

Anemia and its association with glycemia and transaminitis in patients with type 2 diabetes mellitus: A cross-sectional pilot study

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ABSTRACT

Background and Aims: Anemia impairs glucose homeostasis, affects glycemic control, and predisposes to complications in diabetics. It correlates with oxidative stress and increases the risk of developing microvascular and macrovascular complications. However, it is an underrecognized comorbidity in diabetics. This study was conducted to assess the prevalence of anemia in diabetic patients and compare the metabolic profiles of anemic and non-anemic diabetics. **Methods:** This is a cross-sectional study, conducted among type 2 diabetes (T2DM) patients, at the outpatient clinic. Patients with chronic kidney disease (CKD), known hematological disorders, and chronic inflammatory disorders were excluded. **Results:** Of the 97 patients, 37 (38.14%) were found to be anemic (hemoglobin (Hb): male <13 g/dl, female <12 g/dl). The mean values of fasting blood sugar (FBS) in low and normal mean corpuscular volume (MCV) patients were 265.9 ± 43.7 mg/dl and 157.2 ± 7.2 mg/dl, respectively ($P = 0.0026$), and those of postprandial blood sugar (PPBS) were 370.3 ± 58.4 mg/dl and 226.3 ± 10.1 mg/dl, respectively ($P = 0.0015$). It was found that 6 (22.2%) of 27 patients with raised alanine aminotransferase (ALT) had anemia against 27 (45.8%) of 59 patients with normal ALT ($P = 0.03$). The mean Hb levels in patients with raised and normal ALT were 13.31 ± 2.3 gm% and 12.2 ± 2.0 gm% ($P = 0.03$), respectively. **Conclusions:** Blood sugar may have a direct relationship with MCV in T2DM patients. Hb tends to relate to hepatic enzymes likely due to altered dietary patterns in anemics. Further larger studies on the effect of iron supplementation and dietary habits on glycemic control and hepatic steatosis are warranted.

Keywords: Anemia, ALT, corpuscular volume, diabetes, diet, metabolic, microcytic, sugar control

Introduction

Diabetes mellitus (DM) is one of the most common chronic disorders with profound metabolic and organ-specific effects. Anemia has an underrecognized association with DM.

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The prevalence across studies and populations varies from 22 to 50%.^[1] In a study, anemia has been found to be twice as common in type 2 diabetes (T2DM) patients compared with controls.^[2] The inflammation exhibited by the elevated expression of pro-inflammatory cytokines, including interleukin (IL)-6, tumor necrosis factor (TNF)- α , and nuclear factor-kappa B (NF- κ B), is one of the main pathogenic processes. Low hemoglobin (Hb) is because of these cytokines' anti-erythropoietic actions, modifications in progenitors' susceptibility to erythropoietin, and immature erythrocyte death.^[3] In addition, it seems that

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individuals with diabetes have higher rates of iron deficiency anemia (IDA) than people without diabetes.^[4] The prevalence of anemia is significantly greater in older men and women, people with long-standing diabetes, hypertensives, diabetic females, patients with low glomerular filtration rates, and poorly controlled diabetics.^[5-7] In people with T2DM, serum C-peptide concentrations were negatively correlated with anemia.^[8]

In both humans and animals, glucose homeostasis can be compromised by IDA. It might have a detrimental impact on glucose management and put diabetic patients at risk for additional complications. Similarly, taking an iron supplement helps manage DM and reduce the progression of complications.^[4] Oxidative stress and anemia are associated because erythrocytes are a significant source of antioxidants in the blood.^[9] Anemia addressed in DM is important because of metabolic and cardiac implications.^[10,11] In individuals with DM, anemia may exacerbate diabetic retinopathy, diabetic nephropathy, foot ulcers, and cardiovascular disease.^[12-15]

Anemia, particularly IDA, is the most common hematological disorder in the Indian population. Whether or not it is a cause or consequence of adverse glycemic control is a matter of concern. However, anemia has been found to be negatively associated with transaminitis, which implies the importance of Hb in the worsening of fatty liver disease, which is further implicated in the progression of the glycemic and metabolic profiles of diabetic patients.

This study aimed to study the prevalence and hematological classification of anemia in stable diabetic patients and compare the metabolic and biochemical profiles of anemic and non-anemic diabetics.

Methods

This cross-sectional analytical observation study was conducted in the Medicine Department of a tertiary care hospital in New Delhi, wherein stable adult patients with an age more than 18 years with confirmed DM (based on American Diabetes Association guidelines) were invited to participate if they had a recent Hb report within 1 month available. Other blood reports, such as red blood cell (RBC) indices, renal function tests, liver function tests (LFTs), and lipid profiles, were recorded if available at the same time point as Hb. Patients with chronic kidney disease (CKD) and/or end-stage renal disease (eGFR <15 ml/min), critically ill currently or recently admitted patients, and patients with known hematological disorders such as myelofibrosis, myelodysplasia and hematological malignancies, chronic liver disease, and chronic inflammatory disorders such as collagen vascular diseases (CTDs) were excluded from the study. A convenient sample of 97 patients was taken based on feasibility. Patients were assessed clinically and underwent routine fasting blood sugar (FBS) and PPBS levels. Anemia was considered as per the World Health Organization (WHO) guidelines of <13 gm% in

men and <12 gm% in women. Patient consent and institutional ethics committee clearance were obtained.

Results

Of the 97 patients enrolled in the study, 46 (47.4%) were females and 51 (52.6%) were males. Thirty-seven (38.14%) patients were found to be anemic. Twenty (54.1%) among them were males, and 17 (45.9%) were females. The prevalence in males and females comes out to be 39.2% and 36.9%, respectively ($P = 0.819$). The mean Hb of the population was 12.61 ± 2.06 g/dl (10.5–14.6), with mean values in men and women being 13.20 ± 2.16 (11.0–15.4) g/dl and 11.95 ± 2.08 (9.8–14.0) g/dl, respectively. The mean age of the population was 50.5 years, and the anemic group had a mean age of 51.89 years against 49.6 years for the non-anemic group ($P = 0.278$). Sixteen (43.2%), 20 (54.1%), and 1 (2.7%) patients were classified as mild (11–11.9 mg% in females and 11–12.9 mg% in males), moderate (8–10.9 mg%), and severe (<8 mg%) anemia, respectively [Table 1].

The mean FBS of anemic patients (29 patients) was 180.2 ± 92.8 mg%, whereas that of non-anemic patients (54 patients) was 160.9 ± 57.4 mg% ($P = 0.25$). The mean postprandial blood sugar (PPBS) among anemic patients was 253.1 ± 105.2 mg%, whereas that of non-anemic patients was 232.5 ± 86.5 mg% ($P = 0.37$). The mean cholesterol in the anemic population was 165.5 ± 44.8 mg/dl, whereas, in non-anemic patients, it was 174.0 ± 43.8 mg/dl ($P = 0.46$). The mean value of serum triglycerides (TAGs) was 190.1 ± 107.6 mg/dl in the non-anemic population versus 183.7 ± 105.5 mg/dl in the anemic population. Among the 17 patients with raised serum cholesterol, 6 (35.2%) were anemic against 17 of 46 (36.9%) patients with normal cholesterol ($P = 0.741$). Among 36 patients with elevated TAGs (>150 mg/dl), 11 (30.6%) were anemic, whereas among 29 patients with normal TAGs (<150 mg/dl), 13 (44.8%) were anemic ($P = 0.236$). Patients with anemia had a mean AST value of 27.3 ± 11.0 IU/L, whereas in non-anemics, it was 29.8 ± 16.4 IU/L ($P = 0.44$). Similarly, the mean value of ALT in the anemic population was 29.1 ± 20.3 IU/L against 36.1 ± 22.0 IU/L in the non-anemic population ($P = 0.14$) [Tables 1-3].

Among the 54 patients with raised FBS (≥ 130 mg%), 17 (31.4%) were anemic against 12 (41.3%) of 29 in the normal FBS group ($P = 0.31$). Similarly, for PPBS, 20 (38.4%) of 52 patients with raised PPBS (≥ 180 mg%) had anemia against 5 (22.7%) of 22 with normal PPBS ($P = 0.17$). It was found that 5 (29.4%) of 17 patients with raised AST had anemia against 28 (41.1%) of 68 in the normal AST group [Table 2].

The mean Hb among patients with FBS ≥ 130 mg% was 12.8 ± 2.0 mg/dl as compared to 12.7 ± 2.1 mg/dl in the normal FBS group. The mean value of Hb in the elevated and normal TAG groups was 13.1 ± 1.8 and 12.3 ± 2.2 , respectively ($P = 0.44$). Similarly, the mean Hb in groups with raised and normal cholesterol was 12.6 ± 1.5 and

12.7 ± 2.2 mg/dl (*P* = 0.10), respectively. The mean Hb levels in patients with raised and normal AST were 12.7 ± 2.5 IU/L and 12.5 ± 2.1 IU/L (*P* = 0.65), respectively [Table 4]. Six (22.2%) of 27 patients with raised ALT had anemia against 27 (45.8%) of 59 patients with normal ALT. This was found to be statistically significant (*P* = 0.03). Furthermore, the mean Hb levels in patients with raised and normal ALT were 13.31 ± 2.3 gm% and 12.2 ± 2.0 gm% (*P* = 0.03), respectively [Tables 2 and 4].

The mean value of FBS in low and normal mean corpuscular volume (MCV) patients was 265.9 ± 43.7 mg/dl and 157.2 ± 7.2 mg/dl, respectively (*P* = 0.0026). The mean value of PPBS in low and normal MCV patients was 370.3 ± 58.4 mg/dl and 226.3 ± 10.1 mg/dl, respectively (*P* = 0.0015). The mean value of serum TAGs was found to be 188.8 ± 14.8 mg/dl in the normal MCV group and 207.2 ± 59.6 mg/dl in the low MCV group. The corresponding mean cholesterol was found to be 171.9 ± 5.9 mg/dl and 159.6 ± 23.3 mg/dl, respectively. There was no statistically significant difference among the patients with normal and abnormal MCV in terms of other parameters. [Tables 5 and 6].

There was no statistically significant difference among the patients on comparison of biochemical profiles between groups based on low and normal MCH and MCHC as shown in Tables 7 and 8.

Discussion

According to the WHO, the overall prevalence of anemia has been estimated to be 24.8%. In men and non-pregnant women, this has been estimated to be 12.7% and 30.2%, respectively.^[16] The prevalence of anemia in women in India as per the WHO database, 2019, is estimated to be around 53% (43.7–61.6).

The mean Hb of the stable diabetic population was 12.61 ± 2.06 (10.5–14.6) g/dl with mean values in men and women being 13.20 ± 2.16 (11.0–15.4) g/dl and 11.95 ± 2.08 (9.8–14.0) g/dl, respectively. The normal Hb level in men is 13.8 to 17.2 gm/dl, and in women, it is 12.1 to 15.1 g/dl. This shows that a stable diabetic population has a lower value of Hb compared with healthy controls based on the Hb range provided by various health agencies.

An analysis of the prevalence of anemia among Anemia Mukht Bharat Campaign recipients in Uttarakhand revealed that 53.2% of the population was anemic overall, with 45.1% of anemic males and 54.6% of anemic females.

In a study among 227 patients with DM, 126 (55.5%) had anemia. Fifty-six (44.4%) were males, and 70 (55.55%) were females.^[17]

According to a study, the prevalence of anemia is considerably higher in diabetic females (38.5%) compared with males (21.6%) and in diabetics with poorly managed blood

Table 1: Comparison of biochemical profiles between anemic and non-anemic diabetic patients

| Parameter | Overall (SD) | Anemia group mean (SD) | No anemia group mean (SD) | P |
|-----------------|---------------|------------------------|---------------------------|------|
| Age (years) | 50.5 (9.8) | 51.9 (9.7) | 49.5 (9.9) | 0.25 |
| FBS (mg%) | 167.1 (71.8) | 180.2 (92.8) | 160.9 (57.4) | 0.25 |
| PPBS (mg%) | 239.5 (92.5) | 253.1 (105.2) | 232.5 (86.5) | 0.37 |
| Creatinine (mg) | 0.76 (0.17) | 0.76 (0.19) | 0.76 (0.17) | 0.86 |
| TAG (mg%) | 187.8 (106.0) | 183.7 (105.5) | 190.1 (107.6) | 0.82 |
| Chol (mg%) | 171.9 (43.9) | 165.5 (44.8) | 174.0 (43.8) | 0.46 |
| SGOT (U/l) | 28.9 (14.6) | 27.3 (11.0) | 29.8 (16.4) | 0.44 |
| SGPT (U/l) | 33.4 (21.5) | 29.1 (20.3) | 36.1 (22.0) | 0.14 |

Table 2: Comparison of the proportion of diabetic patients with and without anemia across normal and raised fasting and postprandial blood sugars, LFTs, and lipids

| | No anemia | Anemia | Total | P |
|-------------|------------|------------|-------|-----------------|
| FBS <130 | 17 (58.6%) | 12 (41.4%) | 29 | <i>P</i> : 0.31 |
| FBS ≥130 | 37 (68.5%) | 17 (31.5%) | 54 | |
| PPBS <180 | 17 (77.3%) | 5 (22.7%) | 22 | <i>P</i> : 0.17 |
| PPBS ≥180 | 32 (61.5%) | 20 (38.5%) | 52 | |
| AST <35 | 40 (58.8%) | 28 (41.1%) | 68 | <i>P</i> : 0.37 |
| AST ≥35 | 12 (70.6%) | 5 (29.4%) | 17 | |
| ALT <35 | 32 (54.2%) | 27 (45.8%) | 59 | <i>P</i> : 0.03 |
| ALT ≥35 | 21 (77.7%) | 6 (22.2%) | 27 | |
| S.Chol ≥200 | 11 (64.7%) | 6 (35.3%) | 17 | <i>P</i> : 0.90 |
| S.Chol <200 | 29 (63%) | 17 (37%) | 46 | |
| S.TAG ≥150 | 25 (69.4%) | 11 (30.6%) | 36 | <i>P</i> : 0.24 |
| S.TAG <150 | 16 (55.2%) | 13 (44.8%) | 29 | |

Table 3: Comparison of the proportion of patients with and without anemia across diabetics with and without sugar control

| | Sugar control | |
|--------|----------------|---------------|
| | Yes (total=60) | No (total=26) |
| Anemia | | |
| Yes | 23 (38.3%) | 8 (30.7%) |
| No | 37 (61.6%) | 18 (69.2%) |

P=0.50

Table 4: Mean values of hemoglobin and Red Cell Index (MCV) across different metabolic parameters

| Parameter | Mean hemoglobin (mg/dl) (SD) | P | MCV (fl) (SD) | P |
|------------------|------------------------------|------|---------------|------|
| FBS <130 | 12.7 (2.1) | 0.85 | 89.2 (6.2) | 0.14 |
| FBS ≥130 | 12.8 (2.0) | | 86.5 (7.8) | |
| TAG <150 | 12.3 (2.2) | 0.10 | 88.1 (6.7) | 0.44 |
| TAG ≥150 | 13.1 (1.8) | | 89.4 (6.3) | |
| Cholesterol <200 | 12.7 (2.2) | 0.78 | 89.7 (6.7) | 0.10 |
| Cholesterol ≥200 | 12.6 (1.5) | | 86.5 (5.3) | |
| AST <35 | 12.5 (2.1) | 0.65 | 86.9 (7.6) | 0.09 |
| AST ≥35 | 12.7 (2.5) | | 90.8 (7.6) | |
| ALT <35 | 12.2 (2.0) | 0.03 | 87.5 (6.3) | 0.87 |
| ALT ≥35 | 13.3 (2.3) | | 87.8 (10.0) | |

Table 5: Comparison of biochemical profiles between microcytic and normocytic diabetic patients

| | Overall (SD) | Low MCV (<80 fl) (SD) | Normal MCV (80–100 fl) (SD) | P |
|----------------|--------------|-----------------------|-----------------------------|--------|
| Age | 50.1 (1.1) | 47.9 (3.2) | 50.4 (1.2) | 0.46 |
| FBS | 169.0 (8.7) | 265.9 (43.7) | 157.2 (7.2) | <0.001 |
| PPBS | 239.4 (11.6) | 370.3 (58.4) | 226.3 (10.1) | <0.001 |
| Creatinine | 0.77 (0.02) | 0.73 (0.05) | 0.77 (0.02) | 0.54 |
| S.TAG | 190.3 (14.3) | 207.2 (59.6) | 188.8 (14.8) | 0.72 |
| S. Cholesterol | 170.9 (5.7) | 159.6 (23.3) | 171.9 (5.9) | 0.55 |
| SGOT | 28.4 (1.7) | 27.2 (3.4) | 28.6 (1.9) | 0.78 |
| SGPT | 33.1 (2.5) | 29.9 (6.0) | 33.6 (2.7) | 0.63 |

Table 6: Comparison of the proportion of patients with microcytic RBCs between normal and raised fasting and postprandial blood sugars, LFTs, and lipids

| | MCV normal | Low MCV | Total | P |
|-------------|------------|-----------|-------|---------|
| AST <35 | 54 (85.7%) | 9 (14.3%) | 63 | P: 0.47 |
| AST ≥35 | 13 (92.9%) | 1 (7.1%) | 14 | |
| ALT <35 | 47 (87.0%) | 7 (13.0%) | 54 | P: 0.96 |
| ALT ≥35 | 21 (87.5%) | 3 (12.5%) | 24 | |
| S.Chol ≥200 | 14 (93.3%) | 1 (6.7%) | 15 | P: 0.77 |
| S.Chol <200 | 40 (90.9%) | 4 (9.1%) | 44 | |
| S.TAG ≥150 | 30 (90.9%) | 3 (9.1%) | 33 | P: 0.85 |
| S.TAG <150 | 24 (92.3%) | 2 (7.7%) | 26 | |

Table 7: Comparison of biochemical profiles between low and normal MCHC diabetic patients

| | Overall (SD) | Low MCHC (<32) (SD) | Normal MCHC (>32) (SD) | P |
|---------------|--------------|---------------------|------------------------|------|
| Age | 50.5 (1.2) | 49.6 (1.8) | 51.2 (1.5) | 0.48 |
| FBS | 169.8 (9.2) | 180.7 (16.5) | 161.0 (9.8) | 0.29 |
| PPBS | 241.5 (12.3) | 241.9 (20.9) | 241.1 (13.9) | 0.97 |
| Creatinine | 0.76 (0.02) | 0.75 (0.02) | 0.76 (0.02) | 0.84 |
| S.TAG | 188.9 (15.1) | 201.8 (23.8) | 174.5 (17.3) | 0.36 |
| S.Cholesterol | 170.6 (6.1) | 171.5 (8.8) | 169.4 (8.3) | 0.86 |
| SGOT | 27.7 (1.7) | 25.0 (1.2) | 29.9 (3.0) | 0.17 |
| SGPT | 31.0 (2.3) | 28.7 (2.6) | 32.8 (3.6) | 0.37 |

Table 8: Comparison of biochemical profiles between hypochromic and normochromic diabetic patients

| | Overall (SD) | Low MCH (<27.5 pg) (SD) | Normal MCH (27.5–32.5 pg) (SD) | P |
|---------------|--------------|-------------------------|--------------------------------|------|
| Age | 50.5 (1.2) | 48.6 (2.2) | 51.7 (1.3) | 0.20 |
| FBS | 169.9 (9.2) | 178.7 (19.7) | 164.8 (9.2) | 0.47 |
| PPBS | 241.5 (12.3) | 242.3 (26.4) | 241.0 (11.7) | 0.96 |
| Creatinine | 0.76 (0.02) | 0.75 (0.02) | 0.77 (0.03) | 0.62 |
| S.TAG | 188.9 (15.0) | 189.1 (30.4) | 188.8 (15.8) | 0.99 |
| S.Cholesterol | 170.6 (6.1) | 173.8 (10.9) | 168.6 (7.2) | 0.68 |
| SGOT | 27.7 (1.7) | 23.9 (1.3) | 29.9 (2.7) | 0.10 |
| SGPT | 31.0 (2.3) | 27.1 (2.9) | 33.4 (3.2) | 0.18 |

sugar (33.46%) compared with those with under-control blood sugar (27.9%) ($P < 0.05$).^[7] Patients with anemia had an average age of 60.69 ± 0.198 years, while those without anemia had an

average age of 54.07 ± 0.121 years. This suggests that as people age, their risk of anemia rises.

Our study estimates the prevalence of anemia to be 38.14%, with the prevalence in males and females being 39.2% and 36.9%, respectively. This prevalence is lower than the national and international data, but that seems to be due to our stringent criteria to exclude CKD, other chronic disorders such as connective tissue disorders, and liver disease.

Anemia, diabetic micro- and macrovascular renal disease, and cardiovascular problems are all brought on by the rise of pro-inflammatory cytokines, which are particularly important in promoting IL-6. IL-6 induces immature erythrocyte apoptosis and lessens progenitors' susceptibility to erythropoietin (erythroid growth factor).^[3]

In general, females have a higher preponderance for anemia compared with males and are more likely to get tested for anemia, but in our study, we got almost similar prevalence in both sexes.

Further looking at the type of anemia, microcytic and hypochromic pictures were more prevalent compared with other subtypes. Within the anemic population, however, the normocytic picture was more common. This may suggest that although a higher preponderance of iron deficiency was seen among anemic diabetics, a normocytic picture due to dimorphic anemia or chronic inflammation may also be responsible. In a different study, anemia was twice as common in T2DM patients as in controls. Of them, 68.6% had normocytic anemia, whereas 5.7% and 25.7% had microcytic and macrocytic anemia, respectively.^[2]

In our study, the mean FBS of anemic patients (29 patients) was 180.2 ± 92.8 mg%, whereas that of non-anemic patients (54 patients) was 160.9 ± 57.4 mg%. The mean PPBS among anemic patients was 253.1 ± 105.2 mg%, whereas that of non-anemic patients was 232.5 ± 86.5 mg%. Various studies have shown an association between anemia and blood sugar. In one investigation, the HbA1c level was higher in iron-deficient diabetics (7.3 ± 0.9) than in normocytic controls (5.4 ± 0.6).^[18] It was discovered that IDA ($Hb \leq 10.5$ g/dl) was associated with elevated HbA1c levels, which decreased with iron therapy and Hb level improvement.^[19]

In a prospective study with 37 T1DM patients, 11 of them had IDA and the other 26 had adequate iron levels. Following a 3-month iron supplementation period, these patients' HbA1c levels significantly decreased. Furthermore, following iron therapy, the mean HbA1c of IDA nondiabetic individuals dropped from $7.6 \pm 2.6\%$ to $6.2 \pm 1.4\%$ ($P < 0.05$).^[20]

An investigation including 47 students with IDA ($Hb < 12$ g/dl) was conducted to corroborate this result. Following a 20-week oral iron treatment, their HbA1c considerably dropped, falling from $6.2 \pm 0.6\%$ to $5.3 \pm 0.5\%$.^[21]

A study in Indonesia showed a strong relationship ($P = 0.003$) between HbA1c and IDA.^[22]

According to a study, IDA is highly prevalent in diabetic individuals and may be linked to changes in glycemic dynamics and HbA1c levels that are clinically significant. It recommended long-term studies monitoring HbA1c fluctuations both before and during anemia therapy.^[23] The mean value of TAG in the anemic population was 183, whereas, in the non-anemic population, it was 190.1. However, in view of the skewed data on TAGs, the median value was seen. It was 162 in the anemic population versus 141.5 in the non-anemic population. The median value of serum TAGs was found to be 156 in the normal MCV group and 184 in the abnormal MCV group. The corresponding mean was found to be 184.58 and 218.5, respectively. Our findings may be in concurrence with some studies on anemia and lipid profiles. Compared to controls, women with IDA have decreased high-density lipoprotein cholesterol (HDL-C), greater TAGs, and cholesteryl ester transfer protein (CETP) activity.^[24]

Another study conducted in India revealed that the IDA group had considerably ($P < 0.001$) higher levels of TAGs and very low-density lipoprotein cholesterol (30.40 ± 9.71 mg/dl) than the control group (109.99 ± 30.81 mg/dl and 21.96 ± 6.69 mg/dl).^[25]

Lipid parameters such as total cholesterol, low-density lipoprotein, very low-density lipoprotein, and TAG levels were found to be considerably increased in IDA cases compared with controls in another investigation on lipid profiles and anemia. IDA sufferers had a considerably lower amount of high-density lipoprotein than controls.^[25]

Adjusted models with reference group HbA1c values between 5.0 and 5.5% showed that HbA1c of 4.0% was linked to higher ALT (odds ratio (OR) 3.62 (95% CI 1.09–12.02)) and AST (6.80 (2.99–15.43)). Hepatic steatosis and increased GGT were also linked to HbA1c (4.0%); however, these associations were not statistically significant. They did not, however, find a connection between liver illness and low fasting glucose, indicating that the relationship with low HbA1c may not be dependent on glycemic pathways.^[26]

Patients with nonalcoholic fatty liver disease (NAFLD) frequently have iron deficiency, which is linked to female sex, an elevated body mass index, and non-white racial background. Iron-deficient individuals had reduced serum levels of hepcidin, which is a normal physiological reaction to decreasing blood levels of iron. In our study, normal ALT was significantly associated with anemia compared with raised ALT. This may be due to the higher prevalence of malnutrition-related anemia in Indian patients and raised ALT, suggesting the adequacy of food intake and availability and hence the lower likelihood of anemia. The association between hepatic iron stores and steatosis has been established in the literature. NAFLD has been linked to elevated iron levels, hepatic iron deposition, and serum ferritin levels.^[27,28]

The underlying link could be insulin resistance syndrome.^[29] An increased body iron content may contribute to insulin resistance through pathways involving decreased glucose burning, altered adipose tissue function, and adipokine release.^[30] Phlebotomy, iron chelators, nanotechnology, and ferroptosis are a few developments in iron metabolism-targeted therapeutics for the treatment of NAFLD.^[31]

The median values of ALT or AST in the low, normal, and high MCV groups were found to be 22.9/26.5, 26.11/25, and 30/32, respectively. A trend toward lower liver enzymes was seen among patients with low MCV.

Patients with higher blood sugars, both fasting and postprandial, tend to have higher cholesterol levels in our study, but the reverse was not found. Some with higher cholesterol values were found to have fewer fasting and PPBSs.

Increased Hb levels are predictive of elevated serum ALT in teenage girls with dyslipidemia, according to a Chinese study.^[32]

In clinical practice in the primary care of patients with diabetes, it is suggested that a hemogram be performed for all patients and management of glycemic control and anemia should go hand in hand. This should, however, be monitored to ensure that overtreatment is avoided and transaminitis is prevented. The optimal level of Hb, however, needs further research and understanding. Anemia, being a common disorder in the general population, is even more common in diabetics, and because of several dietary restrictions, including fruits, it becomes even more common.

Patients with diabetes, especially if associated with fatty liver and obesity, are advised regarding low-calorie feeds. Patients tend to avoid food in general, leading to deficiencies in micronutrients. Therefore, even if transaminitis (which is likely due to steatosis) is improved, iron deficiency also occurs simultaneously. Hence, the likelihood of fatty liver seems higher in iron-replete diabetic patients.

A study conducted on adult women in the USA found a positive and independent correlation between serum iron and both ALT and AST.^[33]

Serum iron levels may be a biomarker to assess the risk of metabolic dysfunction-associated fatty liver disease (MAFLD) in T2DM patients for improved screening and prevention, according to the findings of another Chinese study. Serum iron levels were found to be independently and positively associated with MAFLD in these patients.^[34]

Conclusion

Glycemic control in T2DM correlates directly with MCV of RBCs and subsequently with Hb levels. Henceforth, early control of sugar levels in T2DM can positively impact Hb levels,

potentially reducing morbidity and mortality associated with anemia in T2DM. Additionally, diabetic patients with anemia exhibit altered dietary patterns, resulting in reduced steatotic load on the liver. Consequently, these patients demonstrate LFTs within normal limits compared to T2DM patients with normal Hb levels, who show deranged LFTs, specifically elevated ALT, possibly due to exacerbated NAFLD in the presence of diabetic inflammatory conditions.

Screening for anemia, particularly microcytic anemia, and diagnosing it in T2DM patients early in the disease course, particularly those with uncontrolled diabetes, is essential. Early diagnosis facilitates simultaneous correction of both anemia and blood glucose levels. Blood sugar control may mitigate anemia of chronic disease associated with chronic inflammation in uncontrolled diabetes. Additionally, managing anemia synergistically enhances glycemic control, exercise capacity, and cardiovascular function.

Additionally, dietary counselling in diabetic patients should emphasise the effects of high-calorie intake on the liver. In dietary management, calorie restriction should be balanced to prevent deficiencies in essential minerals and vitamins. While controlling sugar levels and correcting anemia are crucial for better survival ratios, caution is needed to avoid overcorrection, which may exacerbate fatty liver incidence, potentially due to the pro-inflammatory effects of excess iron.

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Conflicts of interest

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References

- Mahjoub AR, Patel E, Ali S, Webb K, Kalavar M. The prevalence of anemia in diabetic patients with normal kidney function. *Blood* 2015;126:4545.
- Awofisoye OI, Adeleye JO, Olaniyi JA, Esan A. Prevalence and correlates of anemia in type 2 diabetes mellitus: A study of a Nigerian outpatient diabetic population. *Sahel Med J* 2019;22:55-63.
- Angelousi A, Larger E. Anaemia, a common but often unrecognized risk in diabetic patients: A review. *Diabetes Metab* 2015;41:18-27.
- Soliman AT, De Sanctis V, Yassin M, Soliman N. Iron deficiency anemia and glucose metabolism. *Acta Biomed* 2017;88:112-8.
- Fiseha T, Adamu A, Tesfaye M, Gebreweld A. Prevalence of anemia in diabetic adult outpatients in Northeast Ethiopia. *PLoS One* 2019;14:e0222111.
- Siddique A, Nelson JE, Aouizerat B, Yeh MM, Kowdley KV; NASH Clinical Research Network. Iron deficiency in patients with nonalcoholic fatty liver disease is associated with obesity, female gender, and low serum hepcidin. *Clin Gastroenterol Hepatol* 2014;12:1170-8.
- AlDallal SM, Jena N. Prevalence of anemia in type 2 diabetic patients. *J Hematol* 2018;7:57-61.
- Chung JO, Park SY, Cho DH, Chung DJ, Chung MY. Anemia is inversely associated with serum C-peptide concentrations in individuals with type 2 diabetes. *Medicine (Baltimore)* 2018;97:e11783.
- Meroño T, Dauteuille C, Tetzlaff W, Martín M, Botta E, Lhomme M, *et al.* Oxidative stress, HDL functionality and effects of intravenous iron administration in women with iron deficiency anemia. *Clin Nutr* 2017;36:552-8.
- Fujita Y, Doi Y, Hamano T, Hatazaki M, Umayahara Y, Isaka Y, *et al.* Low erythropoietin levels predict faster renal function decline in diabetic patients with anemia: A prospective cohort study. *Sci Rep* 2019;9:14871.
- Sahay M, Kalra S, Badani R, Bantwal G, Bhoraskar A, Das AK, *et al.* Diabetes and anemia: International Diabetes Federation (IDF)-Southeast Asian Region (SEAR) position statement. *Diabetes Metab Syndr* 2017;11(Suppl 2):S685-95.
- Singh DK, Winocour P, Farrington K. Erythropoietic stress and anemia in diabetes mellitus. *Nat Rev Endocrinol* 2009;5:204-10.
- Shareef AM, Ahmedani MY, Waris N. Strong association of anemia in people with diabetic foot ulcers (DFUs): Study from a specialist foot care center. *Pak J Med Sci* 2019;35:1216-20.
- Wu F, Jing Y, Tang X, Li D, Gong L, Zhao H, *et al.* Anemia: An independent risk factor of diabetic peripheral neuropathy in type 2 diabetic patients. *Acta Diabetol* 2017;54:925-31.
- Brenner BM, Cooper ME, de Zeeuw D, Grunfeld JP, Keane WF, Kurokawa K, *et al.* The losartan renal protection study--rationale, study design and baseline characteristics of RENAAL (Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan). *J Renin Angiotensin Aldosterone Syst* 2000;1:328-35.
- McLean E, Cogswell M, Egli I, Wojdyla D, de Benoist B. Worldwide prevalence of anaemia, WHO Vitamin and Mineral Nutrition Information System, 1993-2005. *Public Health Nutr* 2009;12:444-54.
- Salman MA. Anemia in patients with diabetes mellitus: Prevalence and progression. *General Med* 2015;3:1. doi: 10.4172/2327-5146.1000162.
- Sumathi K, Dilliraj G, Shanthi B, Selvi VSK, Rani J. Correlation between iron deficiency anemia and HbA1C levels in type 2 diabetes mellitus. *Int J Clin Biochem Res* 2020;7:400-2.
- Ng JM, Cooke M, Bhandari S, Atkin SL, Kilpatrick ES. The effect of iron and erythropoietin treatment on the A1C of patients with diabetes and chronic kidney disease. *Diabetes Care* 2010;33:2310-3.
- Tarim O, Küçükdoğan A, Günay U, Eralp O, Ercan I. Effects of iron deficiency anemia on hemoglobin A1c in type 1 diabetes mellitus. *Pediatr Int* 1999;41:357-62.
- El-Agouza I, Abu Shahla A, Sirdah M. The effect of iron deficiency anaemia on the levels of haemoglobin subtypes: Possible consequences for clinical diagnosis. *Clin Lab Haematol* 2002;24:285-9.
- Kaltsum TI, Pusparini P. Poor glycemic control correlates with iron deficiency anemia in type 2 diabetes mellitus. *Althea Med J* 2023;10:99-103.
- Elsheikh E, Aljohani SS, Alshaikhmubarak MM, Alhawl MA, Alsubaie AW, Alsultan N, *et al.* Implications of iron deficiency anaemia on glycemic dynamics in diabetes mellitus: A critical risk factor in cardiovascular disease.

- Cureus 2023;15:e49414. doi: 10.7759/cureus.49414.
24. Yang S, Chen XY, Xu XP. The relationship between lipoprotein-associated phospholipase A (2), cholesteryl ester transfer protein and lipid profile and risk of atherosclerosis in women with iron deficiency anaemia. *Clin Lab* 2015;61:1463-9.
 25. Verma U, Shankar N, Madhu SV, Tandon OP, Madan N, Verma N. Relationship between iron deficiency anaemia and serum lipid levels in Indian adults. *J Indian Med Assoc* 2010;108:555-8, 562.
 26. Christman AL, Lazo M, Clark JM, Selvin E. Low glycated hemoglobin and liver disease in the U.S. population. *Diabetes Care* 2011;34:2548-50.
 27. Buzzetti E, Petta S, Manuguerra R, Luong TV, Cabibi D, Corradini E, *et al.* Evaluating the association of serum ferritin and hepatic iron with disease severity in non-alcoholic fatty liver disease. *Liver Int* 2019;39:1325-34.
 28. Ma B, Sun H, Zhu B, Wang S, Du L, Wang X, *et al.* Hepatic steatosis is associated with elevated serum iron in patients with obesity and improves after laparoscopic sleeve gastrectomy. *Obes Facts* 2021;14:64-71.
 29. Macdonald GA, Powell LW. More clues to the relationship between hepatic iron and steatosis: An association with insulin resistance? *Gastroenterology* 1999;117:1241-4.
 30. Dongiovanni P, Fracanzani AL, Fargion S, Valenti L. Iron in fatty liver and in the metabolic syndrome: A promising therapeutic target. *J Hepatol* 2011;55:920-32.
 31. Chen H. Iron metabolism in non-alcoholic fatty liver disease: A promising therapeutic target. *Liver Res* 2022;6:203-13.
 32. Ma W, Hu W, Liu Y, He L. Association between ALT/AST and muscle mass in patients with type 2 diabetes mellitus. *Mediators Inflamm* 2022;2022:9480228.
 33. He A, Zhou Z, Huang L, Yip KC, Chen J, Yan R, *et al.* Association between serum iron and liver transaminases based on a large adult women population. *J Health Popul Nutr* 2023;42:69.
 34. Wang JW, Jin CH, Ke JF, Ma YL, Wang YJ, Lu JX, *et al.* Serum iron is closely associated with metabolic dysfunction-associated fatty liver disease in type 2 diabetes: A real-world study. *Front Endocrinol (Lausanne)* 2022;13:942412.