.7% of the IDA group had HbA1c $\leq 5.0\%$, while 13.3% had HbA1c 5.1–5.5%. After correction, 45.8% had HbA1c 5.6–6.0% and 27.5% had HbA1c 6.1–6.5%. Mean HbA1c increased to $5.816 \pm 0.323\%$ after correction ($p < 0.001$).

Table 2. Distribution of HbA1c before and after correction of iron deficiency anemia. Within-group change in mean HbA1c: $p < 0.001$.

HbA1c (%)	Pre-correction n (%)	Post-correction n (%)	Mean
≤ 5.0	104 (86.7)	0 (0)	$4.619 \pm 0.308 \rightarrow 5.816 \pm 0.323$
5.1–5.5	16 (13.3)	32 (26.7)	
5.6–6.0	0 (0)	55 (45.8)	
6.1–6.5	0 (0)	33 (27.5)	
>6.5	0 (0)	0 (0)	

Hemoglobin and HbA1c showed a weak positive correlation before treatment ($r=0.26$, $p=0.005$). After correction, the correlation was weakly negative and not statistically significant ($r=-0.15$, $p=0.111$).

DISCUSSION

The present study reveals that HbA1c was significantly lower in adults with IDA than in age- and sex-matched controls and increased significantly after correction of iron deficiency anemia. This direction of effect differs from several reports in which IDA was associated with higher HbA1c values.

The demographic pattern, with 68.3% females and most participants in the second to fourth decades, is compatible with the recognized vulnerability of women to iron deficiency because of menstrual blood loss and increased iron requirements. The severity of anemia was also notable: mean hemoglobin was 6.8 g/dL and 85.8% of participants had hemoglobin below 8 g/dL.

The hematological response to treatment supports effective correction of the underlying anemia. Hemoglobin, MCV, MCH, serum iron and ferritin all improved substantially. The accompanying increase in HbA1c suggests that erythrocyte-related factors may have contributed to the baseline HbA1c measurement. Horton and Huisman reported lower HbA1c in patients with iron deficiency anemia than in healthy individuals. Sinha et al. similarly reported an increase in HbA1c after iron treatment. In contrast, Brooks and colleagues and several later studies reported elevated HbA1c during iron deficiency with a decline after treatment. Other investigations, including work by van Heyningen and Ford, found little or no clinically important effect.

HbA1c reflects glycation accumulated during the life of the erythrocyte; therefore, altered erythropoiesis and the age distribution of circulating red cells can influence the measured percentage independently of glucose concentration. Increased production of young erythrocytes after iron therapy may alter the circulating red-cell population.

The present study should not be interpreted as evidence that HbA1c is inaccurate in every patient with IDA. In this cohort, HbA1c changed substantially after hematological correction. The study excluded diabetes and several major conditions known to affect HbA1c, reducing some important confounding.

The weak positive correlation between hemoglobin and HbA1c before treatment is statistically significant, whereas the post-treatment correlation is weak and nonsignificant. This suggests that the relationship between erythrocyte parameters and HbA1c may not be linear throughout anemia correction.

Clinically, the findings are relevant when HbA1c is close to a diagnostic or treatment threshold. In patients with substantial anemia, corroboration with plasma glucose-based testing may be appropriate when clinical and biochemical findings are discordant.

CONCLUSION

In adults with iron deficiency anemia, HbA1c was significantly lower than in matched controls and increased significantly following correction of anemia. Hemoglobin and HbA1c showed a weak positive correlation before correction, while the post-correction correlation was weak and statistically nonsignificant. These findings support consideration of iron deficiency anemia as a non-glycemic factor when interpreting HbA1c, particularly around clinically important thresholds. Larger, multicenter studies with longer follow-up and standardized HbA1c methodology are required.

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Conflict of Interest: The authors report no conflict of interest.

Ethics Approval: Ethical committee clearance was obtained and individual written informed consent was taken.

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