RESEARCH ARTICLE/ARAŞTIRMA MAKALESİ

Type 2 Diabetes and Iron Deficiency: The Effect of Oral and Intravenous Iron Therapy on HbA1c

Tip 2 Diyabet ve Demir Eksikliği: Oral ve İntravenöz Demir Tedavisinin HbA1c Üzerindeki Etkisi

Esra SUAY TIMURKAAN[1], Mustafa TIMURKAAN[1], Muhammed Fuad USLU[1]

[1] *Department of Internal Medicine, Fethi Sekin City Hospital, Elazig, Turkey*

Yazışma Adresi/Correspondence:

Mustafa TIMURKAAN

E-posta/E-mail: mustafatimurkan@gmail.com

Department of Internal Medicine

Address Elazig Fethi Sekin City Hospital, Department of Internal Medicine, 23280 Elazig, Turkey

Geliş Tarihi/Received: 30.11.2025 Kabul Tarihi/Accepted:08.12.2025

Esra SUAY TIMURKAAN https://orcid.org/0000-0001-5654-7070 dresrasuay@gmail.com

Mustafa TIMURKAAN https://orcid.org/0000-0003-1950-0489 mustafatimurkan@gmail.com

Muhammed Fuad USLU https://orcid.org/0000-0001-6300-5130 dr.fuslu@gmail.com

Hippocrates Medical Journal / Hippocrates Med J 2025, 5(3): 96-102 DOI: 10.58961/hmj.1833166

Abstract

Introduction	The relationship between iron deficiency anemia (IDA) and HbA1c has been the subject of many recent studies. However, there are serious inconsistencies among studies in the literature. Our aim is to investigate how HbA1c levels are affected before and after treatment in diabetic patients diagnosed with IDA and to clarify unresolved issue.
Materials and Methods	This retrospective analysis was conducted on 899 patients diagnosed with IDA and Type 2 Diabetes Mellitus (T2DM). A total of 166 patients who met the inclusion criteria were included in the study. Participants were divided into three groups: those receiving intravenous iron therapy, those receiving oral iron therapy, and those not receiving any treatment.
Results	The study included 166 patients, 104 of whom were female (62.7%) and 62 were male (37.3%). The average age of the patients was 59.10 ± 13.31 years. In all groups—IV, oral, and no treatment—the second glucose measurement showed a significant increase compared to the first ($p<0.001$). In the no-treatment group, the second HbA1c measurement showed a significant increase compared to the first ($p<0.01$). When comparing HbA1c levels between groups, we found no significant difference either before or after treatment.
Conclusion	In this retrospective cohort of patients with T2DM and IDA, HbA1c levels remained largely stable in iron-treated patients, while increases in HbA1c and glucose levels were observed in the untreated group, paralleling a decrease in ferritin. These findings are consistent with the hypothesis that unresolved iron deficiency may lead to higher HbA1c values. Clinicians should interpret HbA1c values cautiously in the presence of anemia, as iron status may cause HbA1c values to be artificially higher or lower than expected.
Keywords	HbA1c, Iron deficiency anemia, oral iron, parenteral iron, Type 2 Diabetes Mellitus

Özet

Giriş	Demir eksikliği anemisinin (IDA) HbA1c ile ilişkisini incelemek, yakın zamana kadar birçok çalışmanın konusunu olmuştur. Fakat bu çalışmalar arasında ciddi tutarsızlıklar mevcuttur. Amacımız IDA tanılı diyabetik hastalarda, tedavi önecesi ve sonrası HbA1c düzeylerinin nasıl etkilendiğinin incelenmesi ve aydınlatılmamış bu konunun açıklığa kavuşturulmasıdır.
Gereç ve Yöntemler	Bu retrospektif analiz, IDA ve T2DM tanısına sahip 899 hasta üzerinde gerçekleştirilmiştir. Dahil edilme kriterlerini karşılayan toplam 166 hasta çalışmaya alınmıştır. Katılımcılar intravenöz demir tedavisi alanlar, oral demir tedavisi alanlar ve tedavi almayanlar olmak üzere üç gruba ayrılmıştır.
Bulgular	Çalışmaya 104'ü kadın (%62,7) ve 62'si (%37,3) erkek olmak üzere toplam 166 hasta dahil edilmiştir. Hastaların yaş ortalaması 59,10±13,31dir. Hem IV grubunda, hem oral grubunda hem de tedavi almayan grupta ikinci glukoz ölçümü birinciye göre anlamlı şekilde artış göstermiştir ($p<0,001$). Tedavi almayan grupta ikinci HbA1c ölçümü birinciye göre anlamlı şekilde artış göstermiştir ($p=0,01$). HbA1c düzeylerini gruplar arası kıyasladığımızda ise hem tedavi öncesi hemde tedavi sonrası anlamlı bir fark bulamadık.
Sonuç	Bu çalışmada, IDA ve T2DM'li hastalarda demir tedavisi alan gruplarda HbA1c düzeyleri genel olarak stabil seyrederken, tedavi almayan grupta ferritin düzeylerindeki azalma ile birlikte HbA1c ve glukoz değerlerinde artış gözlendi. Bu bulgular, demir eksikliğinin giderilmediği olgularda HbA1c'nin gerçek glisemik durumu olduğundan daha yüksek yansıtabileceği yönündeki hipotezle uyumludur. Anemi varlığında HbA1c'nin değerlendirilmesinde literatürdeki tutarsızlıklar ve HbA1c düzeylerinin normalden hem yüksek hem de düşük olabileceği olasılığı göz önünde bulundurulmalı, diyabet yönetiminde bu parametre dikkatle yorumlanmalıdır.
Anahtar Kelimeler	Demir eksikliği anemisi, HbA1c, oral demir, parenteral demir, Tip 2 Diyabet Mellitus

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a common metabolic disorder in modern societies, characterized by hyperglycemia, insulin resistance, and/or impaired insulin secretion (1). The World Health Organization (WHO) has defined HbA1c, a marker reflecting long-term blood sugar levels, as a diagnostic parameter for T2DM (2). Iron deficiency anemia is particularly common in diabetic patients, with prevalence rates ranging from 13% to 47% depending on the population studied. The presence of anemia may actually precede the development of diabetes (3). The higher incidence of IDA in diabetic patients can be attributed to multiple mechanisms, including suboptimal intake, malabsorption, blood loss due to diabetic enteropathy such as gastroparesis, and increased urinary loss associated with diabetic nephropathy (3,4).

The first study investigating the effects of iron deficiency anemia on HbA1c levels was conducted by Brooks et al., who evaluated HbA1c levels before and after iron treatment in 35 non-diabetic patients with IDA (5). They observed that HbA1c levels were significantly higher in patients with IDA and decreased after iron treatment. The mechanisms leading to increased glycated HbA1c levels were not clear. However, some researchers have argued that the increase in HbA1c levels is not solely due to hyperglycemia but may also be caused by IDA. Therefore, they suggested that HbA1c may lose its reliability in the presence of IDA (6-9). It is also known that certain hemoglobin variants, pregnancy (second and third trimesters and postpartum period), glucose-6-phosphate dehydrogenase deficiency, HIV, hemodialysis, recent blood loss or transfusion, hemolysis, or erythropoietin treatment can alter the relationship between HbA1c and hyperglycemia, leading to misinterpretation. In such cases, it is more appropriate to diagnose diabetes based on plasma glucose criteria (10). This situation can affect treatment strategies and complicate interventions aimed at glucose regulation.

Although studies have been conducted on the effects of metabolic deficiencies on laboratory tests, and these effects are partially understood, studies on post-treatment follow-up are quite limited. While oral and intravenous iron therapy are widely used to treat iron deficiency, the effects of these treatments on glucose metabolism in diabetic patients are not yet fully understood.

The first-line treatment for iron deficiency anemia is oral iron therapy. It involves long-term oral intake by the patient. Generally, 80-100 mg/day of elemental iron is used. It is the most cost-effective and easily accessible form of iron therapy (11). Intravenous iron formulations, which tightly bind elemental iron to different carbohydrate cores, can be safely and effectively preferred in cases where oral therapy fails to overcome iron deficiency, where gastrointestinal complaints increase and the patient cannot tolerate it, in patients with a history of bariatric surgery, in those with inflammatory bowel disease, etc. (12). Understanding the interactions during the treatment process is important for improving the patient's quality of life, minimizing treatment duration, and planning health budgets. Glucose and iron play irreplaceable roles in many reactions in body homeostasis. The increasing frequency of their co-occurrence has highlighted the causal relationship, complex interactions, and the need to identify variables after treatment over time.

In this article, we aimed to examine the effects of oral and intravenous iron preparations used in the treatment of iron deficiency in T2DM patients on HbA1c and glucose regulation. Based on literature reviews and clinical findings, we will discuss the advantages and disadvantages of these treatments. Our primary outcome was the change in HbA1c between baseline and follow-up according to iron treatment status; secondary outcomes included changes in haemoglobin, mean corpuscular volume, ferritin and fasting glucose.

MATERIALS AND METHODS

Research Design

This study used a retrospective cohort design to investigate the relationships between iron deficiency anaemia (IDA), HbA1c levels, and glycaemic dynamics in patients with Type 2 Diabetes Mellitus (T2DM). This analysis was conducted on 899 patients diagnosed with IDA and T2DM who were treated and/or followed up at Elazig Fethi Sekin City Hospital Internal Medicine Clinics between January 2024 and December 2024. Groups were formed after a rigorous screening process based on inclusion/exclusion criteria. A total of 166 patients who met the inclusion criteria were included in the study (Figure 1).

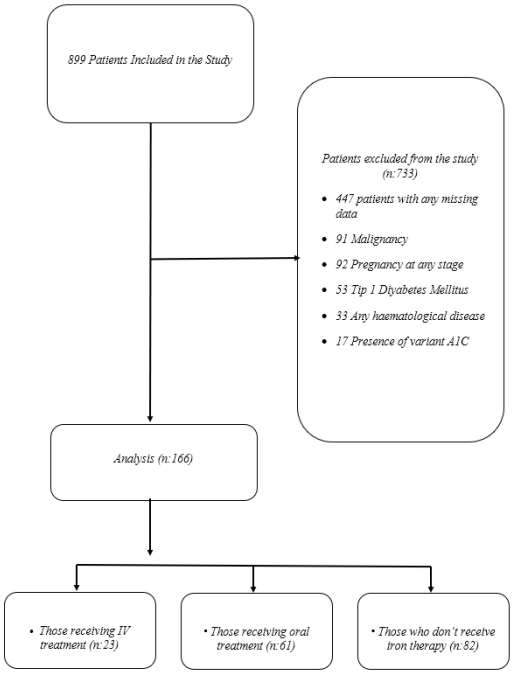

Figure 1

Participants were divided into three groups: those receiving intravenous iron therapy (single or two doses of 1000 to 2000 mg IV carboxymaltose), those receiving oral iron therapy (daily oral 80-100 mg Fe^2 or Fe^3 equivalent iron preparation), and those not receiving any treatment. This classification allowed for the comparison of the effects of treatment on glucose regulation and HbA1c.

For all patients, baseline laboratory values (including HbA1c and indices of iron metabolism) were defined as the measurements obtained at the time of iron deficiency anaemia diagnosis, before initiation of iron therapy. Follow-up values were taken from the routine control visit performed approximately three months after treatment initiation (or after the diagnostic visit for patients who did not receive iron), at which both glycaemic control (HbA1c) and anaemia status were reassessed. Inclusion and exclusion criteria were determined to obtain a more homogeneous patient population.

Inclusion Criteria

- Individuals diagnosed with Type 2 Diabetes and iron deficiency.
- Patients aged 18 years or older.
- Patients who are regularly followed up and can provide data suitable for the study design.

Exclusion Criteria

- Patients with Type 1 Diabetes.
- Pregnant or pediatric populations.
- Presence of variant A1c.
- Glucose-6-phosphate dehydrogenase deficiency.
- Patients with any hemolytic disease.
- Patients with any hematological malignancy.
- Patients using drugs or diagnosed with diseases that may depress bone marrow.
- Patients with chronic kidney disease (CKD) and/or on hemodialysis.
- Patients who could not provide data collected at the appropriate time for the study design.

Data Collection

Patient demographics and laboratory results were analyzed in detail and systematically. Pre- and post-treatment hematological and biochemical parameters were examined within the study. To be included in the analysis, patients were required to have complete hematological and biochemical data at both the time of iron deficiency anemia diagnosis and at the three-month follow-up visit. Specifically, Hgb, MCV, ferritin, glucose, and HbA1c levels were considered key parameters for assessing the relationship between iron deficiency anemia and glycemic control. All data were collected retrospectively from the hospital's electronic database, and the records were meticulously checked for accuracy. Patients with complete and reliable records were included in the study, and those with incomplete or inaccurate data were excluded from the analysis. Furthermore, demographic characteristics such as age, gender, medical history, and comorbidities were comprehensively assessed. These procedures are likely to improve internal validity.

Statistical Analysis

Analyses were performed using the SPSS (Statistical Package for Social Sciences; SPSS Inc., Chicago, IL) version 22. In this study, descriptive data in the study are presented as n and percentages for categorical variables, and all continuous variables were summarized as medians (IQR) due to non normal distributions. The normality of continuous variables was assessed using the Kolmogorov–Smirnov test. The Mann–Whitney U test was used for comparisons between two independent groups. Within-group pre–post comparisons were performed using the Wilcoxon signed-rank test. For comparisons among the three iron-treatment groups, the Kruskal–Wallis test was applied; where the global test was significant, pairwise post-hoc comparisons were examined to identify which groups differed. A two-sided p value <0.05 was considered statistically significant.

RESULTS

The study included 166 patients, 104 of whom were female (62.7%) and 62 were male (37.3%). The average age of the patients was 59.10 ± 13.31 years, with a median age of 62.00 (51.00-69.00) years. Of the patients, 13.9% received IV iron, 36.7% received oral iron therapy, and 49.4% did not receive any iron treatment (Table 1).

Table 1. Characteristics of all patients

		N	%
Gender	Female	104	62.7
	Male	62	37.3
Iron intake status	IV	23	13.9
	Oral	61	36.7
	None	82	49.4
		Median (IQR)	
Age		62.00 (51.00-69.00)	
Hgb1		11.10 (10.20-12.70)	
Hgb2		11.60 (10.70-13.20)	
MCV1		80.25 (76.20-83.60)	
MCV2		81.10 (77.00-84.50)	
Ferritin1		25.50 (12.00-109.00)	
Ferritin2		56.00 (19.00-138.00)	
Hb1Ac1		10.20 (8.60-11.00)	
HbA1c2		10.25 (7.70-11.20)	
Glucose1		115.00 (105.00-137.00)	

Glucose2	130.00 (116.00-163.00)
Hgb change	0.25 (0.10-0.60)
MCV change	0.50 (0.20-1.00)
Ferritin change	9.00 (1.00-72.00)
HbA1c change	0.30 (0.0-0.70)
Glucose change	12.00 (4.00-28.00)

***Hgb:** Hemoglobin, MCV: Mean Corpuscular Volume.

In all groups—IV, oral, and no treatment—the second Hgb levels showed a significant increase compared to the first (p<0.001). In all groups—IV, oral, and no treatment—the second MCV measurement showed a significant increase compared to the first (p<0.001). In both the IV (p<0.001) and oral (p<0.001) groups, the second ferritin measurement showed a significant increase compared to the first, while in the no-treatment group, it showed a significant decrease (p=0.007).

In the no-treatment group, the second HbA1c measurement showed a significant increase compared to the first (p=0.01). In all groups—IV, oral, and no treatment—the second glucose measurement showed a significant increase compared to the first (p<0.001) (Table 2).

Table 2. Comparison of laboratory values before and after treatment by iron intake status

	IV		**Oral**		**None**	
	Before	**After**	**Before**	**After**	**Before**	**After**
	Median (IQR)	***Median (IQR)***	***Median (IQR)***	***Median (IQR)***	***Median (IQR)***	***Median (IQR)***
Hgb	10.30 (10.00-10.80)	11.40 (11.20-11.90)	10.30 (10.00-10.80)	10.60 (10.10-11.10)	12.60 (11.50-13.90)	13.10 (11.80-14.20)
p*	**<0.001**		**<0.001**		**<0.001**	
MCV	76.60 (62.60-80.60)	77.70 (69.50-80.90)	76.80 (70.40-79.60)	77.90 (70.80-81.70)	83.05 (80.70-85.40)	84.00 (81.10-85.90)
p*	**<0.001**		**<0.001**		**<0.001**	
Ferritin	10.00 (5.00-12.00)	134.00 (100.00-150.00)	15.00 (11.00-32.00)	19.00 (15.00-50.00)	109.50 (31.00-139.00)	81.50 (32.00-156.00)
p*	**<0.001**		**<0.001**		**0.007**	
HbA1c	10.10 (10.00-10.30)	10.20 (7.60-10.70)	10.40 (8.40-10.70)	10.30 (7.30-11.20)	10.10 (8.60-11.30)	10.25 (7.90-11.20)
p*	0.073		0.122		**<0.01**	
Glucose	118.00 (108.00-138.00)	130.00 (121.00-165.00)	107.00 (102.00-125.00)	122.00 (110.00-148.00)	118.00 (112.00-148.00)	134.50 (121.00-186.00)
p*	**<0.001**		**<0.001**		**<0.001**	

*Wilcoxon analysis was applied.

**Hgb: Hemoglobin, MCV: Mean Corpuscular Volume.

Significant differences were observed between iron intake statuses in terms of the first measured Hgb (p<0.001), the first measured MCV (p<0.001), and the second measured MCV (p<0.001), and these differences were due to the differences between the no-treatment group and the other two groups. Significant differences were observed between iron intake statuses in terms of the second measured Hgb (p<0.001), the first measured ferritin (p<0.001), and the second measured ferritin (p<0.001), and these differences were due to the differences between all groups. Significant differences were observed between iron intake statuses in terms of the first measured glucose (p<0.001), and these differences were due to the differences between the oral treatment group and the other two groups. Significant differences were observed between iron intake statuses in terms of the second measured glucose (p=0.01), and these differences were due to the differences between the oral treatment group and the no-treatment group. Significant differences were observed between iron intake statuses in terms of Hgb change (p<0.001) and ferritin change (p<0.001), and these differences were due to the differences between the IV treatment group and the other two groups (Table 3).

Table 3. Comparison of laboratory values by iron intake status

	IV	**Oral**	**None**	**p***
	Median (IQR)	***Median (IQR)***	***Median (IQR)***	
Hgb1	10.30 (10.00-10.80)[a]	10.30 (10.00-10.80)[a]	12.60 (11.50-13.90)[b]	**<0.001**
Hgb2	11.30 (11.20-11.90)[a]	10.60 (10.10-11.10)[b]	13.10 (11.80-14.20)[c]	**<0.001**
MCV1	76.60 (62.60-80.60)[a]	76.80 (70.40-79.60)[a]	83.05 (80.70-85.40)[b]	**<0.001**
MCV2	77.70 (69.50-80.90)[a]	77.90 (70.80-81.70)[a]	84.00 (81.10-85.90)[b]	**<0.001**
Ferritin1	10.00 (5.00-12.00)[a]	15.00 (11.00-32.00)[b]	109.50 (31.00-139.00)[c]	**<0.001**
Ferritin2	134.00 (100.00-150.00)[a]	19.00 (15.00-50.00)[b]	81.50 (32.00-156.00)[c]	**<0.001**
HbA1c1	10.10 (10.00-10.30)	10.40 (8.40-10.70)	10.10 (8.60-11.30)	0.464
HbA1c2	10.20 (7.60-10.70)	10.30 (7.30-11.20)	10.25 (7.90-11.20)	0.670
Glucose1	118.00 (108.00-138.00)[a]	107.00 (102.00-125.00)[b]	118.00 (112.00-148.00)[a]	**<0.001**
Glucose2	130.00 (121.00-165.00)[a,b]	122.00 (110.00-148.00)[a]	134.50 (121.00-186.00)[b]	**0.010**
Hgb change	1.00 (0.50-1.20)[a]	0.20 (0.10-0.40)[b]	0.20 (0.10-0.50)[b]	**<0.001**
MCV change	0.70 (0.10-1.10)	0.60 (0.30-1.30)	0.40 (0.20-0.90)	0.231
Ferritin change	126.00 (90.00-139.00)[a]	5.00 (1.00-29.00)[b]	−8.00 (−32.00 – 1.00)[b]	**<0.001**
HbA1c change	0.30 (0.00-0.70)	0.20 (0.00-0.70)	0.30 (0.00-0.70)	0.693
Glucose change	13.00 (3.00-28.00)	12.00 (3.00-28.00)	13.00 (5.00-29.00)	0.767

* Kruskal–Wallis test was applied for comparisons among the three iron-treatment groups.

****a,b,c:** Different superscripts (different letters within a column or group) indicate statistically significant differences between groups (p<0.05). There are no significant differences between groups sharing the same letter.

*****Hgb:** Hemoglobin, **MCV:** Mean Corpuscular Volume.

DISCUSSION

In this retrospective cohort of patients with T2DM and iron deficiency anaemia, HbA1c levels remained broadly stable over time in those who received either intravenous or oral iron therapy, whereas a modest but statistically significant increase in HbA1c was observed only in the untreated group (p=0.01). Fasting glucose increased in all three groups with a similar magnitude of change, suggesting that iron replacement per se did not exert a major additional effect on glycaemic control beyond background clinical care. Haemoglobin, mean corpuscular volume and ferritin differed significantly between groups, reflecting more severe iron deficiency at baseline and greater improvement in iron indices in the intravenous iron group. In the untreated group, serial measurements demonstrated a decline in ferritin concentrations over time, and this worsening of iron stores was temporally associated with concomitant increases in HbA1c and fasting plasma glucose. In our cohort, this combination of falling ferritin and rising HbA1c in patients whose anaemia was not actively treated is compatible with the hypothesis that progressive deterioration in iron stores may be accompanied by an upward drift in HbA1c values. However, given the retrospective design, strict exclusion criteria and the modest sample size, this association should be interpreted as hypothesis-generating rather than causal.

Iron deficiency anaemia (IDA) is one of the most common nutritional deficiencies worldwide and is characterised by reduced total body iron, impaired haemoglobin synthesis and a wide spectrum of systemic manifestations, including fatigue, weakness, headache, irritability, tissue hypoxia and impaired immune function (13,14). HbA1c is widely used in diabetic follow-up and is generally regarded as less susceptible than plasma glucose to short-term variation related to diet, physical activity, intercurrent inflammation and local laboratory conditions (15). However, HbA1c reflects glycaemic exposure over the lifespan of circulating erythrocytes. In IDA, changes in red blood cell indices and turnover can alter this exposure window and may therefore lead to spuriously increased or decreased HbA1c values that are not fully explained by concomitant glycaemia (16). Consistent with this biological plausibility, classic reports such as the study by Brooks et al., which described spuriously elevated HbA1c in IDA, and more recent work by Altuntaş et al., in which low baseline HbA1c in IDA increased after iron therapy, illustrate how anaemia and its treatment can both modify HbA1c and contribute to the apparently conflicting conclusions in the literature (5,17).

Many epidemiological and clinical studies have reported that IDA is associated with higher HbA1c levels independent of plasma glucose (18–24). Conversely, a meta-analysis in diabetic populations suggested that HbA1c may be significantly lower in anaemic than in non-anaemic patients, and that this difference is related to the severity of anaemia; in that analysis, resolution of anaemia by iron supplementation was accompanied by an increase in HbA1c (25). Studies examining iron biomarkers and glycaemic indices in T2DM have also yielded heterogeneous results: serum iron has been linked to the glycaemic course of T2DM, whereas total iron-binding capacity, transferrin saturation and ferritin have not shown consistent associations with glucose or HbA1c (26). Other investigations comparing HbA1c before and after iron replacement have found higher baseline HbA1c in IDA than in controls, followed by a significant decrease after iron therapy, emphasising that IDA can produce misleading elevations in HbA1c that should not be ignored when interpreting this marker (27). In the study by Altuntaş et al., HbA1c increased after treatment in anaemic patients; furthermore, patients with more severe anaemia had lower baseline HbA1c than those with milder anaemia, again suggesting that IDA may in some contexts be associated with low, rather than high, HbA1c (17). In contrast, Gan et al. did not identify a robust association between HbA1c and anaemia, and highlighted the role of confounding factors such as age, diabetes duration and control, comorbid conditions and iron deficiency without overt anaemia (28). This helps explain why different studies have reported opposite directions of association: even small differences in study design, population or iron indices can change both the direction and the size of the observed HbA1c shift.

In this setting, our results offer a few practical points for clinicians. First, in this cohort of patients with T2DM, after excluding conditions that directly distort red blood cell indices, we did not see any clear differences in HbA1c between the groups at either baseline or follow-up, despite marked differences in haematological indices and ferritin responses, particularly in the intravenous iron group. This suggests that, under routine care conditions, correcting iron deficiency with either oral or intravenous iron may not substantially shift HbA1c in patients with established T2DM, at least over the time frame captured in our study. Second, the untreated group showed a pattern in which declining ferritin was accompanied by increases in both HbA1c and fasting glucose. This profile is compatible with the hypothesis that unresolved iron deficiency can contribute to upward drift in HbA1c, but also emphasises that any such effect is intertwined with genuine deterioration in glycaemic control rather than purely analytic artefact. Because we did not perform formal correlation or multivariable modelling between changes in haematological indices and HbA1c, our study cannot quantify the independent contribution of iron-related mechanisms to the observed HbA1c changes. In this direct comparison of intravenous iron, oral iron and no iron therapy within the same T2DM cohort, our data suggest that active iron repletion does not produce large, systematic distortions in HbA1c, whereas failure to correct worsening iron deficiency may be associated with modest, but potentially clinically relevant, increases in HbA1c over time. Prospective

studies that combine alternative glycaemic markers (e.g. glycated albumin) with continuous glucose monitoring could further disentangle biological changes in glycaemia from measurement artefacts related to iron status and anaemia.

Limitations

Strengths of our study include the use of standardised HbA1c measurements and the systematic exclusion of conditions that directly affect the red blood cell series, such as haemoglobinopathies, haematological malignancies, myelodysplastic syndromes and aplastic anaemia. By removing these potential confounders, we sought to reduce bias in the assessment of the relationship between iron status and HbA1c. Nevertheless, several limitations should be acknowledged. First, the study is retrospective and single-centre, and both the total sample size and the numbers within each treatment group are relatively small, so external generalisability may be limited. Second, the time interval between baseline and follow-up measurements was not fully standardised, and only two time points were available for analysis. Third, we did not perform formal correlation or multivariable analyses between changes in haematological indices and changes in HbA1c, so our data cannot establish a causal relationship. For these reasons, larger prospective studies, ideally incorporating alternative glycaemic markers such as glycated albumin, are needed to confirm and extend our findings.

CONCLUSIONS

As can be seen, the results regarding the relationship between HbA1c and anaemia in the literature are complex and sometimes contradictory. In our cohort of patients with T2DM and iron deficiency anaemia, iron therapy improved haematological indices while HbA1c remained stable in the treated groups and increased only in patients who did not receive iron replacement. HbA1c analysis is affected by dynamic processes such as red blood cell kinetics, iron status and assay methodology, and these processes may vary between individuals and populations. Therefore, HbA1c values in the presence of anaemia should be interpreted with caution, and iron status should always be considered when HbA1c appears discordant with the clinical picture of glycaemic control.

Ethics Committee Approval: Ethical approval was obtained from the Elazig Fethi Sekin City Hospital Non-Interventional Research Ethics Committee on 19.12.2024-2024/06-13. Our study was conducted in accordance with the Helsinki Declaration. Due to the retrospective design of the study, informed consent forms were waived.

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from Patients.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

Abbreviations

IDA: Iron deficiency anaemia

T2DM: Type 2 Diabetes Mellitus

HbA1c: Glycated haemoglobin

IV: Intravenous

CKD: Chronic kidney disease

REFERENCES

1.ElSayed NA, Grazia Aleppo, Bannuru RR, et al. American Diabetes Association Professional Practice Committee. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes. Diabetes Care. 2024;47: 20-42.

2.World Health Organization. Use of glycated haemoglobin (HbA1c) in the diagnosis of diabetes mellitus: abbreviated report of a WHO consultation. Geneva, Switzerland: World Health Organization; 2011. Accessed February 20, 2025. Available from: https://pubmed.ncbi.nlm.nih.gov/26158184/

3.Soliman AT, De Sanctis V, Yassin M, Soliman N. Iron deficiency anemia and glucose metabolism. Acta Biomed. 2017; 88:112-118.

4.Taderegew MM, Gebremariam T, Tareke AA, Woldeamanuel GG. Anemia and its associated factors among type 2 diabetes mellitus patients attending Debre Berhan Referral Hospital, North-East Ethiopia: a cross-sectional study. J Blood Med. 2020; 11:47-58.

5.Brooks AP, Metcalfe J, Day JL, Edwards MS. Iron deficiency and glycosylated haemoglobin A. Lancet. 1980 Jul 19;2(8182):141-144.

6.English E, Idris I, Smith G, Ketan Dhatariya, Kilpatrick ES, John WG. The effect of anaemia and abnormalities of erythrocyte indices on HbA1c analysis: a systematic review. Diabetologia. 2015; 58:1409-1421.

7.Kim C, Bullard KM, Herman WH, Beckles GL. Association Between Iron Deficiency and A1C Levels Among Adults Without Diabetes in the National Health and Nutrition Examination Survey, 1999–2006. Diabetes Care. 2010; 33:780-785.

8.Rajagopal L, Ganapathy S, Arunachalam S, Raja V, Ramraj B. Does iron deficiency anaemia and its severity influence HbA1c level in non-diabetics? An analysis of 150 cases. J Clin Diagn Res. 2017; 11:13-15.

9.Shanthi B, Revathy C, Devi AJ, Subhashree. Effect of iron deficiency on glycation of haemoglobin in nondiabetics. J Clin Diagn Res. 2013; 7:15-17.

10.ElSayed NA, McCoy RG, Grazia Aleppo, et al. American Diabetes Association Professional Practice Committee. 2. Diagnosis and classification of diabetes: Standards of Care in Diabetes. Diabetes Care. 2025;48: S27-S49.

11.Batchelor EK, Kapitsinou P, Pergola PE, Kovesdy CP, Jalal DI. Iron Deficiency in Chronic Kidney Disease: Updates on Pathophysiology, Diagnosis, and Treatment. J Am Soc Nephrol. 2020; 31:456-468.

12. DeLoughery TG, Jackson CS, Ko CW, Rockey DC. AGA Clinical Practice Update on Management of Iron Deficiency Anemia: Expert Review. Clin Gastroenterol Hepatol. 2024; 22:1575-1583.e4.

13. Kumar A, Sharma E, Marley A, Samaan MA, Brookes MJ. Iron deficiency anaemia: pathophysiology, assessment, practical management. BMJ Open Gastroenterol. 2022;9: e000759.

14.Bae H, Kim KT, Heo MH, Do YR, Cho YW. The prevalence and clinical characteristics of restless legs syndrome in patients with iron deficiency anemia in Korea. J Clin Sleep Med. 2021; 17:1447-1452.

15.Tarim O, AYGUN Kucukerdogan, UNSAL Gunay, OZGEN Eralp, Ilhan Ercan. Effects of iron deficiency anemia on hemoglobin A1c in type 1 diabetes mellitus. Ped Intern. 1999; 41:357-362.

16.Radin MS. Pitfalls in hemoglobin A1c measurement: when results may be misleading. J Gen Intern Med. 2014; 29:388-394.

17.Altuntas SC, Evran M, Gürkan E, Sert M, Tetiker T. HbA1c level decreases in iron deficiency anemia. Wien Klin Wochenschr. 2020; 133:102-106.

18.Ahmad J, Rafat D. HbA1c and iron deficiency: A review. Diabetes Metab Syndr. 2013; 7:118-122.

19.Christy AL, Manjrekar PA, Babu RP, Hegde A, Rukmini MS. Influence of iron deficiency anemia on hemoglobin A1c levels in diabetic individuals with controlled plasma glucose levels. Iran Biomed J. 2014; 18:88-93.

20.Hardikar PS, Joshi SM, Bhat DS, et al. Spuriously High Prevalence of Prediabetes Diagnosed by HbA1c in Young Indians Partly Explained by Hematological Factors and Iron Deficiency Anemia. Diabetes Care. 2012; 35:797-802.

21.Ford ES, Cowie CC, Li C, Handelsman Y, Bloomgarden ZT. Iron-deficiency anemia, non-iron-deficiency anemia and HbA1c among adults in the US. J Diabetes. 2011; 3:67-73.

22.Son JI, Rhee SY, Woo J, et al. Hemoglobin A1c May Be an Inadequate Diagnostic Tool for Diabetes Mellitus in Anemic Subjects. Diabetes Metab J. 2013; 37:343-348.

23.Silva JF, Pimentel AL, Camargo JL. Effect of iron deficiency anaemia on HbA1c levels is dependent on the degree of anaemia. Clin Biochem. 2016; 49:117–120.

24.Patil S, Biradar SM, Renuka Holyachi, Shashidhar Devarmani, Reddy S. Assessment of Serum Electrolytes and Glycated Hemoglobin Level in Non-diabetic Iron-Deficient Anaemic Patients. Cureus. 2023;15: e38656.

25.Kuang L, Li W, Xu G, You M, Wu W, Li C. Systematic review and meta-analysis: influence of iron deficiency anemia on blood glycosylated hemoglobin in diabetic patients. Ann Palliat Med. 2021; 10:11705-11713.

26.Liang Y, Luo S, Hon T, He B, Schooling CM, Shiu. Association of iron homeostasis biomarkers in type 2 diabetes and glycaemic traits: a bidirectional two-sample Mendelian randomization study. Int J Epidemiol. 2023; 52:1914-1925.

27.Madhu SV, Raj A, Gupta S, Giri S, Rusia U. Effect of iron deficiency anemia and iron supplementation on HbA1c levels—implications for diagnosis of prediabetes and diabetes mellitus in Asian Indians. Clin Chim Acta. 2017; 468:225-229.

28.Gan T, Liu X, Xu G. Glycated albumin versus HbA1c in the evaluation of glycemic control in patients with diabetes and CKD. Kidney Int Rep. 2018; 3:542-554.