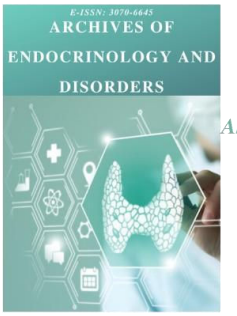

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Research Article

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Anemia and its Metabolic Correlates in Patients with Type 2 Diabetes Mellitus

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Abstract

Introduction: Anemia is a common but underrecognized comorbidity in patients with Type 2 Diabetes Mellitus (T2DM), with implications for metabolic and hepatic function. This study aimed to evaluate the association of hemoglobin with glycemic, hepatic and lipid parameters in T2DM patients.

Methods: This cross-sectional observational study was conducted on 146 adult T2DM patients. Participants were categorized as anemic or non-anemic and hematological, hepatic, glycemic, lipid and iron indices were compared between categories. Correlations between hemoglobin, liver enzymes and lipid ratios were assessed using Pearson's coefficient and ROC analysis was performed for the Hemoglobin-to-HDL Ratio (HHR) in predicting elevated ALT.

Results: A total of 146 patients were enrolled in the study, with 59 (40.4%) classified as anemic and 87(59.6%) as non-anemic. Anemic patients had lower MCV, MCH, MCHC, serum iron and ferritin ($p<0.05$). Median ALT was lower in anemics (20.5 U/L) vs non-anemics (30.5 U/L), $p=0.0001$. Mean CAP was lower in anemics (267.9 dB/m) vs non-anemics (297.0 dB/m), $p=0.0398$. Hemoglobin correlated weakly but positively with ALT ($\varrho=0.3565$, $p<0.001$). Patients with elevated ALT had higher hemoglobin, serum iron and HHR (HHR mean 0.37 vs 0.31, $p=0.0034$). HHR predicted elevated ALT modestly (AUC=0.669; cut-off >0.3217; sensitivity 59.5%, specificity 57.9%).

Conclusion: Anemia, particularly iron deficiency, is prevalent in T2DM and is associated with distinct hepatic and metabolic alterations. Lower hemoglobin and iron indices correlate with lower ALT and CAP, suggesting a possible protective effect of mild anemia on hepatic steatosis. Monitoring anemia in diabetic patients may offer insights into metabolic risk modulation.

Keywords: Type 2 Diabetes Mellitus; Anemia; Iron deficiency; Alanine Aminotransferase Hemoglobin/HDL Ratio

Introduction

Diabetes Mellitus (DM) is a prevalent chronic disorder with significant metabolic and organ-specific complications [1]. Type 2 Diabetes Mellitus (T2DM) is rising in asians driven by genetic predisposition, visceral adiposity and higher insulin resistance [2].

Anemia is a frequent comorbidity in patients with T2DM. A study indicated that anemia is twice as prevalent in diabetics compared to non-diabetics [3]. Studies report a prevalence ranging from 22% to 50% [1,4-6]. Anemia tends to develop earlier and more severely in diabetic nephropathy than in renal impairment from other causes [7]. However, its causes in diabetes are multifactorial, including chronic inflammation, nutritional deficiencies including restricted diets, autoimmune disorders, medication side effects and hormonal imbalances [5,8].

Addressing anemia in DM is crucial due to its metabolic and cardiovascular implications. It worsens both microvascular (nephropathy, retinopathy, neuropathy) and macrovascular (ischemic heart disease, cerebrovascular disease, peripheral vascular disease) complications. Anemia is associated with poorer glycemic control, increased hospitalization and higher mortality [9,10]. Beyond these complications, anemia may be of significance in the management of T2DM, as it reduces exercise capacity, predisposing patients to lower physical activity and weight gain. However, iron itself may have some detrimental toxic effects on the liver mediated by oxidative injury, which can lead to worsening of fatty liver and metabolic regulation. So, excessive correction is also questionable.

Anemia in T2DM may also interact with key metabolic pathways. Iron status, liver health and lipid metabolism are particularly relevant in this context. The effect of the iron status of the body on the health of the liver has been studied before, with therapeutic phlebotomy having been explored as a management option in patients with fatty liver disease [11]. However, the association between anemia and elevated liver enzymes in T2DM has not been adequately studied. Dyslipidemia is a well-established factor in Metabolic dysfunction Associated Steatotic Liver Disease (MASLD) and iron deficiency is prevalent in patients with MASLD [8,12]. However, evidence for the association of anemia with dyslipidemia is limited. Studies suggested that iron deficiency anemia is associated with lower levels of total cholesterol, triglycerides and High-Density Lipoprotein-Cholesterol (HDL-C), indicating a possible metabolic link that warrants further exploration [13,14].

The aim of this study is to understand the classification of anemia and its association with metabolic parameters including glycemic, hepatic and lipid profiles in patients with Type 2 Diabetes Mellitus.

Material And Methods

This was a cross-sectional observational study conducted at the Medicine outpatient and Metabolic clinics of a tertiary care teaching hospital, from January to December 2024. Adult Type 2 Diabetes patients were invited to participate in the study. Patients with CKD and/or End-stage renal disease (eGFR < 15 ml/min), critically ill, currently or recently admitted patients, patients with known hematological disorders like myelofibrosis, myelodysplasia and hematological malignancies, chronic liver disease and chronic inflammatory disorders like Collagen Vascular Diseases (CVDs) were excluded from the study.

The patients were divided into 2 groups, anemic (n= 59) and non-anemic (n=87). Anemia was considered as per the World Health Organisation (WHO) guidelines of Hb <13 g/dL in men and <12 g/dL in women. All patients underwent hematological, biochemical and metabolic profile assessment. These included CBC with red blood cell indices, Renal and hepatic function tests, Fasting and post-prandial blood sugars, glycosylated hemoglobin, lipid profile, folate and vitamin B12, ESR, iron studies including serum ferritin, total iron and TIBC. Data on elastography (Fibroscan)-Controlled Attenuation Parameter (CAP) and Liver Stiffness Measurement (LSM) were obtained from some patients who underwent these investigations.

Data obtained from patients were entered into MS Excel and statistical analysis was performed using STATA version 14 (StataCorp., USA). Normally distributed data were presented as mean ± SD and analyzed using the paired t-test, whereas non-normally distributed data were expressed as median (IQR) and analyzed using the Wilcoxon rank-sum test. Categorical variables were analyzed using Fisher's exact test. Correlation analysis was performed using the Pearson correlation coefficient. Receiver Operating Characteristic (ROC) curve analysis was carried out to evaluate the predictive ability of specific parameters and the Area Under the Curve (AUC) was used to assess their diagnostic performance. A P-value < 0.05 was considered statistically significant.

All ethical guidelines were followed and appropriate institutional review board approval was obtained. All procedures followed the guidelines laid down in the Declaration of Helsinki 1964 and as revised later.

Results

A total of 146 patients were enrolled in the study, with 59 (40.4%) classified as anemic and 87 (59.6%) as non-anemic. 79 (54.1%) patients were female and 67 (45.9%) were male. 86 (70.49%) of 122 patients were found to be iron-deficient, 21 (17.21%) folate deficient and 25 (19.38%) out of 129 patients were vitamin B12 deficient. Among the 51 anemics, 39 (76.47%) patients had iron deficiency, 8 (15.38%) of 52 patients had folate deficiency and 6 of 53 patients (11.32%) had vitamin B12 deficiency. Among the non-anemics, 13 (18.57%) of 70 had Folate deficiency, 19 (25%) of 76 had Vitamin B12 deficiency and 47 (66.19%) out of 71 had iron deficiency. 31 (72.09%) of the 43 patients in the anemic group and 43 (65.15%) of the 66 in the non-anemic group had iron deficiency with normal/raised ferritin.

On the analysis of Blood parameters and iron studies between the anemic and non-anemic groups, MCV, MCH and MCHC were significantly lower in the anemic group compared to the non-anemic group (P=0.0273, P=0.0001, P=0.0000 respectively) (Table 1). The mean serum iron level was significantly lower in anemic patients (58.05 ± 24.13 μg/dL) than in non-anemic patients (66.71 ± 22.62 μg/dL, P = 0.0442) (Table 1). The median serum ferritin concentration was also lower in anemics (30.3 [17.4-89] μg/L) compared to non-anemics (71.8 [33.2-131] μg/L) (Table 2).

The median ALT was significantly lower in anemic patients (20.5(17-27) U/L) compared to non-anemics (30.5 (22-44) U/L, P = 0.0001) (Table 2). On subgroup analysis by sex, serum ALT levels remained significantly lower in the anemic group compared to the non-anemic group in both males and females. Among males, the mean ALT was 22.89 ± 7.11 U/L in anemic patients and 36.85 ± 18.71 U/L in non-anemic patients (P = 0.0026, independent t-test). Among females, the median ALT was 22 U/L (IQR: 17-27) in anemic patients and 28.5 U/L (IQR: 20.5-39) in non-anemic patients (P = 0.0225, Wilcoxon rank-sum test).

Categorical analysis using Fisher's exact test revealed that 50 out of 58 anemics (86.21%) had normal ALT values, whereas 53 of 86 non-anemics (61.63%) had normal ALT values, a difference that was statistically significant (P = 0.001) (Table 3). Correlation analysis demonstrated a weak positive correlation between hemoglobin and ALT (rho = 0.3565, P < 0.001). There were no significant associations found between Urea, Creatinine, Uric Acid, Total Bilirubin, FBG, PPBG, Folate, Vitamin B12, ESR levels and the presence of Anemia.

Correlation analysis done between TC/HDL-C ratio and Hemoglobin revealed a weak positive correlation (rho=0.2871) that was significant (P=0.0262), only in the male sex. CAP values assessed by FibroScan were significantly lower in anemics (267.88 ± 12.11 dB/m) compared to non-anemics (297 ± 7.38 dB/m) (P = 0.0398) (Table 1). In categorical analysis, 66.67% of anemics and 93.02% of non-anemics had raised CAP values, a difference that was also statistically significant (P = 0.015) (Table 3). However, the median difference in LSM between the two groups was not statistically significant (Table 2). No significant correlations were found between CAP and serum ferritin or between CAP and ALT levels. Among patients stratified by ALT levels using a threshold of 33 U/L, those with elevated ALT had significantly higher mean hemoglobin (13.52 ± 1.77 g/dL) than those with normal ALT (12.29 ± 1.89 g/dL) (P=0.0005) (Table 4). The mean serum iron level was also significantly higher in patients with elevated ALT (72.94 ± 22.36 μg/dL) compared to those with normal ALT (59.37 ± 23.03 μg/dL, P = 0.0039) (Table 4). Among lipid parameters, HDL-c was significantly lower in the raised ALT group (38.17 ± 7.75 mg/dL) versus the normal ALT group (42.24 ± 11.32 mg/dL, P = 0.0465) (Table 4).

The HHR (Hemoglobin HDL ratio) was significantly higher in the high-ALT group (0.37 ± 0.09) than in the normal-ALT group (0.31 ± 0.10) (p = 0.0034, independent t-test) (Table 5). Correlation analysis demonstrated a weak positive correlation between ALT and HHR (rho= 0.2845, P=0.001). No significant correlation was found between CAP and HHR. Among patients stratified by CAP values using a threshold of >238 dB/m, the median HHR was higher in those with deranged CAP (n=5) compared to those with normal CAP (n=25) in female sex alone.; 0.22 [0.21-0.26] vs. 0.30 [0.25-0.36], respectively (P = 0.0626, Wilcoxon rank-sum test). ROC curve analysis was performed to evaluate the ability of the HHR to predict elevated ALT levels. The AUC was 0.669 (95% CI: 0.574-0.764), indicating a modest discriminatory power. The optimal cut-off value of HHR > 0.3217, determined using the Youden index, yielded a sensitivity of 59.5% and a specificity of 57.9% for identifying individuals with high ALT levels. (Fig. 1).

Biochemical Parameter	0(No Anemia) (n)	1(Anemia) (n)	P-value	Reference Range	UOM
Hemoglobin	13.86±1.26 (87)	10.89±1.27 (59)	0.0000	13.0-17.0 (male) 12.0-15.0 (female)	g/dL
Total Leukocyte Count	8.76±2.12 (87)	8.27±2.31 (59)	0.1888	4.0-10.0	10^6/uL
Platelet	203.47±72.7(87)	204.35±84.55(59)	0.9463	150-410	10^3/uL
MCV	88.64±6.36(87)	85.99±7.93(59)	0.0273	83-101	fL
MCH	27.87±2.80(87)	25.83±3.08(59)	0.0001	27-32	pg
MCHC	31.42±1.52(87)	30.21±1.63(59)	0.0000	31.5-34.5	g/dL
ALP	111.21±33.71(86)	108.31±37.28(58)	0.6289	40-129(male) 35-104(female)	U/L
AST	28.50±13.94 (86)	25.38±15.11(58)	0.2053	<=40(male) <=32(female)	U/L
HbA1c	8.38±1.87 (87)	7.91±1.52(59)	0.1102	Non diabetic range-4.8-5.6 Prediabetic range- 5.7-6.4 Diabetes range- >=6.5 High risk- >7.0	%
Serum Iron	66.71±22.62 (72)	58.05±24.13(51)	0.0442	59-158(male) 37-145(female)	ug/dL
TIBC	376.02±78.12(72)	384.54±65.70(51)	0.5262	250-450	ug/dL
Total Cholesterol	164.50±44.54(77)	152.88±40.44(55)	0.1272	no risk - <200 moderate risk -200-239 high risk ->240	mg/dL
LDL	89.71±35.28(75)	81.03±35.29(52)	0.1750	Adult levels Optimal - <100 Near optimal - 100-129 Borderline high -130 -159 High -160-189	mg/dL
VLDL	32.58±16.01 (72)	28.80±12.70 (52)	0.1609	0-40	mg/dL
HDL	40.94±10.36 (77)	41.32±10.96(55)	0.8399	>=55	mg/dL
FBG	164.49 ±72.03 (87)	153.50±61.64(59)	0.3397	<100	mg/dL
PPBG	232.49±80.90(74)	231.17±81.75(55)	0.9278	Normal- <140 Prediabetics- 140-199 Diabetic ->=200	mg/dL
CAP (Fibroscan)	297 ± 7.38(43)	267.88 ± 12.11(18)	0.0398	Grade 0- <237 Grade 1 fatty liver- 237-259 Grade 2 fatty liver- 260-292 Grade 3 fatty liver- >292	dB/m

Table 1: Results of two-sample t-test analysis for comparison of laboratory biomarkers between non-anemic and anemic participant groups.

Biochemical Parameter	0(Non-anemic) Median (p50) [p25-p75](n)	1(Anemic) Median (p50) [p25-p75] (n)	p-value	Reference Range	UOM
DLC -E	2.6 [1.2-4.0] (87)	2.7[1.7-3.9] (59)	0.7300	0.02-0.5	10^3/uL
DLC-B	0.4[0.3-0.6] (87)	0.4[0.3-0.5] (59)	0.6641	0.02-0.1	10^3/uL
S. Ferritin	71.8[33.2-131] (71)	30.3 [17.4-89] (51)	0.0034	30-400 male 15-150 female	ng/mL
Triglyceride	135[111-210] (77)	130[106-174] (53)	0.2381	Normal- <150 Borderline high- 150-199 High risk-200-499 Very high risk- >500	mg/dL
Folate	5.06[3.38-8.39] (70)	5.63[4.01-9.33] (52)	0.5094	3.1-17.5	ng/mL
ESR	20[11-30] (64)	36[28-40] (38)	0.0001	0-20 (male) 0-20 (0-50y female) 0-30(50-100y female)	mm/hr
ALT	30.5 (22-44) (87)	20.5(17-27) (59)	0.0001	<=41 male <=33 female	U/L
Transferrin saturation	17.57(12.83-22.60) (71)	14.58(10.23-19.73) (51)	0.053	200-360	mg/dL
LSM (Fibroscan)	6.4 (4.8-8.6) (43)	6.8 (5.3-8.2) (18)	0.72	Normal- 0-7 Mild fibrosis- 7-10 Moderate fibrosis- 10-13 Severe fibrosis- 13+	kPa

Table 2: Results of Wilcoxon Rank Sum analysis for comparison of laboratory biomarkers between non-anemic and anemic participant groups.

Biochemical Parameter	Category	0(Non-Anemic)	1(Anemic)	p-value
MCV	Low	12 (13.79%)	12 (20.34%)	0.621
	Normal	73 (83.91%)	46 (77.97%)	
	High	2 (2.30%)	1 (1.69%)	
MCH	Low	36 (41.38%)	39 (66.10%)	0.004
	Normal	51 (58.62%)	20 (33.90%)	
MCHC	Low	48 (55.17%)	47 (79.66%)	0.004
	Normal	37 (42.53%)	12 (20.34%)	
	High	2 (2.30%)	0 (0%)	
ALP	Low	0 (0%)	1 (1.72%)	0.170
	Normal	41 (47.67%)	33 (56.90%)	
	High	45 (52.33%)	24 (41.38%)	
ALT	Normal	53 (61.63%)	50 (86.21%)	0.001
	High	33 (38.37%)	8 (13.79%)	
AST	Normal	67 (77.01%)	49 (83.05%)	0.411
	High	20 (22.99%)	10 (16.95%)	
HbA1c	Controlled	22 (25.29%)	20 (33.90%)	0.376
	Uncontrolled	36 (41.38%)	25 (42.37%)	
	Poorly Controlled	29 (33.33%)	14 (23.73%)	
Iron	Low	5 (6.94%)	11 (21.57%)	0.028
	Normal	67 (93.06%)	40 (78.43%)	
TIBC	Low	3 (4.11%)	1 (1.96%)	0.930

	Normal	58 (79.45%)	42 (82.35%)	
	High	12 (16.44%)	8 (15.69%)	
Ferritin	Low	4 (5.63%)	8 (15.69%)	0.046
	Normal	50 (70.42%)	38 (74.51%)	
	High	17 (23.94%)	5 (9.80%)	
Total Cholesterol	Low Risk	62 (80.52%)	49 (87.50%)	0.349
	Moderate to High risk	15 (19.48%)	7 (12.50%)	
Triglyceride	Normal	41 (53.25%)	35 (66.04%)	0.284
	High Risk	35 (45.45%)	17 (32.08%)	
	Very High Risk	1 (1.3%)	1 (1.89%)	
LDL	Normal Range	45 (60.00%)	36 (69.23%)	
	High	30 (40.00%)	16 (30.77%)	
HDL	Not ReachingTarget	50 (64.94%)	39 (70.91%)	0.573
	Reached Target	27 (35.06%)	16 (29.09%)	
VLDL	Normal Range	55 (75.34%)	44 (84.62%)	0.266
	High	18 (24.66%)	8 (15.38%)	
FBG	Achieved Target	41 (47.13%)	25 (42.37%)	0.614
	Above Target Range	46 (52.87%)	34 (57.63%)	
PPBG	Achieved Target	23 (30.26%)	16 (29.09%)	1.000
	Above Target Range	53 (69.74%)	39 (70.91%)	
Folate	Deficient	13 (18.57%)	8 (15.38%)	0.809
	Normal	57 (81.43%)	44 (84.62%)	
Vitamin B12	Deficient	20 (26.32%)	6 (11.32%)	0.045
	Normal	56 (73.68%)	47 (88.68%)	
ESR	Normal	40 (63.49%)	8 (21.62%)	0.0000
	Abnormal	23 (36.51%)	29 (78.38%)	
CAP	Normal	3 (6.98%)	6 (33.33%)	0.015
	Abnormal	40 (93.02%)	12 (66.67%)	
LSM	Normal	26(60.47%)	10 (55.56%)	0.78
	Abnormal	17(39.53%)	8 (44.44%)	

Table 3: Distribution of categorical classifications of biochemical measures among Non-Anemic and Anemic participant groups with corresponding statistical significance.

Biochemical Parameter	1(ALT <=33) (n)	2(ALT>33) (n)	P-value	Reference Range	UOM
Hemoglobin	12.29±1.89 (103)	13.52±1.77 (41)	0.0005	13.0-17.0 (male) 12.0-15.0 (female)	g/dL
MCV	87.01±7.49 (103)	88.87±6.18 (41)	0.1614	83-101	fL
MCH	26.76±3.19 (103)	27.73±2.76 (41)	0.0908	27-32	pg
MCHC	30.82±1.69 (103)	31.20±1.65 (41)	0.2208	31.5-34.5	g/dL
Total Bilirubin	0.51±0.27 (103)	0.59±0.25 (41)	0.1127	0-1.2	mg/dL
ALP	106.11±33.93 (103)	119.92±36.43 (41)	0.0327	40-129(male) 35-104(female)	U/L
ALT	22.00±6.27 (103)	56.88±23.83 (41)	0.0000	<=41 male <=33 female	U/L

AST	22.32±9.30 (103)	39.60±17.54 (41)	0.0000	<=40(male) <=32(female)	U/L
HbA1c	8.12±1.86 (103)	8.37±1.45 (41)	0.4474	Non diabetic range-4.8-5.6 Prediabetic range- 5.7-6.4 Diabetes range- >=6.5 High risk- >7.0	%
Serum Iron	59.37±23.03 (89)	72.94±22.36 (34)	0.0039	59-158(male) 37-145(female)	ug/dL
TIBC	380.85±66.93 (89)	376.18±88.16 (34)	0.7527	250-450	ug/dL
TS	16.44±7.98(89)	19.40±7.33 (34)	0.0654	200-360	mg/dL
Total Cholesterol	157.93±44.80 (95)	164.10±38.63 (37)	0.4619	no risk - <200 moderate risk -200-239 high risk ->240	mg/dL
LDL	85.32±37.59(92)	88.37±29.26 (35)	0.6658	Adult levels Optimal - <100 Near optimal - 100-129 Borderline high - 130 -159 High -160-189	mg/dL
VLDL	29.94±14.36 (91)	33.92±15.74 (33)	0.1860	0-40	mg/dL
HDL	42.24±11.32 (95)	38.17±7.75 (37)	0.0465	>=55	mg/dL
FBG	159.54±68.39 (103)	162.84±68.89 (41)	0.7947	<100	mg/dL
PPBG	231.63±82.68 (92)	233.14±78.93 (35)	0.9261	Normal- <140 Prediabetics- 140-199 Diabetic ->=200	mg/dL
CAP	280.27±50.94 (40)	303.90±47.63 (21)	0.0838	Grade 0- <237 Grade 1 fatty liver- 237-259 Grade 2 fatty liver- 260-292 Grade 3 fatty liver- >292	dB/m
HHR	0.31+0.10 (95)	0.37+0.09 (37)	0.0034		

Table 4: Results of two-sample t-test analysis for comparison of laboratory biomarkers between participants with normal ALT values and those with elevated ALT values.

Biochemical Parameter	1 (ALT<=33) Median (p50) [p25-p75] (n)	2 (ALT>33) Median (p50) [p25-p75] (n)	p-value	Reference range	UOM
S.Ferritin	60.2[25.9-106] (85)	78[24.2-188.35] (37)	0.1407	30-400 male	ng/mL

				15-150 female	
Triglyceride	130.5[104-185] (94)	118[140.25-235.09] (36)	0.0735	Normal- <150 Borderline high- 150-199 High risk-200-499 Very high risk- >500	mg/dL
Folate	5.63[3.4-9.53] (87)	4.83[3.38-8.02] (35)	0.3723	3.1-17.5	ng/mL
Vitamin B12	378[236-543] (92)	327[194-421] (37)	0.1442	197-771	pg/mL
ESR	26[14-37] (69)	21[12-35] (33)	0.3725	0-20 (male) 0-20 (0-50y female) 0-30(50-100y female)	mm/hr
LSM	6.4(5.05-7.95) (40)	7.6(5.9-9.1) (21)	0.22	Normal- 0-7 Mild fibrosis- 7-10 Moderate fibrosis- 10-13 Severe fibrosis- 13+	kPa

Table 5: Results of Wilcoxon Rank Sum test for comparison of laboratory biomarkers between participants with normal ALT values and those with elevated ALT values.

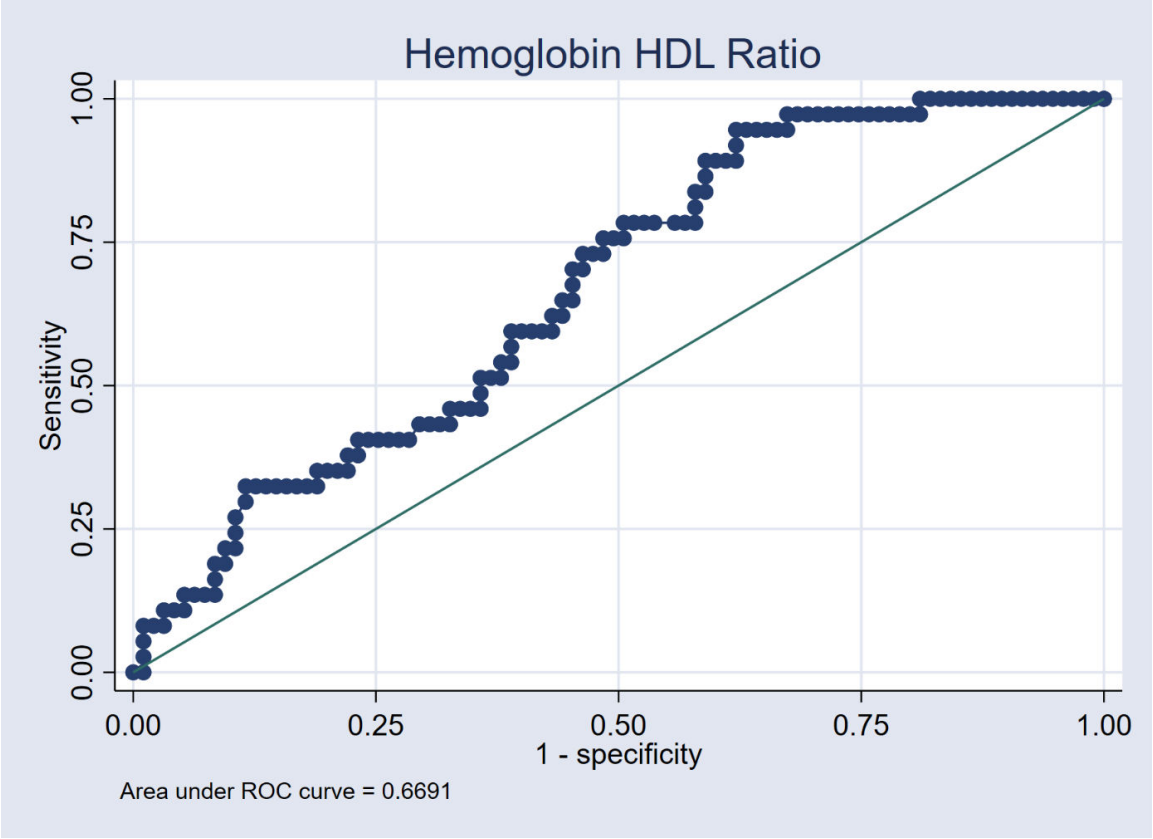

Figure 1: Receiver Operating Characteristic (ROC) curve showing the diagnostic performance of the Hemoglobin-to-HDL cholesterol Ratio (HHR) for predicting elevated ALT levels.

Discussion

This study aimed to explore the types of anemia in patients with T2DM, as well as assess differences in biochemical, metabolic and hepatic parameters between anemic and non-anemic diabetic individuals. The global prevalence of anemia among adult T2DM patients is estimated to be 27% [15]. A study reported the prevalence of iron deficiency anemia to be 39.3% among individuals with type 2 diabetes across various diabetic care centres in India [16]. A study found the prevalence of vitamin B12 deficiency to be 37.76% in people with pre-diabetes and 18.25% in people with diabetes and folate deficiency to be 12% [17,18]. Our study found iron deficiency anemia to be the predominant type of anemia with prevalence of 76% in the anemic group. Folate and B12 deficiencies were seen in 15.38% and 11.32% respectively.

In our study, anemic patients exhibited significantly lower red blood cell indices (MCV, MCH, MCHC) as well as serum iron and ferritin values. Most of our anemic patients tend to have iron deficiency anemia, as is common in the general population. Iron deficiency is recognized as the leading cause of anemia in India, with dietary habits playing a major contributory role. Nonheme iron, found in plant-based foods, eggs and milk, has low absorption efficiency (2%-20%), whereas heme iron, present only in meat, is absorbed more effectively with a bioavailability of 15%-35% [19].

Metabolic Differences Between Anemic and Non-Anemic Groups

Anemic patients had significantly lower ALT levels and lower CAP scores, possibly suggesting less hepatic fat accumulation and inflammation. However, there was no significant difference between the anemic and non-anemic groups in terms of liver stiffness. These findings were also reflected in another study on the association between hemoglobin levels and MASLD and this positive association persisted even after adjusting for multiple confounders [20]. Another study concluded that individuals with MASLD exhibited higher circulating hemoglobin levels [21]. Therefore, our data may suggest anemia as a protective factor for liver health. This can either be attributed to low dietary intake in general, leading to less fat and minerals in the diet and hence corresponding low values of hemoglobin and low ALT and CAP scores. However, another plausible explanation is that iron itself is toxic to the liver and an iron-deficient state may be protective. In our study, on the assessment of the correlation between Hemoglobin and ALT, a weak positive correlation was found. Similarly, a Scandinavian study found a positive correlation between serum ALT and Hematocrit (HCT) in 1,200 healthy Amish individuals, which was confirmed in 9,842 participants from NHANES III. ALT levels were also associated with RBC count, hemoglobin and HCT [22].

Significance of Iron Status and Liver Health

In our study, patients with higher Iron levels had significantly higher ALT values; however, there was no significant association between serum ferritin and high serum ALT values. Similar to our study, another study indicated a positive association between serum iron and liver transaminases, indicating that serum iron may be a potential biomarker of liver function [23]. Contrasting with our study, several studies have demonstrated a significant association between ALT and serum ferritin levels, indicating a potential correlation between elevated serum ferritin and liver dysfunction [17,20]. In U.S. adults, there was a positive correlation between serum ferritin levels and liver stiffness, which was more pronounced when serum ferritin exceeded 440 ng/mL [24]. Current literature suggests that iron dysmetabolism independently drives liver inflammation, fibrosis and lipid accumulation, promoting the progression of MASLD in individuals without obesity [25].

Significance of Liver Steatosis and Elevated Liver Enzymes

In our study, there was no correlation found between CAP and ALT. However, abundant studies and clinical practices have proven that the liver enzyme levels, such as ALT, were usually increased in the MASLD patients and these liver enzymes could be used as diagnostic markers for the MASLD to some extent [26]. Similar to our study, not all the studies supported the above conclusion. Sheng, et al., reported that some MASLD patients possessed a normal ALT value and the residual MASLD patients had an elevated level of ALT [27].

Significance of Dyslipidemia and HHR (Hemoglobin HDL ratio) as a Potential Biomarker in MASLD

HDL-C alleviates the early stages of hepatic inflammation by inhibiting the recruitment and activation of neutrophils and macrophages, thereby alleviating hepatocyte damage and hepatic steatosis [28]. Our study found that HDL levels were significantly lower in the raised ALT group of patients. Additionally, the HHR was found to be significantly correlated with ALT. This is supported in the literature. A study found that specific HDL lipids, including phosphatidylglycerol and

sphingomyelin, were inversely associated with hepatocellular ballooning, inflammation and fibrosis. This suggests that beyond cholesterol transport, alterations in HDL composition and function contribute to MASLD, insulin resistance and liver injury [29]. Another study concluded that HDL-C levels negatively correlate with the risk of developing MASLD [12].

In our study, females showed that HHR is close to significantly higher in the deranged CAP group. This suggests a potential association in females between a higher HHR and deranged CAP. ROC curve analysis demonstrated that the HHR possesses a modest capacity to predict elevated ALT levels (Fig. 1). Abundant studies and clinical practices have proven that the liver enzyme levels, such as ALT, are usually increased in the MASLD patients [26]. In a study, a significant positive correlation between HHR and MASLD was found, suggesting that HHR could potentially be used as an important biomarker for MASLD risk [30].

Our findings suggest a potentially protective role of mild iron deficiency in reducing hepatic fat accumulation, supported by lower CAP and ALT in anemic patients. This may be explained through nutritional pathways where dietary restriction in obese diabetics may limit intake of both obesogenic and iron-rich foods-as well as physiological mechanisms such as hepcidin-mediated suppression of iron absorption in chronic inflammation. However, another view is that iron is toxic to the liver and may cause oxidative injury and hence higher chances of fatty liver. So, mild iron deficiency may be a protective factor for the liver. So, in patients with anemia, this protective mechanism is maintained, but in certain patients, this may be overwhelmed and hence, non-protective with high hemoglobin, iron stores and fatty liver.

The positive correlation between hemoglobin and ALT, alongside higher serum iron in patients with raised ALT, suggests that higher iron availability may be linked to increased hepatic stress and metabolic dysfunction. Furthermore, the observed relationship between HDL and ALT adds to the evidence linking liver dysfunction with dyslipidemia, reinforcing the need to consider liver health as a core aspect of metabolic syndrome in diabetic care.

Diabetes management should include a comprehensive approach that addresses the patient's diet, monitors and treats dyslipidemia and evaluates for hepatic steatosis. While heme -iron-rich foods and supplements may help improve anemia, they could also contribute to underlying liver dysfunction and should be assessed carefully. However, larger multicenter studies across diverse populations are needed to validate and expand upon these results.

Strengths and Limitations

The study's strengths include a well-defined cohort with detailed assessment of red cell indices, iron parameters and liver enzymes. However, limitations must be acknowledged. Causal inference may have been restricted due to the cross-sectional nature of our study. Dietary intake, inflammatory markers and insulin resistance indices were not assessed, which could provide further insights into the observed associations. Not all the values of elastography were available to be assessed in every patient. Potential selection bias due to a single-centre setting may limit generalizability. Additionally, multiple statistical comparisons increase the risk of type I error.

Conclusion

Anemia is a prevalent but often underappreciated comorbidity in patients with type 2 diabetes. Anemic patients tend to have a favorable hepatic steatosis profile and this raises concerns about normalizing hemoglobin and the impact of dietary iron. More targeted prospective research with a higher sample size is warranted to unravel these complex interactions and inform clinical guidelines.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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Data Availability Statement

The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

Ethical Statement

All ethical guidelines were followed, and appropriate institutional review board approval was obtained. The Institute Ethics Committee for Post Graduate Research, All India Institute of Medical Sciences, New Delhi [IECPG-663/25.08.2022] approved the study protocol on 25-08-2022. All procedures followed the guidelines laid down in the Declaration of Helsinki 1964 and as revised later.

Informed Consent Statement

Informed consent was taken for this study.

Authors' Contributions

All authors contributed equally to this paper.

References

1. Mahjoub AR, Patel E, Ali S, Webb K, Kalavar M. The prevalence of anemia in diabetic patients with normal kidney function. Blood. 2015;126(23):4545.
2. Shah A, Kanaya AM. Diabetes and associated complications in the South Asian population. Curr Cardiol Rep. 2014;16(5):476.
3. Awofisoye O, Adeleye J, Olaniyi J, 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(2):55.
4. Thomas MC, MacIsaac RJ, Tsalamandris C, Power D, Jerums G. Unrecognized anemia in patients with diabetes: a cross-sectional survey. Diabetes Care. 2003;26(4):1164-9.
5. Abate A, Birhan W, Alemu A. Association of anemia and renal function test among diabetes mellitus patients attending Fenote Selam Hospital, West Gojam, Northwest Ethiopia: A cross-sectional study. BMC Hematol. 2013;13(1):6.
6. Thomas MC. Anemia in diabetes: Marker or mediator of microvascular disease? Nat Clin Pract Nephrol. 2007;3(1):20-30.
7. Ritz E, Haxsen V. Diabetic nephropathy and anaemia. Eur J Clin Invest. 2005;35(Suppl 3):66-74.
8. Siddique A, Nelson JE, Aouizerat B, Yeh MM, Kowdley KV. Iron deficiency in patients with nonalcoholic fatty liver disease is associated with obesity, female sex and low serum hepcidin. Clin Gastroenterol Hepatol. 2014;12(7):1170-8.
9. Thomas MC, Cooper ME, Rossing K, Parving HH. Anaemia in diabetes: Is there a rationale to TREAT? Diabetologia. 2006;49(6):1151-7.
10. Soliman AT, De Sanctis V, Yassin M, Soliman N. Iron deficiency anemia and glucose metabolism. Acta Biomed. 2017;88(1):112-8.
11. Khodadoostan M, Zamanidoost M, Shavakhi A, Sanei H, Shahbazi M, Ahmadian M. Effects of phlebotomy on liver enzymes and histology of patients with nonalcoholic fatty liver disease. Adv Biomed Res. 2017;6:12.
12. Xie J, Huang H, Liu Z, Li Y, Yu C, Xu L, et al. The associations between modifiable risk factors and nonalcoholic fatty liver disease: A comprehensive Mendelian randomization study. Hepatology. 2023;77(3):949.
13. Patel M, Priya P, Nivedita N. Association between iron indices and dyslipidemia among patients with iron deficiency anemia: A cross-sectional study. J Clin Diagn Res. 2024.
14. Shirvani M, Vakili Sadeghi M, Hosseini SR, Bijani A, Ghadimi R. Does serum lipid profile differ in anemia and non-anemic older subjects? Casp J Intern Med. 2017;8(4):305-10.
15. Arkew M, Asmerom H, Gemechu K, Tesfa T. Global prevalence of anemia among type 2 diabetic adult patients: A systematic review and meta-analysis. Diabetes Metab Syndr Obes. 2023;16:2243-54.
16. Pradeepa R, Shreya L, Anjana RM, Jebarani S, Kamal Raj N, Kumar MS, et al. Frequency of iron deficiency anemia in type 2 diabetes: Insights from tertiary diabetes care centres across India. Diabetes Metab Syndr. 2022;16(11):102632.
17. Singla R, Garg A, Surana V, Aggarwal S, Gupta G, Singla S. Vitamin B12 deficiency is endemic in the Indian population: A perspective from North India. Indian J Endocrinol Metab. 2019;23(2):211.
18. Sivaprasad M, Shalini T, Balakrishna N, Sudarshan M, Lopamudra P, Suryanarayana P, et al. Status of vitamin B12 and folate among the urban adult population in South India. Ann Nutr Metab. 2015;68(2):94-102.

19. Natekar P, Deshmukh C, Limaye D, Ramanathan V, Pawar A. A micro review of a nutritional public health challenge: Iron deficiency anemia in India. Clin Epidemiol Glob Health. 2022;14:100992.
20. Yao K, Chen Z, Zhou W, Liu Z, Cui W. Association between hemoglobin and non-alcoholic fatty liver disease in United States adults: Results from NHANES 2017-2020. Prev Med Rep. 2024;44:102798.
21. Juárez-Hernández E, Chavez-Tapia N, Brizuela-Alcántara D, Uribe M, Ramos-Ostos M, Nuño-Lámbarri N. Association between serum hemoglobin levels and nonalcoholic fatty liver disease in a Mexican population. Ann Hepatol. 2018;17:577-84.
22. Hu Y, Snitker S, Ryan KA, Yang R, Mitchell BD, Shuldiner AR, et al. Serum alanine aminotransferase is correlated with hematocrit in healthy human subjects. Scand J Clin Lab Invest. 2012;72(3):258-64.
23. 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(1):69.
24. Han H, Chen Y, Zhang S, Ji X, Zhu M, Ma W, et al. Association between serum ferritin and liver stiffness in adults aged ≥20 years: A cross-sectional study based on NHANES. Medicine (Baltimore). 2023;102(35):e34838.
25. Guo W, Weng T, Song Y. Association of serum iron status with MASLD and liver fibrosis. PLoS One. 2025;20(4):e0319057.
26. Martin-Rodriguez JL, Gonzalez-Cantero J, Gonzalez-Cantero A, Arrebola JP, Gonzalez-Calvin JL. Diagnostic accuracy of serum alanine aminotransferase as biomarker for nonalcoholic fatty liver disease and insulin resistance in healthy subjects using 3T MR spectroscopy. Medicine (Baltimore). 2017;96(17):e6770.
27. Sheng X, Che H, Ji Q, Yang F, Lv J, Wang Y, et al. The relationship between liver enzymes and insulin resistance in type 2 diabetes patients with nonalcoholic fatty liver disease. Horm Metab Res. 2018;50(5):397-402.
28. Säemann MD, Poglitsch M, Kopecky C, Haidinger M, Hörl WH, Weichhart T. The versatility of HDL: A crucial anti-inflammatory regulator. Eur J Clin Invest. 2010;40(12):1131-43.
29. Wu J, Yu W, Huang L, Hou S, Huang Y, Huang Z, et al. The HbA1c/HDL-C ratio as a screening indicator of NAFLD in U.S. adults: A cross-sectional NHANES analysis (2017-2020). BMC Gastroenterol. 2025;25(1):369.
30. Liu Z, Yin H, Li W, Zhang J. Linkage between hemoglobin to high-density lipoprotein cholesterol ratio and metabolic dysfunction-associated steatotic liver disease: A nationally representative study. Clin Transl Sci. 2025;18(7):e70308.

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