Red Cell Osmotic Fragility Status and its Contributing Factors in Type 2 Diabetes Mellitus Patients at South Valley University Hospital

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Abstract

Background: Diabetes mellitus (DM) is a growing public health issue in Egypt. Chronic hyperglycemia, impaired erythropoietin production, and increased RBC fragility, lead to increased destruction.

Objective: To assess the red cell osmotic fragility status and its determinants in type 2 DM (T2DM) patients.

Patients and methods: A cross-sectional study involving 200 participants, 100 with T2DM, and 100 controls, subjected to clinical, physical examination, and laboratory investigations, including an osmotic fragility test.

Results: Anemia was prevalent in 56% of T2DM; 93% had HbA1c > 7, a higher rate of infection, and the presence of complications and associated comorbidities. Anemic patients have higher WBC, platelets, reticulocyte counts, CRP, and ferritin; hemolysis starts at higher NaCl%, especially in females. Hemolysis is linked to various health indicators, including age, disease duration, blood pressure, red cell indices, inflammatory markers, kidney function, and lipid levels. The HbA1c positively correlated with disease duration (r=0.3321, p=0.001), systolic BP (r=0.3342, p=0.001), serum creatinine (r=0.456, p < 0.00001), cholesterol (r=0.5552, p < 0.00001), and VLDL (r=0.3342, p=0.001), and negatively correlation with diastolic BP (r=-0.3318, p=0.001), MCV (r=-0.317, p=0.001), triglycerides (r=-0.3212, p=0.001), and eGFR (r=-0.2391, p=0.0166).

Conclusion: Anemia was prevalent in T2DM patients, accompanied by the presence of comorbidities and complications. Poor glycemic control leads to a decline in RBC count, indices, and increased fragility, which may exacerbate disease progression and worsen complications. Regular monitoring and strict glycemic control aid in complication prevention.

Keywords: Anemia; Hyperglycemia; Nephropathy; Red cell osmotic fragility, Type 2 diabetes mellitus.

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Introduction

Diabetes mellitus (DM) is a global health problem with a prevalence of 9.9% in Egypt in 1995 and is expected to rise to 13.3% by 2025, making it one of the top ten countries with the highest DM cases **(Yameny, 2024).**

Chronic hyperglycemia in diabetes leads to organ damage and dysfunction, affecting the eyes, kidneys, nervous system, heart, and blood vessels. The hypoxic environment in the renal interstitium impairs erythropoietin production, resulting in anemia. Anemia is common in patients with diabetes, with 30% of type 2 patients suffering from it **(Vlacho et al., 2024).**

Anemia in diabetes is multifactorial **(Fathi et al., 2024)**, with red blood cell (RBC) hemolysis being a key factor. Hyperglycemia correlates with increased RBC osmotic fragility and susceptibility to destruction because of reduced surface area-to-volume ratios and altered deformability **(Rownak et al., 2017; Ebenuwa et al., 2024; Tujara et al., 2024).**

This study aimed to assess the osmotic fragility status of red cells and its determinants in T2DM patients.

Patients and methods

A cross-sectional study at Qena University Hospital, Egypt, included 200 participants: 100 were T2DM patients over 18 years attending the diabetes clinic for follow-up for at least 3 years, and 100 were age- and sex-matched controls. The study excluded T2DM patients with known chronic renal disease or pregnancy.

Patients were subjected to a full history, including personal, medical, and special habits; comorbidities; drug and family history; and a thorough physical examination to assess physical signs, body weight, height, and calculation of body mass index (BMI).

All participants were subjected to the following laboratory investigations:

Sampling: six ml of venous blood was collected under aseptic conditions; 2 ml was put into an EDTA tube for complete blood count (CBC), reticulocyte count, and glycosylated hemoglobin (HbA1c). One ml was added to a heparin tube for osmotic fragility test, and 3 ml was placed in a plain tube to obtain serum to estimate ferritin, C-reactive protein (CRP), and kidney function tests.

CBC parameters were measured using the Cell-Dyne Ruby automated cell counter.

The erythrocyte osmotic fragility (EOF) test measures the erythrocytes' resistance to hemolysis under osmotic stress conditions. It measures resistance to varying concentrations of NaCl solution, with normal hemolysis starting at 0.5% NaCl and ending at 0.3% NaCl **(Pagana et al., 2019).**

Ferritin was measured using the Tosoh AIA-360 automated enzyme immunoassay system (Tosoh Corporation, India). Assay range: 3 - 1000 ng/mL.

C-reactive protein (CRP) levels were assessed using a latex-enhanced immunoturbidimetric assay (Beckman Coulter AU 480 analyzer).

Glycosylated hemoglobin (HbA1c) was estimated using the high-performance liquid chromatography (HPLC) Variant II Turbo analyzer (Bio-Rad Laboratories, CA, USA).

Lipid profile, and kidney function tests were performed using the Cobas 6000 analyzer (Roche Diagnostics). The estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI formula **(Levey et al., 2009).**

Ethical approval code: SVU-MED-CCP031-1-24-3-823.

Statistical analysis

SPSS version 26 used data analysis. Data normality was checked using the Shapiro–Wilk test. Qualitative variables were expressed as numbers and percentages, while quantitative variables were expressed as mean ± standard deviation. The student's t-test, Welch's t-test, Mann-Whitney, ANOVA, Fisher exact, and chi-square tests were used for data comparison

as appropriate. Pearson correlation analysis was applied to determine relationships between variables. A P-value < 0.05 was significant.

Results

The study involved 100 T2DM patients, with diabetic complications affecting nephropathy and macrovascular diseases 11%, retinopathy 24%, cardiomyopathy 35%, neuropathy 65%, and microvascular diseases 70%. Common metabolic syndrome (MetS) components include abdominal obesity, high blood pressure, impaired fasting glucose, and low HDL cholesterol levels. Anemia was the most common comorbidity, affecting 56% of cases **(Table.1).**

Table 1. Disease characteristics among T2DM cases

Clinical data		**T2DM (N = 100)**
Duration of disease (years) (mean ± SD)		8.52 ± 5.44
Age of onset of disease (years) (mean ± SD)		42.18 ± 11.92
Diabetic complications	Nephropathy	11 (11%)
	Retinopathy	24 (24%)
	Cardiomyopathy	35 (35%)
	Neuropathy	65 (65%)
	Macrovascular disease	70 (70%)
Medications	Insulin	30 (30%)
	Tablets	70 (70%)
Metabolic syndrome (N = 24)	No metabolic syndrome	76(76%)
	abdominal obesity	6 (6%)
	high blood pressure	6 (6%)
	impaired fasting glucose	6 (6%)
	High triglyceride levels	0 (0%)
Associated comorbidity (N = 30	Anemia	56(56%)
	infected gangrene	18 (18%)
	GIT bleeding	6 (6%)
	venous ulcer	6 (6%)

We found a higher prevalence of infection and family history of diabetes in cases compared to controls. Systolic blood pressure was higher, and the WBCs, MCV, ferritin, uric acid, eGFR, cholesterol, triglyceride, and HDL were at considerably lower levels in the T2DM group than in the controls. However, Hb, platelets count, reticulocyte count, CRP, HbA1c, RBG, creatinine, urea, LDL, and VLDL were significantly higher **(Table.2).**

Table 2. Demographic and laboratory data of the studied groups

Demographic and laboratory data		**T2DM Cases (N = 100)**	**Controls (N = 100)**	**P-Value**
Age (years) Median (range)		52.5 (19 - 92)	52 (14 - 85)	$0.252^{[MWU]}$
Sex	Male	46 (46%)	42 (42%)	$0.5711^{[X]}$
	Female	54 (54%)	58 (58%)	
Residency	Urban	53 (53%)	50 (50%)	$0.6731^{[X]}$
	Rural	47 (47%)	50 (50%)	
Infections		59 (59%)	0 (0%)	$< 0.0001^{*[X]}$
Drink alcohol		0 (0%)	0 (0%)	-
Smoking		0 (0%)	0 (0%)	-
Family history of DM		54 (54%)	8 (8%)	$< 0.0001^{*[X]}$
BMI (Kg/m²)		23.3 (14.4 - 35.7)	23.4 (21.1 - 26.4)	$0.4509^{[MWU]}$

Systolic blood pressure (mmHg)	130 (80 - 240)	118 (100 - 141)	< 0.0001*[MWU]
Diastolic blood pressure (mmHg)	79.76 ± 17.51	82.66 ± 7.15	0.1295[w.t]
WBCs ($\times 10^3/mm^3$)	5.65 (2.79 - 26.59)	8.445 (3.96 - 17.15)	<0.0001*[MWU]
Hemoglobin (g/dL)	11.65 (5.3 - 24.2)	10 (7.9 - 12.1)	<0.0001*[MWU]
MCV (fl)	81.6 (50 - 121.8)	84.15 (72.3 - 94)	0.023*[MWU]
MCHC (g/dL)	31.45 (21.4 - 47.7)	31.35 (27.34 - 37)	0.5649[MWU]
Platelet count ($\times 10^3/mm^3$)	267.5 (33 - 685)	155.5 (95 - 186)	< 0.0001*[MWU]
Reticulocyte count	0.9 (0.2-2.8)	0.7 (0.1-1.4)	< 0.0001*[MWU]
OFT hemolysis starts at NaCl conc. %	0.45 (0.4 – 0.5)	0.45 (0.41–0.5)	0.121 [MWU]
OFT completes at NaCl conc. %	0.2 (0.2 – 0.25)	0.2 (0.16 – 0.26)	0.2646 [MWU]
CRP (mg/L)	12 (0 - 23)	9 (4.9 - 15.2)	0.0488*[MWU]
HBA1c (%)	10 (5.8 - 20.1)	6 (4.9 - 8.1)	< 0.0001*[MWU]
Ferritin (ng/mL)	83.09 (21.22 - 692.86)	270 (167 - 451)	< 0.0001*[MWU]
RBG (mg/dL)	235 (64 - 747)	101 (84 - 154)	< 0.0001*[MWU]
Creatinine (mg/dL)	0.825 (0.37 - 1.7)	0.7 (0.2 - 1.5)	<0.0001*[MWU]
Urea (mg/dL)	33 (12 - 83)	15 (11 - 24)	<0.0001*[MWU]
Uric acid (mg/dL)	4.2 (2.1 - 8.5)	6.05 (3.6 - 7.3)	< 0.0001*[MWU]
eGFR (mL/min/1.73m²)	93.72 ± 32.14	125.09 ± 21.91	< 0.0001*[MWU]
Cholesterol (mg/dl)	131.5 (87 - 271)	144.5 (111 - 184)	0.0384*[MWU]
Triglyceride (mg/dl)	88 (39 - 168)	121.5 (95 - 144)	<0.0001*[MWU]
HDL (mg/dl)	36 (14 - 85)	64 (57 - 73)	<0.0001*[MWU]
LDL (mg/dl)	128 (80 - 245)	78 (57 - 95)	<0.0001*[MWU]

*: significant; MWU: Mann-Whitney U Test; X: Chi square test, w.t.: Welch's t-test; *: significant; BMI: body mass index; BP: blood pressure; WBCs: white blood cells; MCV: mean corpuscular volume; MCHC: mean corpuscular hemoglobin concentration; Conc.: concentration, OFT: osmotic fragility test; CRP: C-reactive protein; HBA1C: hemoglobin A1c; RBG: random blood glucose, eGFR: estimated glomerular filtration rate, HDL: high-density lipoprotein; LDL: low-density lipoprotein; VLDL: very low-density lipoprotein.

Most of the studied cases (93%) had HbA1c > 7. The T2DM cases with HbA1c ≤ 7 and HbA1c > 7 were significantly older than controls (P = 0.0290). The T2DM group had a substantial rise in infection rates (85.71% for HbA1c ≤ 7 and 56.99% for HbA1c > 7) and a considerably higher family history of DM (85.71% for HbA1c ≤ 7 and 90.32% for HbA1c > 7) (P < 0.0001). Diabetic nephropathy (P = 0.0021), micro- and macrovascular complications (P < 0.05). The HbA1c > 7 group had significantly higher mean BP, anemia, and MetS components than in the HbA1c ≤ 7 groups (P < 0.05) (**Table.3).**

Table 3. Demographic and clinical data in the studied groups concerning glycemic control

Demographic data		T2DM HbA1c		Controls (N = 100)	P-Value
		≤ 7 (N = 7)	> 7 (N = 93)		
Age (Years)		53.86 ± 11.51	53.32± 13.07	46.27 ± 22.86	0.0290* [F]
		P1= 0.9959, P2= 0.4371, P3= 0.4888			
Sex	Male	3 (42.86%)	43 (46.24%)	42 (42%)	0.7941 [X]
	Female	4 (57.14%)	50 (53.76%)	58 (58%)	
Residency	Urban	3 (42.86%)	50 (53.76%)	50 (50%)	0.7826 [X]
	Rural	4 (57.14%)	43 (46.24%)	50 (50%)	
Infections		6 (85.71%)	53 (56.99%)	0 (0%)	<0.0001* [X]
Drink alcohol		0 (0%)	0 (0%)	0 (0%)	-
Smoking		0 (0%)	0 (0%)	0 (0%)	-

Family history	6 (85.71%)	84 (90.32%)	8 (8%)	<0.0001* [X]
BMI (Kg/m²)	23.54 ± 4.34	23.38 ± 3.91	23.51 ± 1.52	0.95361 [F]
	P1 = 0.98512, P2 = 0.99931, P3 = 0.99081			
Systolic BP (mmHg)	112.29± 30.22	131.48 ± 26.15	118.59 ± 9.88	0.00002* [F]
	P1 = 0.0109*, P2 = 0.60410, P3 = 0.12499			
Diastolic BP (mmHg)	92.57 ± 26.94	78.80 ± 16.50	82.66 ± 7.15	0.009918 [F]
	P1 = 0.0053*, P2 = 0.6296, P3 = 0.6512			

Clinical data of T2DM		**≤ 7 (N = 7)**	**> 7 (N = 93)**	**P-Value**
Duration of disease (years) (mean ± SD)		7.29 ± 3.25	8.61 ± 5.60	0.4703 [t]
Age of onset of disease (years) (mean ± SD)		52.71 ± 5.91	41.39 ± 11.96	0.1226 [t]
Diabetic complications	Nephropathy	3(42.86%)	8(8.60%)	0.0021* [f]
	Retinopathy	1(14.29%)	23(24.73%)	0.462 [X]
	Cardiomyopathy	3(42.86%)	32(34.41%)	0.5543 [X]
	Neuropathy	6(85.71%)	59(63.44%)	0.052 [X]
	Macrovascular disease	6(85.71%)	64(68.82%)	0.0028 [X]
Medications	Insulin	3(42.86%)	27(29.03%)	0.1986 [X]
	Tablets	4(57.14%)	66(70.97%)	
Metabolic syndrome (N = 24)	No metabolic syndrome	1(14.29%)	75(80.64%)	0.0001*[X]
	abdominal obesity	3(42.86%)	3(3.23%)	0.0332* [f]
	high blood pressure	0	6(6.46%)	0.0039* [f]
	impaired fasting glucose	0	6(6.46%)	0.0332* [f]
	Low HDL	3(42.86%)	3(3.23%)	0.0001* [f]
Associated comorbidity (N = 30	Anemia	7(100%)	49(52.67%)	0.0332* [f]
	infected gangrene	3(42.86%)	3(3.23%)	< 0.0001* [f]
	GIT bleeding	3(42.86%)	3(3.23%)	0.0332* [f]
	venous ulcer	0	6(6.46%)	0.0039* [f]

*: significant; X: chi square test; f: fisher exact test; F: ANOVA test; post-hoc; P1: Comparison between T2DM with HbA1c ≤ 7 and T2DM with HbA1c > 7; P2: Comparison between T2DM with HbA1c ≤ 7 and the control group; P3: Comparison between T2DM with HbA1c > 7 and the control group. BP: blood pressure

Cases with HbA1c > 7 had significantly lower mean WBC, MCV, MCH, reticulocyte count, CRP, ferritin, RBG, urea, uric acid, TG, LDL, VLDL, HDL, and eGFR. While having significantly higher mean cholesterol (P < 0.05) (**Table.4).**

Table 4. Laboratory data in the studied groups concerning glycemic control

Variables	**T2DM with HbA1c**		**Controls (N = 100)**	**P-Value**
	≤ 7 (N = 7)	**> 7 (N = 93)**		
WBCs (×10³/mm³)	10.869 ± 8.754	7.439 ± 4.679	9.13 ± 3.48	0.009* [F]
	P1 = 0.0453*, P2 = 0.44264, P3 = 0.46593			
Hemoglobin (g/dL)	7 ± 1.48	12.09 ± 3.38	9.87 ± 1.13	< 0.00001* [F]
	P1 = 0.00001*, P2 = 0.0014*, P3 = 0.0185*			
MCV (fl)	90.63 ± 18.0	80.95 ± 13.99	84.48 ± 5.68	0.01465* [F]
	P1 = 0.02045*, P2 = 0.20150, P3 = 0.5876			
MCHC (g/dL)	35.86 ± 7.23	31.49 ± 4.88	31.75 ± 2.61	0.02308* [F]
	P1= 0.00341*, P2= 0.00645*, P3= 0.9786			
Platelet count (×10³/mm³)	148.429 ± 52.188	84.657 ± 119.809	154.79 ± 21.850	< 0.00001* [F]
	P1 = 0.0001*, P2 = 0.97132, P3 = 0.00002*			

Reticulocyte (%)	1.714 ± 0.82	0.964 ± 0.59	0.66 ± 0.38	< 0.00001* [F]
	P1 = 0.0003*, P2 = 0.00001*, P3 = 0.15387			
OFT hemolysis starts at NaCl conc. %	0.47 ± 0.27	0.46 ± 0.33	0.45± 0.02	0.050797 [F]
	P1 = 0.4584, P2 = 0.10633, P3 = 0.64843			
OFT hemolysis completes at NaCl conc. %	0.22 ± 0.27	0.21 ± 0.21	0.21 ± 0.03	0.371084 [F]
	P1 = 0.35768, P2 = 0.23845, P3 = 0.96589			
CRP (mg/L)	16.03 ± 6.72	10.37 ± 5.70	9.78 ± 3.01	0.002707* [F]
	P1 = 0.0007*, P2 = 0.0002*, P3 = 0.9189			
HbA1c (%)	6.37 ± 0.45	10.82 ± 2.40	6.16 ± 0.93	< 0.00001* [F]
	P1 = 0.00001*, P2 = 0.93045, P3 = 0.00001*			
Ferritin (ng/mL)	270.07 ± 278.36	164.92 ± 168.231	262.15 ± 73.94	< 0.00001* [F]
	P1 = 0.0514, P2 = 0.9829, P3 = 0.0784			
RBG (mg/dL)	308.43± 106.74	273.63 ± 144.63	105.72 ± 15.82	< 0.00001* [F]
	P1 = 0.5519, P2 = 0.00001*, P3 = 0.00001*			
Creatinine (mg/dL)	0.54 ± 0.09	0.86 ± 0.25	0.62 ± 0.3	< 0.00001* [F]
	P1 = 0.0088*, P2 = 0.7347, P3< 0.0001*			
Urea (mg/dL)	45 ± 29.05	34.88 ± 14.18	15.62 ± 3.64	< 0.00001* [F]
	P1 = 0.0584, P2 < 0.0001*, P3 < 0.0001*			
Uric acid (mg/dL)	5.1 ± 2.71	4.38 ± 1.44	5.67 ± 1.12	< 0.00001* [F]
	P1 = 0.2482, P2 = 0.4158, P3 = 0.0127*			
eGFR (mL/min/1.73m²)	128.39 ± 85.28	91.11 ± 23.46	125.09 ± 21.91	< 0.00001* [F]
	P1 = 0.00012*, P2 = 0.92654, P3 = 0.00051*			
Cholesterol	120.43 ± 16.28	143.36 ± 39.16	145.89 ± 21.01	0.10742 [F]
	P1 = 0.0648, P2 = 0.0348*, P3 = 0.9663			
Triglyceride	119 ± 17.21	86.150 ± 27.62	118.64 ± 14.19	<0.00001* [F]
	P1 = 0.0002*, P2 = 0.9986, P3 = 0.00003*			
HDL	26.714 ± 16.13	38.054 ± 17.58	64.55 ± 4.6	<0.00001* [F]
	P1 = 0.0211*, P2 = 0.00001*, P3 = 0.00001*			
LDL	162.43 ± 53.58	128.07 ± 26.61	77.29 ± 10.84	<0.00001* [F]
	P1 = 0.00001*, P2 = 0.00001*, P3 = 0.00001*			
VLDL	39.57 ± 8.68	33.75 ± 12.79	16.44 ± 8.77	<0.00001* [F]
	P1 = 0.2372, P2 = 0.00001*, P3 = 0.0001*			

*: significant; F: ANOVA test; post-hoc; P1: Comparison between T2DM with HbA1c ≤ 7 and T2DM with HbA1c > 7; P2: Comparison between T2DM with HbA1c ≤ 7 and the control group; P3: Comparison between T2DM with HbA1c > 7 and the control group; OFT: osmotic fragility test.

The T2DM group with and without anaemia was older than the control group (P = 0.0291). T2DM with anaemia had a higher incidence of infections (P < 0.00001). Nephropathy, microvascular and macrovascular disease, MetS symptoms, infected gangrene, GIT bleeding, and venous ulcers were substantially prevalent in the anaemic patients (**Table.5)**.

Table 5. Demographic data in the studied groups concerning anemia

Demographic data		**T2DM with anemia (N = 56)**	**T2DM no anemia (N = 44)**	**Controls (N = 100)**	**P-Value**
Age (Years)		53.33 ± 9.97	53.23 ± 15.97	46.27 ± 22.86	0.0291* [F]
Sex	**Male**	31(55.36%)	15(34.09%)	42 (42%)	0.0886 [X]
	Female	25(44.64%)	29(65.91%)	58 (58%)	
Residency	**Urban**	32(57.14%)	22(50%)	50 (50%)	0.63096 [X]
	Rural	24(42.86%)	22(50%)	50 (50%)	

Infections	46(82.14%)	13(29.54%)	0 (0%)	<0.0001* [X]
Family history	27(48.21%)	28(63.64%)	8 (8%)	<0.0001* [X]
BMI (Kg/m²)	23.21 ± 4.22	23.62 ± 24	23.51 ± 1.52	0.7642 [F]
	P1 = 0.73622; p2 = 0.85143; p3 = 0.97693			
Systolic BP (mmHg)	123.89± 25.98	138.09 ± 25.84	118.59 ± 9.88	< 0.00001* [F]
	P1 = 0.0003*; p2 = 0.3056; p3 = 0.00001*			
Diastolic BP (mmHg)	81.46± 17.36	77.59 ± 17.85	82.66 ± 7.15	0.1137
	P1 = 0.2595; p2 = 0.87816; p3 = 0.10112			

Clinical data		**Cases with anemia**	**Cases no anemia**	**P-Value**
Duration of disease (years) (mean ± SD)		8.87 ± 5.63	8.07 ± 5.28	0.4703 [t]
Age of onset of disease (years) (mean ± SD)		43.82 ± 10.83	40.09 ± 13.12	0.1226 [t]
Diabetic complications	Nephropathy	11(19.64%)	0	0.0021* [f]
	Retinopathy	15(26.77%)	9(20.45%)	0.462 [X]
	Cardiomyopathy	21(37.5%)	14(31.82%)	0.5543 [X]
	Neuropathy	41(73.21%)	24(54.55%)	0.052 [X]
	Macrovascular disease	46(82.14%)	24(54.55%)	0.0028 [X]
Medications	Insulin (N = 30)	16(28.57%)	14(31.82%)	0.7251 [X]
	Tablets (N = 70)	40(71.43%)	30(68.18%)	
Metabolic syndrome (N = 24)	No metabolic syndrome	32(57.14%)	44(100%)	< 0.0001* [f]
	abdominal obesity	6(10.71%)	0	0.0332* [f]
	high blood pressure	6(10.71%)	0	0.0332* [f]
	impaired fasting glucose	6(10.71%)	0	0.0332* [f]
	Low HDL	6(10.71%)	0	0.0332* [f]
Associated comorbidity (N = 30)	infected gangrene	18(32.14%)	0	< 0.0001* [f]
	GIT bleeding	6(10.71%)	0	0.0332* [f]
	venous ulcer	6(10.71%)	0	0.0332* [f]

*: significant; X: chi-square test; F: ANOVA test; post-hoc; f: Fisher exact test. t: student t-test; P1: Comparison between T2DM with anemia and T2DM without anemia; P2: Comparison between T2DM with anemia and the control group; P3: Comparison between T2DM without anemia and the control group; BP: blood pressure.

Moreover, anaemic patients showed significantly higher WBC, platelets count, reticulocytes count, CRP, and ferritin levels. However, the erythrocyte osmotic fragility test showed that red cell haemolysis starts at a higher NaCl concentration in non-anaemic than in anaemic T2DM patients (P = 0.00002). Both T2DM groups had significantly higher urea and lower uric acid and eGFR levels than controls. Triglyceride, LDL, and VLDL levels were significantly higher in anaemic T2DM, while HDL levels were considerably lower (P < 0.00001) (**Table.6).**

Table 6. Laboratory data in the studied groups concerning anemia

Laboratory data	**T2DM with anemia (N = 56)**	**T2DM without anemia (N = 44)**	**Controls (N = 100)**	**P-Value**
WBCs (×10³/mm³)	8.645± 5.335	6.449 ± 2.146	9.13 ± 3.48	0.003* [F]
	P1 = 0.01630*; p2 = 0.81573; p = 0.00243*			
Hemoglobin (g/dL)	9.32± 1.86	14.81 ± 2.65	9.87 ± 1.13	< .00001* [F]
	P1 = 0.00001*; p2 = 0.21352; p3 = 0.00001*			
MCV (fl)	81.73± 12.91	81.50 ± 16.26	84.48 ± 5.68	0.1879 [F]
	P1 = 0.99298; p2= 0.91399; p3 = 79641			
MCHC (g/dL)	31.45± 4.90	32.24 ± 5.47	31.75 ± 2.61	0.63301 [F]

	P1 = 0.54902; p2 = 0.36284; p3 = 0.30506			
Platelet count (×10³/mm³)	285.198± 154.323	262.295 ± 56.021	154.791±21.855	< 0.00001* [F]
	P1 = 0.32606; p2 = 0.00001*; p3 = 0.00001*			
Reticulocyte (%)	1.25 ± 0.68	0.72± 0.41	0.66 ± 0.38	< 0.00001* [F]
	P1 = 0.00001*; p2 = 0.00001*; P3 = .73622			
OFT hemolysis starts at NaCl conc. %	0.454 ± 0.267	0.473 ± 0.349	0.454 ± .016	0.00002* [F]
	P1 = 0.00003*; p2 = 0.981; p3 = 0.00006*			
OFT hemolysis completes at NaCl conc. %	0.213 ± 0.228	0.208 ± 0.185	0.209 ± 0.026	0.2974 [F]
	P1 = 0.3102; p2 = 0.4143; p3 = 0.9792			
CRP (mg/L)	12.61± 5.73	8.43 ± 5.35	9.78 ± 3.01	0.000012* [F]
	P1 = 0.00001*; p2 = 0.00201*; p3 = 0.23019			
HBA1c (%)	10.07± 2.52	11.06 ± 2.58	6.16 ± 0.93	< 0.00001* [F]
	P1 = 0.01495*; p2 = 0.00001*; p3 = 0.00001*			
Ferritin (ng/mL)	240.63± 209.44	85.30 ± 55.66	262.15 ± 73.94	< 0.00001* [F]
	P1 = 0.00001*; p2 = 0.61854; p3 = 0.00001*			
RBG (mg/dL)	265.38± 109.03	289.68 ± 176.01	105.72 ± 15.82	< 0.00001* [F]
	P1 = 0.39127; p2 = 0.00001*; p3 = 0.00001*			
Creatinine (mg/dL)	0.755 ± 0.257	0.95 ± 0.22	0.62 ± 0.3	< .00001* [F]
	P1 =0.0014*; p2 = 0.0089*; p3 < 0.0001*			
Urea (mg/dL)	35.64 ± 15.61	35.52 ± 15.87	15.62 ± 3.64	< .00001* [F]
	P1 =0.9948; p2 < 0.0001*; p3 < 0.0001*			
Uric acid (mg/dL)	4.60 ± 1.66	4.21 ± 1.40	5.67 ± 1.12	< .00001* [F]
	P1 = 0.26306; p2 = 0.00009*; p3 = 0.00001*			
eGFR (mL/min/1.73m²)	101.27 ± 38.35	84.10 ± 18.76	125.09 ± 21.91	< .00001* [F]
	P1 = 0.00191*; p2 = 0.00001*; p3 = 0.00001*			
Cholesterol (mg/dl)	135.57± 40.53	149.61 ± 34.39	145.89 ± 21.01	0.0502 [F]
	P1 = 0.03583*; p2 = 0.16190; p = 0.78630			
Triglyceride (mg/dl)	98.30 ± 27.03	75. 91 ± 24.78	118.64 ± 14.19	< .00001* [F]
	P1 = 0.00001*; p2 = 0.00001*; p3 = 0.00001*			
HDL (mg/dl)	31.20 ± 16.75	44.98 ± 15.78	64.55 ± 4.6	< 0.00001* [F]
	P1 = 0.00001*; p2 = 0.00001*; p3 = 0.00001*			
LDL (mg/dl)	145.20 ± 29.11	111.98 ± 19.21	77.29 ± 10.84	< 0.00001* [F]
	P1 = 0.00001*; p2 = 0.00001*; p3 = 0.00001*			
VLDL (mg/dl)	35.30± 10.81	32.69 ± 14.57	16.44 ± 8.77	< 0.00001* [F]
	P1 = 0.39137; p2 = 0.00001*; p3 = 0.00001*			

*: significant; F: ANOVA test; post-hoc; P1: Comparison between T2DM with anemia and T2DM without anemia; P2: Comparison between T2DM with anemia and the control group; P3: Comparison between T2DM without anemia and the control group; OFT: Osmotic fragility test.

T2DM females were older (P = 0.0003) and had a longer disease duration (P = 0.0008), higher family history (P < 0.0001), higher systolic BP (P = 0.0293), more frequent retinopathy (P < 0.0001), neuropathy (P = 0.0034), cardiomyopathy (P = 0.0321), abdominal obesity (P = 0.0196), and gastrointestinal bleeding (P = 0.0196). Males have considerably higher prevalence of infection history (P = 0.0011) and macrovascular disease (P = 0.0005), high blood pressure, impaired fasting glucose (P = 0.0059), anaemia (P = 0.03417), infected gangrene (P < 0.0001),

and venous ulcers (P = 0.0059). However, the erythrocyte osmotic fragility test showed that red cell haemolysis starts at a higher NaCl concentration in females than in males with T2DM (P < 0.0001). Males have significantly higher reticulocyte count, platelets count, RBG, triglyceride, LDL, CRP, and ferritin levels (P < 0.0001). Whereas females have higher HbA1c (P = 0.0031), and lower eGFR (P < 0.0001) (**Table.7).**

Table 7.Demographic, clinical, and laboratory data in the studied groups concerning gender

Demographic and clinical data		**T2DM Male (N = 46)**	**T2DM Female (N = 54)**	**P-value**
Age (years)		50.3 ± 15.23	55.96 ± 9.66	0.0347*[w.t]
Residency	Urban	35 (76.09%)	18 (33.33%)	<0.0001*[X]
	Rural	11 (23.91%)	36 (66.67%)	
Infections		35 (76.09%)	24 (44.44%)	0.0011*[X]
Family history		12 (26.09%)	42 (77.78%)	<0.0001*[X]
Duration of disease (years)		6 (1 - 17)	8 (4 - 27)	0.0003*[MWU]
Age of onset of disease (years)		41.7 ± 12.6	42.59 ± 11.29	0.7135[t]
BMI (Kg/m²)		22.8 ± 3.25	23.9 ± 4.31	0.152[t]
Systolic blood pressure (mmHg)		124.5 (81 - 171)	135 (80 - 240)	0.0293*[MWU]
Diastolic blood pressure (mmHg)		78.43 ± 19.32	80.89 ± 15.71	0.4971[t]
Duration of disease (years) (mean ± SD)		6.56±4.12	8.46±5.44	0.0008* [t]
Age of onset of disease (years) (mean ± SD)		41.69±12.74	41.89±12.21	0.71101 [t]
Diabetic complications	Retinopathy	0 (0%)	24 (44.44%)	<0.0001*[X]
	Nephropathy	5 (10.87%)	6 (11.11%)	0.9697[X]
	Neuropathy	23 (50%)	42 (77.78%)	0.0034*[X]
	Macrovascular disease	40 (86.96%)	30 (55.56%)	0.0005*[X]
	Cardiomyopathy	11 (23.91%)	24 (44.44%)	0.0321*[X]
Medications	Insulin	6 (13.04%)	24 (44.44%)	0.0005*[X]
	Tablets	40 (86.96%)	30 (55.56%)	
Metabolic syndrome	No metabolic syndrome	28 (60.87%)	48 (88.89%)	0.0009*[X]
	Abdominal obesity	0 (0%)	6 (11.11%)	0.0196*[f]
	High blood pressure	6 (13.04%)	0 (0%)	0.0059*[f]
	Impaired fasting glucose	6 (13.04%)	0 (0%)	0.0059*[f]
Associated comorbidity	Anemia	31(67.39%)	25 (46.30%)	0.03417*
	Infected Gangrene	18 (39.13%)	0 (0%)	<0.0001*[f]
	GIT bleeding	0 (0%)	6 (11.11%)	0.0196*[f]
	Venous Ulcer	6 (13.04%)	0 (0%)	0.006*[f]
WBCs (×10³/mm³)		5.48 (2.79 - 26.59)	6.455 (3.07 - 21.8)	0.3346[MWU]
Hemoglobin (g/dL)		9.95 (6.6 - 24.2)	12.25 (5.3 - 16.2)	0.2595[MWU]
MCV (fl)		83.65 ± 12.51	79.91 ± 15.53	0.1903[t]
MCHC (g/dL)		30.08 ± 4.26	33.26 ± 5.35	0.0015*[t]
Platelet count (×10³/mm³)		271.5 (162 - 685)	258.5 (33 - 374)	0.0663[MWU]
Reticulocyte count (%)		1.2 (0.2 - 2.8)	0.8 (0.2 - 2)	0.0091*[MWU]
OFT hemolysis starts at NaCl conc. %		0.45 (0.4–0.5)	0.5 (0.45–0.5)	<0.0001*[MWU]
OFT completes at NaCl conc. %		0.2 (0.2–0.25)	0.2 (0.2–0.25)	0.8458[MWU]
CRP (mg/L)		12.3 (5 - 23)	11.8 (1- 21)	0.0074*[MWU]
HBA1c (%)		9.73 ± 1.47	11.17 ± 3.07	0.0031*[w.t]
Ferritin (ng/mL)		227.13 (22.05 - 692.86)	66.165 (21.22 - 215.31)	<0.0001*[MWU]
RBG (mg/dL)		243 (160 - 540)	222 (64 - 747)	0.1473[MWU]
Creatinine (mg/dL)		0.8 (0.37 - 1.28)	0.85 (0.57 - 1.7)	0.0658[MWU]

Urea (mg/dL)	33.5 (18 - 74)	32 (12 - 83)	0.2104[MWU]
Uric acid (mg/dL)	3.5 (2.1 - 6.8)	4.8 (2.4 - 8.5)	0.0002*[MWU]
eGFR (mL/min/1.73m²)	99.95 (68.03 - 246.1)	79.455 (46 - 129.09)	<0.0001*[MWU]
Cholesterol (mg/dl)	115.17 ± 16.58	164.39 ± 36.83	< 0.0001*[w.t]
Triglyceride (mg/dl)	106 (42 - 139)	74 (39 - 168)	< 0.0001*[MWU]
HDL (mg/dl)	23 (14 - 57)	45.5 (18 - 85)	< 0.0001*[MWU]
LDL (mg/dl)	144 (80 - 245)	113.8 (86 - 171)	< 0.0001*[MWU]
VLDL (mg/dl)	33.5 (16 - 56)	36.5 (12 - 66)	0.9669[MWU]

*: significant; w.t.: Welch's t-test; MWU: Mann-Whitney U test; t: student t-test; X: chi-square; t: student t-test; f: Fisher exact test; GIT: gastrointestinal tract; WBCs: white blood cells; MCV: mean corpuscular volume; MCHC: mean corpuscular hemoglobin concentration; Conc.: concentration; OFT: osmotic fragility test.

T2DM patients with MetS are younger than those without MetS (P = 0.0197). They have higher incidence of infection rates (100%) (P < 0.0001), nephropathy (0.0211), macrovascular diseases (0.001), anaemia (< 0.00001), infection gangrene (< 0.05), GIT bleeding (0.001), and venous ulcers (0.001). (**Table.8).**

Table 8. Demographic and clinical data in the studied groups concerning metabolic syndrome

Variables		**MetS (N = 24)**	**No MetS (N = 76)**	**Controls (N = 100)**	**P-Value**
Age (Years)		50.42 ± 6.18	54.29 ± 14.19	46.27 ± 22.86	0.0197* [F]
		P1= 0.6491, P2= 0.5914, P3= 0.0143*			
Sex	Male	18 (75%)	28 (36.84%)	42 (42%)	0.0036* [X]
	Female	6 (25%)	48 (63.16%)	58 (58%)	
Residency	Urban	18 (75%)	35 (46.05%)	50 (50%)	0.0428* [X]
	Rural	6 (25%)	41 (53.95%)	50 (50%)	
Infections		24 (100%)	35 (46.05%)	0 (0%)	<0.0001* [f]
Family history		12 (50%)	42 (55.26%)	8 (8%)	<0.0001* [X]
BMI (Kg/m²)		22.85 ± 3.12	23.56 ± 4.1	23.51 ± 1.52	0.5658 [F]
		P1= 0.5573, P2= 0.5904, P3= 0.9914			
Systolic BP (mmHg)		112.08 ± 20.8	135.84 ± 25.68	118.59 ± 9.88	<0.0001* [F]
		P1= <0.0001*, P2= 0.2858, P3= <0.0001*			
Diastolic BP (mmHg)		82.04 ± 17.4	79.04 ± 17.48	82.66 ± 7.15	0.2009 [F]
		P1= 0.607, P2= 0.9777, P3= 0.1825			
Clinical data			**MetS (N = 24)**	**No MetS (N = 76)**	**P-Value**
Duration of disease (years) (mean ± SD)			6.75±2.42	9.08±6.03	0.0688[t]
Age of onset of disease (years) (mean ± SD)			45.5±11.59	41.13±12.11	0.11987[t]
Diabetic complications	Retinopathy		0	24(31.58%)	0.0069 [X]
	Nephropathy		6(25%)	5(6.58%)	0.0211* [f]
	Neuropathy		18(75%)	47(61.84%)	0.23873[X]
	Macrovascular disease		24(100%)	46(60.53%)	0.001*[X]
	Cardiomyopathy		6(25%)	29(38.16%)	0.23872 [X]

Medications	Insulin	6(25%)	24(31.58%)	0.53978[X]
	Tablets	18(75%)	52(68.42%)	
Associated comorbidity	Anemia	24(100%)	32(41.01%)	< 0.00001*[f]
	Infected Gangrene	12(50%)	6(7.89%)	< 0.05*[f]
	GIT bleeding	6(25%)	0	0.001* [f]
	Venous Ulcer	6(25%)	0	0.001* [f]

*: significant; X: chi square test; f: Fisher exact test; t: student t-test; F: ANOVA test; post-hoc; P1: Comparison between T2DM with metabolic syndrome and T2DM without metabolic syndrome; P2: Comparison between and T2DM with metabolic syndrome and control group; P3: Comparison between T2DM with metabolic syndrome and control group.

T2DM patients with MetS had higher WBC, MCV, MCHC, reticulocyte count, CRP, ferritin, RNG, urea, eGFR, triglyceride, LDL, and VLDL. But lower hemoglobin (P < 0.0001), platelet counts (P = 0.0009), HbA1c, creatinine, cholesterol, and HDL (P < 0.0001) (**Table.9).**

Table 9. Laboratory data in the studied groups concerning metabolic syndrome

Variables	T2DM with MetS (N = 24)	T2DM No MetS (N = 76)	Controls (N = 100)	P-Value
WBCs ($\times 10^3/mm^3$)	8.28 ± 6.68	7.49 ± 4.4	9.13 ± 3.48	0.0499* [F]
	P1= 0.7232, P2= 0.6676, P3= 0.0388*			
Hemoglobin (g/dL)	8.39 ± 1.73	12.79 ± 3.26	9.87 ± 1.13	<0.0001* [F]
	P1= <0.0001*, P2= 0.012*, P3= <0.0001*			
MCV (fl)	86.6 ± 11.17	80.06 ± 14.86	84.48 ± 5.68	0.007* [F]
	P1= 0.028*, P2= 0.6629, P3= 0.0212*			
MCHC (g/dL)	34.28 ± 4.84	31.01 ± 4.96	31.75 ± 2.61	0.0025* [F]
	P1= 0.0016*, P2= 0.0157*, P3= 0.4395			
Platelet count ($\times 10^3/mm^3$)	219.92 ± 54.02	292.55 ± 130.36	154.79 ± 21.85	<0.0001* [F]
	P1= 0.0009*, P2= 0.0024*, P3= <0.0001*			
Reticulocyte (%)	1.45 ± 0.78	0.88 ± 0.5	0.66 ± 0.38	<0.0001* [F]
	P1= <0.0001*, P2= <0.0001*, P3= 0.0082*			
OFT hemolysis starts at NaCl conc. %	0.462 ± 0.022	0.462 ± 0.034	0.454 ± 0.016	0.078 [F]
	P1= 0.9948, P2= 0.3347, P3= 0.0894			
OFT hemolysis completes at NaCl conc. %	0.212 ± 0.022	0.211 ± 0.021	0.209 ± 0.026	0.6972 [F]
	P1= 0.9696, P2= 0.7678, P3= 0.7803			
CRP (mg/L)	13.77 ± 4.04	9.82 ± 6.06	9.78 ± 3.01	0.0004* [F]
	P1= 0.0008*, P2= 0.0005*, P3= 0.9978			
HBA1C (%)	9.05 ± 1.93	10.97 ± 2.57	6.16 ± 0.93	<0.0001* [F]
	P1= <0.0001*, P2= <0.0001*, P3= <0.0001*			
Ferritin (ng/mL)	260.64 ± 212.74	144.38 ± 154.23	262.15 ± 73.94	<0.0001* [F]

	P1= 0.0007*, P2= 0.9986, P3= <0.0001*			
RBG (mg/dL)	281.67 ± 88.87	274.3 ± 154.32	105.72 ± 15.82	<0.0001* [F]
	P1= 0.9483, P2= <0.0001*, P3= <0.0001*			
Creatinine (mg/dL)	0.62 ± 0.15	0.91 ± 0.25	0.62 ± 0.3	<0.0001* [F]
	P1< 0.0001*, P2= 0.9948, P3< 0.0001*			
Urea (mg/dL)	39.96 ± 20.28	34.21 ± 13.45	15.62 ± 3.64	<0.0001* [F]
	P1= 0.072, P2< 0.0001*, P3< 0.0001*			
Uric acid (mg/dL)	4.88 ± 2.17	4.29 ± 1.26	5.67 ± 1.12	<0.0001* [F]
	P1= 0.1553, P2= 0.0295*, P3= <0.0001*			
eGFR (mL/min/1.73m²)	116.06 ± 49.09	86.66 ± 19.77	125.09 ± 21.91	<0.0001* [F]
	P1= <0.0001*, P2= 0.2862, P3= <0.0001*			
Cholesterol	118.67 ± 12.55	149.04 ± 40.63	145.89 ± 21.01	0.0001* [F]
	P1= 0.0001*, P2= 0.0002*, P3= 0.7651			
Triglyceride	115.67 ± 20.45	79.86 ± 24.48	118.64 ± 14.19	<0.0001* [F]
	P1= <0.0001*, P2= 0.7828, P3= <0.0001*			
HDL	20.92 ± 4.07	42.42 ± 17.01	64.55 ± 4.6	<0.0001* [F]
	P1= <0.0001*, P2= <0.0001*, P3= <0.0001*			
LDL	163 ± 29.29	120.21 ± 21.78	77.29 ± 10.84	<0.0001* [F]
	P1= <0.0001*, P2= <0.0001*, P3= <0.0001*			
VLDL	37.33 ± 6.84	33.15 ± 13.71	16.44 ± 8.77	<0.0001* [F]
	P1= 0.2272, P2= <0.0001*, P3= <0.0001*			

*: significant; F: ANOVA test; Post-hoc; P1: Comparison between T2DM with metabolic syndrome and T2DM without metabolic syndrome; P2: Comparison between and T2DM with metabolic syndrome and control group; P3: Comparison between T2DM with metabolic syndrome and control group. WBCs: white blood cells; MCV: mean corpuscular volume; MCHC: mean corpuscular hemoglobin concentration; Conc.: concentration.

The EOF (start of hemolysis) was positively correlated with Hb (r = 0.2485, p = 0.0127), MCHC (r = 0.5768, p < 0.00001), creatinine (r = 0.2702, p = 0.006), uric acid (r = 0.283, p = 0.004), cholesterol (r = 0.2551, p = 0.01), HDL (r = 0.4439, p < 0.00001), EOF (end of hemolysis) (r = 0.2327, p = 0.0198), and negatively correlated with reticulocyte count (r = -0.2903, p = 0.003), platelets count (r = -0.284, p = 0.005), eGFR (r = -0.335 , p = 0.001), ferritin (r = -0.5458, p < 0.00001), CRP (r = -0.209, p = 0.0369), triglycerides (r = -0.3318, p = 0.001), and LDL (r = -0.4181, p = 0.00001).

The EOF (end of hemolysis) was positively correlated with disease duration (r = 4149, p = 0.0001), diastolic BP (r = 4382, p = 0.0004), WBC (r = 6554, p < 0.00001), creatinine (r = 2519, p = 0.0115), urea (r = 4388, p < 0.4388, 0.00001), RBG (r = 2806, p = 0.0198), CRP(r = 2662, p = 0.007), EOF (start of hemolysis) (r = 2327, p = 0.007), and negatively correlated with age (r = -0.3279, p = 0.001) and VLDL (r = -2106, p = 0.03599).

The HbA1c showed significant positive correlation with disease duration (r = 0.3321, p = 0.001), systolic BP (r =

0.3342, p = 0.001), serum creatinine (r = 0.456, p < 0.00001), cholesterol (r = 0.5552, p < 0.00001), and VLDL (r = 0.3342, p = 0.001), and a significant negative correlation with diastolic BP (r = -0.3318, p = 0.001), MCV (r = -0.317, p = 0.001), triglycerides (r = -0.3212, p = 0.001), and eGFR (r = -0.2391, p = 0.0166).(**Table.10**)

Table 10. Correlation between EOF and HbA1c with clinical and laboratory parameters

Variables	Erythrocyte osmotic fragility (EOF)				HbA1c	
	Haemolysis starts		Haemolysis complete			
	r	P-Value	r	P-Value	r	P-Value
Age	-0.1329	0.19049	-0.3279	0.001*	0.184	0.0669
Disease duration	0.0432	0.6695	0.4149	0.0001*	0.3328	0.001*
BMI	-0.09	0.37320	-0.1196	0.238305	0.048	0.6353
Systolic BP	-0.0085	0.93704	-0.1038	0.3078	0.3342	0.001*
Diastolic BP	0.1673	0.09678	0.3482	0.0004*	-0.3318	0.001*
EOF (H. starts)	-	-	0.2327	0.0198*	0.0317	0.754
EOF (H. complete)	0.2327	0.0198*	-	-	-0.11	0.276
WBC count	0.0546	0.5936	0.6554	< 0.00001*	-0.147	0.145
HB	0.2485	0.0127*	-0.0565	0.57999	0.132	0.189
MCV	-0.1726	.08705	-0.0664	0.514134	-0.317	0.002*
MCHC	0.5768	< 0.00001*	0.0194	0.84807	-0.139	0.169
Reticulocyte count	-0.2903	0.003*	0.0382	0.70592	-0.134	0.182
Platelets	-0.284	0.005*	0.1832	0.06808	0.1602	0.111802
eGFR	-0.335	0.001*	-0.1383	0.17093	-0.2391	0.016584
Creatinine	0.2702	0.006*	0.2519	0.0115*	0.456	< 0.00001*
Urea	0.1371	0.17377	0.4388	< 0.00001	-0.1407	0.162634
Uric acid	0.283	0.004*	0.1262	0.21088	0.1355	0 .178893
RBG	0.007	0.94489	0.2806	0.005*	0.167	0.0967
Ferritin	-0.5458	< 0.00001*	-0.1435	0.155804	-0.1279	0.20798
CRP	-0.209	0.0369*	0.2662	0.007*	-0.1332	0.1871
Cholesterol	0.2551	0.01*	0.0645	0.52376	0.5552	< 0.00001*
Triglycerids	-0.3318	0.001*	-0.0341	0.737005	- 0.3212	0.001*
LDL	-0.4181	0.00001*	-0.0731	0.470426	-0.1582	0.11594
HDL	0.4439	< 0.00001*	-0.0866	0.3949	0.0528	0.60186
VLDL	0.0789	0.43522	-0.2106	.03599*	-0.4669	< 0.00001*
HbA1c	0.0317	0.754	-0.11	0.276	-	-

*: significant; r: Pearson correlation; EOF: Erythrocyte osmotic fragility, WBCs: White Blood Cells, HB: Hemoglobin, MCV: Mean Corpuscular Volume, MCHC: Mean Corpuscular Hemoglobin Concentration, Reticulocyte count: Reticulocyte Count; CRP: C-reactive protein; HBA1C: hemoglobin A1c; RBG: random blood glucose, eGFR: estimated glomerular filtration rate, HDL: high-density lipoprotein; LDL: low-density lipoprotein; VLDL: very low-density lipoprotein.

Discussion

Diabetes mellitus is a syndrome characterized by hyperglycemia, disrupting metabolic, cellular, and hematological processes **(Tujara et al., 2024).** Prolonged hyperglycemia causes glycation in Hb and RBC membrane proteins, triggering structural and functional alterations that lead to increased RBC aggregation, reduced deformability, and impaired membrane fluidity, affecting blood viscosity and microcirculation **(Pretorius et al., 2015).**

T2DM, increased glycations, chronic inflammation, and oxidative stress cause endothelial damage, leading to vascular complications, which further impact RBC integrity, erythropoiesis, and reticulocyte counts **(Wang et al., 2021).**

Anemia, a common hematological abnormality in T2DM patients, is often underdiagnosed, with its prevalence varying across different populations **(Fayed et al., 2013).** Anemia is multifactorial, including chronic hyperglycemia, Hb glycation, kidney function decline, functional erythropoietin deficiency, oxidative stress, inflammation, and oral antidiabetic medication effects **(Arkew et al., 2022).**

This study aimed to assess the red cell osmotic fragility status and its determinants in T2DM patients.

The study found a 59% infection rate in T2DM patients, consistent with **uk (2013) and Wu et al. (2017)**. The mean disease duration was 8.52 years, with a 65% diabetic neuropathy complication rate. This is higher than the 16% prevalence reported by **Aikaeli et al. (2022),** possibly due to the longer disease duration.

In this study, cardiomyopathy was reported in 35% of T2DM cases, lower than the 75% reported by **Tarquini et al. (2011)**. Diabetic retinopathy reported in 24%, aligns with **Voigt et al. (2018)** and **Govindarajan Venguidesvarane et al. (2020).** Diabetic nephropathy is found in 11%, consistent with **Govindarajan Venguidesvarane et al. (2020)** and **Kebede et al. (2021).** Furthermore, macrovascular complications were reported at 70%, higher than the 29.7% reported by **Govindarajan Venguidesvarane et al. (2020)**.

Our study found that 65% of T2DM patients had neuropathy; this was in contrast to 17.8% reported by **Liu et al. (2010)**, and 70% were treated with oral medications, as per **Nicolucci et al. (2019)**.

The study found that T2DM patients had significantly higher systolic blood pressure compared to controls, contradicting **Tsimihodimos et al. (2018)**, suggesting hypertension is prevalent among individuals with increased BMI, a significant independent predictor of hypertension.

The study found that T2DM patients showed higher infection rates and family history of diabetes compared to controls, as per **Carey et al. (2018).** Furthermore, 56% had anemia, with higher reticulocyte and platelet counts and lower WBCs and MCV than the controls. This was consistent with **Arkew et al. (2021);** however, they reported anemia in 17.9% of T2DM patients; **Fathi et al. (2024)** reported that 38.4% of T2DM patients had anemia.

We found no significant differences in the start or complete hemolysis between T2DM cases and controls, unlike **Tujara et al.'s (2024),** who reported greater erythrocyte osmotic fragility in DM.

In our study, T2DM had higher LDL and VLDL levels but lower HDL; consistent with **Ozder (2014)** and **Stamouli et al. (2014)**.

The study found that 93% of cases had HbA1c > 7, with a higher prevalence of nephropathy, micro- and macrovascular complications, anemia, and MetS. They had significantly lower mean eGFR but higher platelet counts. However, those with HbA1c ≤ 7 had higher mean WBC

and reticulocyte counts but lower hemoglobin levels. In contrast, **Bhutto et al. (2019)** reported insignificant differences in platelet counts between controlled and uncontrolled T2DM patients.

In this study, T2DM patients with HbA1c > 7 had higher systolic BP, suggesting poor glycemic control is linked to elevated blood pressure. This aligns with **Chen et al. (2023).**

The study found higher CRP levels and random blood glucose in the HbA1c ≤ 7 and HbA1c > 7 groups, with ferritin being the highest in T2DM with the HbA1c ≤ 7 group, indicating poor glycemic control is linked to systemic inflammation (**Gautam et al., 2023)**.

Females with T2DM experience longer disease duration, higher family history, higher systolic BP, and higher prevalence of retinopathy, neuropathy, cardiomyopathy, abdominal obesity, and gastrointestinal bleeding. Consistent with **Kautzky-Willer et al. (2023)**. **O'Neill and O'Driscoll (2015).**

Males with T2DM have higher prevalence of infection, macrovascular disease, high blood pressure, anemia, infected gangrene, and venous ulcers, while females have higher red cell hemolysis, HbA1c, and lower eGFR. Males have higher levels of reticulocytes, platelet count, RBG, triglycerides, LDL, CRP, and ferritin.

The study found that males had significantly lower cholesterol and HDL levels compared to females, while triglyceride levels were higher in the male group, consistent with **Russo et al. (2015).**

Males have a higher prevalence of anemia than females. In contrast, **Fathi et al. (2024)** reported that 38.4% of T2DM patients had anemia, with a higher prevalence in females (67.4%) compared to males (7.7%).

Our study supports **Du et al.'s (2016)** finding that HbA1c-defined diabetic men have higher ferritin levels than women, possibly due to increased inflammation and oxidative stress **(Beydoun et al., 2020)**.

The study found no significant difference in BMI between males and females, but females had higher systolic blood pressure. consistent with **Regensteiner and Reusch (2022)**.

The study found that males had lower uric acid levels and higher eGFR compared to females, consistent with **Cherian et al. (2024)**. However, **Yang et al. (2021)** reported higher average serum uric acid levels in men.

The study found that T2DM patients with and without anemia were older than controls, infections were prevalent in patients with anemia. The family history of diabetes was more prevalent in T2DM patients, with higher frequency in those without anemia. The study supports **Chávez-Reyes et al. (2021)** showing increased susceptibility to severe infectious diseases in individuals with diabetes.

In our study, T2DM patients with anemia had a similar disease duration and age of onset, but had diabetic nephropathy, microvascular, and macrovascular complications. Anemia was linked to MetS features like abdominal obesity, high blood pressure, impaired fasting glucose, and low HDL. This is consistent with **Shaheen (2019)** and **Rupasinghe and Jayasinghe (2024)** and **Kelem et al. (2023)**.

In our study, T2DM patients without anemia had higher systolic blood pressure than those with anemia and controls. This aligns with **Salazar-Vazquez et al. (2006)** and **Fathi et al. (2024)**.

In our study, T2DM patients with anemia had higher WBC, platelet count, and reticulocytes but lower hemoglobin levels than those without anemia and controls. The osmotic fragility test showed that hemolysis was higher in T2DM patients with anemia, consistent with **Arkew et al. (2021) and Tujara et al. (2024)**.

In our study, T2DM patients with anemia had higher CRP levels, HbA1c, ferritin, and RBG levels. This aligns with **Ndevahoma et al. (2021)**, which suggest an inflammatory influence on iron metabolism.

In our study, the T2DM group with anemia had lower creatinine, uric acid, and eGFR levels. In contrast to **Tikki et al. (2022)**, who suggest a link between anemia and hyperuricemia in T2DM patients. **Wang et al. (2023)** found a U-shaped relationship between serum uric acid and anemia, indicating that both high and low uric acid levels increase anemia risk.

In our study, T2DM with anemia had lower cholesterol and HDL levels. But higher triglyceride, LDL, and VLDL levels. Align with **Stamouli et al. (2014)**.

In our study, T2DM patients without MetS were older. MetS was more prevalent in males and urban residents, had higher infection rate. A family history of DM was more common in non-MetS cases. This finding aligns with **Wang et al. (2013)** and **Ghassab-Abdollahi et al. (2023)**.

MetS T2DM patients were younger, had higher infection rates, MCV, MCHC, reticulocyte count, CRP, ferritin, RBG, HbA1c, eGFR, triglyceride, and LDL. But lower WBC, haemoglobin, platelet counts, cholesterol, and HDL. With insignificant differences in red cell osmotic fragility tests. This aligns with **Abril-Ulloa et al. (2014), Arkew et al. (2021)**, **Essawi et al. (2023)**, **and Bambo et al. (2024)**, who reported a potential association between MetS and anemia in diabetes.

Lower hemoglobin levels in the MetS group may be due to inflammation and comorbidities impairing RBC production **(Mozos, 2015)**. Higher MCV and MCHC indicate macrocytic anemia and altered hemoglobin concentration, while the lower MCV in the non-MetS group could be linked to iron deficiency or anemia of chronic disease. Whereas increased reticulocyte count reflects a compensatory response to anemia, with more pronounced effects in the MetS group due to greater oxidative stress and inflammation **(Kuhn et al., 2017)**.

In our study, T2DM patients without MetS had higher systolic blood pressure. This was in agreement with **Huo et al. (2013).** Moreover; had higher creatinine levels but lower eGFR than in those with MetS and controls. Whereas urea levels were higher in the T2DM group with MetS than those without MetS and controls. This was consistent with **Moehlecke et al. (2010)** and **Lin et al. (2022)**. The differences in renal parameters can be attributed to metabolic disturbances.

In our study, T2DM patients with MetS had higher triglycerides and LDL but lower cholesterol and HD. This aligns with **Paredes et al. (2019)**, indicating distinct lipid profile enhancing cardiovascular diseases risk.

The EOF (start of hemolysis) was positively correlated with Hb, MCHC, creatinine, uric acid, cholesterol, and HDL, while negatively correlated with reticulocytes, platelets count, eGFR, ferritin, CRP, triglycerides, and LDL**.**

The EOF (end of hemolysis) was positively correlated with disease duration, diastolic BP, WBC, creatinine, urea, RBG, and CRP, while negatively correlated with age and VLDL**.**

HbA1c levels positively correlated with disease duration, systolic BP, serum creatinine, cholesterol, and VLDL, but negatively correlated with diastolic BP, MCV, triglycerides, and eGFR**.** This aligns with **Anandhasayanam et al. (2024)**. In contrast, **Findikli et al. (2022)** found a positive correlation between HbA1c levels and MCV, RDW, and MPV. Additionally, **Bhutto et al. (2019)** found a non-significant correlation between MCV and hemoglobin.

Study limitations: This study has limitations, including a small sample size, cross-sectional nature, single medical

center's selection bias, inability to establish causality, not considering long-term medication use or environmental factors, and gender-specific differences, which could limit applicability to different populations or healthcare settings.

Conclusion

Anemia affects 56% of T2DM patients, often accompanied by metabolic syndrome and the presence of complications such as retinopathy, nephropathy, neuropathy, cardiomyopathy, or macrovascular and microvascular diseases and associated comorbidities like GIT bleeding, venous ulcers, and infected gangrene. Poor glycemic control led to a decline in RBC count and indices and increased reticulocyte count. The increased red cell hemolysis was correlated with various health indicators, including age, disease duration, blood pressure, kidney function, inflammatory markers, and lipid profile abnormalities. These exacerbate disease progression and increase the risk of complications. Therefore, regularly monitoring and strict glycemic control aid in reducing the disease progression and complication prevention.

References

- **Abril-Ulloa V, Flores-Mateo G, Solà-Alberich R, Manuel-y-Keenoy B, Arija V. (2014).** Ferritin levels and risk of metabolic syndrome: meta-analysis of observational studies. BMC public health, 14(1): 1-8.
- **Aikaeli F, Njim T, Gissing S, Moyo F, Alam U, Mfinanga S G, et al. (2022).** Prevalence of microvascular and macrovascular complications of diabetes in newly diagnosed type 2 diabetes in low-and-middle-income countries: A systematic review and meta-analysis. PLOS global public health, 2(6): 59-79.
- **Aikens RC, Zhao W, Saleheen D, Reilly M P, Epstein SE, Tikkanen E, et al. (2017).** Systolic blood pressure and risk of type 2 diabetes: a Mendelian randomization study. Diabetes, 66(2): 543-550.
- **Anandhasayanam A, Kannan S, Hemanandhini H, Rajamurugan R, Ranjith R, Rajamani S. (2024).** Correlation between Red Cell Distribution Width (RDW) and Mean Corpuscular Volume (MCV) as a Prognostic Biomarker for Diabetic Nephropathy Patients in a South Indian Hospital. Journal of Pharmaceutical Research International, 36(4): 1-10.
- **Arkew M, Yemane T, Mengistu Y, Gemechu K, Tesfaye G. (2021).** Hematological parameters of type 2 diabetic adult patients at Debre Berhan Referral Hospital, Northeast Ethiopia: A comparative cross-sectional study. Plos one, 16(6): 20-36.
- **Bambo G M, Asmelash D, Alemayehu E, Gedefie A, Duguma T, Kebede SS. (2024).** Changes in selected hematological parameters in patients with type 1 and type 2 diabetes: a systematic review and meta-analysis. Frontiers in Medicine, 11(1): 1-21.
- **Beydoun, MA, Obhi HK, Weiss J, Canas JA, Beydoun HA, Evans MK., et al. (2020).** Systemic inflammation is associated with depressive symptoms differentially by sex and race: a longitudinal study of urban adults. Molecular psychiatry, 25(6): 1286-1300.
- **Bhutto AR, Abbasi A, Abro AH. (2019).** Correlation of hemoglobin A1c with red cell width distribution and other parameters of red blood cells in type II diabetes mellitus. Cureus, 11(8): 16-32.
- **Carey IM, Critchley JA, DeWilde S, Harris T, Hosking FJ, Cook DG. (2018).** Risk of infection in type 1 and

type 2 diabetes compared with the general population: a matched cohort study. Diabetes Care, 41(3): 513-521.

- C**hávez-Reyes J, Escárcega-González CE, Chavira-Suárez E, León-Buitimea A, Vázquez-León P, Morones-Ramírez JR, et al. (2021).** Susceptibility for some infectious diseases in patients with diabetes: the key role of glycemia. Frontiers in Public Health, 9(1): 55-95.
- **Chen S, Zhu Y, Jin S, Zhao D, Guo J, Chen L, et al. (2023).** Association of glycemic control with hypertension in patients with diabetes: a population-based longitudinal study. BMC Cardiovascular Disorders, 23(1): 501-520.
- **Cherian S, Raman LM, Pujari S, Goudappala P. (2024).** Plasma uric acid levels and renal function in Type 2 Diabetes Mellitus. African Journal of Biomedical Research, 27(3): 253-256.
- **Du T, Yuan G, Zhou X, Sun X. (2016).** Sex differences in the effect of HbA1c-defined diabetes on a wide range of cardiovascular disease risk factors. Annals of Medicine, 48(2): 34-41.
- **Ebenuwa I, Violet P-C, Tu H, Lee C, Munyan N, Wang Y, et al. (2024).** Altered RBC deformability in diabetes: clinical characteristics and RBC pathophysiology. Cardiovascular Diabetology, 23(1): 370-377.
- **Essawi K, Dobie G, Shaabi MF, Hakami W, Saboor M, Madkhali AM, et al. (2023).** Comparative Analysis of Red Blood Cells, White Blood Cells, Platelet Count, and Indices in Type 2 Diabetes Mellitus Patients and Normal Controls: Association and Clinical Implications. Diabetes, Metabolic Syndrome and Obesity, 1(1): 3123-3132.
- **Fathi AE, Shahwan M, Hassan N, Jairoun AA, Shahwan M. (2024).** Prevalence of Anemia in Type 2 Diabetic Patients and correlation with Body Mass Index and Kidney function in Palestine. Diabetes, Metabolic Syndrome and Obesity, 1(2): 2293-2301.
- **Findikli HA, Sirikci V, Kirac CO, Erdogan M. (2022).** Evaluation of the Relationship between Blood Glucose Regulation and Hematological Indices in Patients with diabetes Mellitus. Eurasian Journal of Medical Investigation, 6(2): 6-15.
- **Gautam D, Adhikari S, Thapa R, Kharel L. (2023).** Study to determine between HbA1C and C-reactive protein in Diabetes mellitus. Journal of Pathology of Nepal, 13(1): 1979-1982.
- **Ghassab-Abdollahi N, Nadrian H, Pishbin K, Shirzadi S, Sarbakhsh P, Saadati F, et al. (2023).** Gender and urban–rural residency-based differences in the prevalence of type-2 diabetes mellitus and its determinants among adults in Naghadeh: Results of IraPEN survey. Plos one, 18(3): 21-39.
- **Govindarajan Venguidesvarane A, Jasmine A, Varadarajan S, Shriraam V, Muthuthandavan AR, Durai V, et al. (2020).** Prevalence of vascular complications among type 2 diabetic patients in a rural health center in South India. Journal of Primary Care & Community Health, 11(1): 1-21.
- **Huo D, Tao L, Li X, Wang W, Wang Z, Chen D, et al. (2013).** Association of blood pressure with development of metabolic syndrome

components: a five-year Retrospective Cohort study in Beijing. BMC public health, 13(1): 1-9.

- **Kautzky-Willer A, Leutner M, Harreiter J. (2023).** Sex differences in type 2 diabetes. Diabetologia, 66(6): 986-1002.
- **Kebede SA, Tusa BS, Weldesenbet AB, Tessema ZT, Ayele TA. (2021). I**ncidence of diabetic nephropathy and its predictors among type 2 diabetes mellitus patients at university of gondar comprehensive specialized hospital, Northwest Ethiopia. Journal of Nutrition and Metabolism, 2021(1): 675-915.
- **Kelem A, Shiferaw E, Adane T. (2023).** Hematological abnormalities and associated factors among metabolic syndrome patients at the University of Gondar comprehensive specialized hospital, Northwest Ethiopia. Plos one, 18(5): 23-86.
- **Kuhn V, Diederich L, Keller IV TS, Kramer CM, Lückstädt W, Panknin C, et al. (2017).** Red blood cell function and dysfunction: redox regulation, nitric oxide metabolism, anemia. Antioxidants & redox signaling, 26(13): 718-742.
- **Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, et al. (2019).** CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. Ann Intern Med. 150(9): 604-12.
- **Lin L, Tan W, Pan X, Tian E, Wu Z, Yang J. (2022).** Metabolic syndrome-related kidney injury: a review and update. Frontiers in endocrinology, 13(1): 30-91.
- **Liu Z, Fu C, Wang W, Xu, B. (2010).** Prevalence of chronic complications of type 2 diabetes mellitus in outpatients-a cross-sectional hospital-based survey in urban China. Health and quality of life outcomes, 8(1): 1-9.
- **Moehlecke M, Leitão CB, Kramer CK, Rodrigues TdC, Nickel C, Silveiro SP, et al. (2010).** Effect of metabolic syndrome and of its individual components on renal function of patients with type 2 diabetes mellitus. Brazilian Journal of Medical and Biological Research, 4(3): 687-693.
- **Mozos I. (2015).** Mechanisms linking red blood cell disorders and cardiovascular diseases. BioMed research international, 2015(1): 54-68.
- **Ndevahoma F, Nkambule BB, Dludla PV, Mukesi M, Natanael KN, Nyambuya, TM. (2021).** The effect of underlying inflammation on iron metabolism, cardiovascular risk and renal function in patients with type 2 diabetes. EJHaem, 2(3): 357-365.
- **Nicolucci A, Charbonnel B, Gomes MB, Khunti K, Kosiborod M, Shestakova, MV, et al. (2019).** Treatment patterns and associated factors in 14 668 people with type 2 diabetes initiating a second-line therapy: results from the global DISCOVER study programme. Diabetes, Obesity and Metabolism, 21(11): 2474-2485.
- **O'Neill S, O'Driscoll L. (2015).** Metabolic syndrome: a closer look at the growing epidemic and its associated pathologies. Obesity reviews, 16(1): 1-12.
- **Ozder A. (2014).** Lipid profile abnormalities seen in T2DM patients in primary healthcare in Turkey: a cross-sectional study. Lipids in health and disease, 13(1): 1-6.
- **Pagana KD, Pagana TJ, Pagana TN. (2019).** Mosby's Diagnostic and

Laboratory Test Reference. 14th ed. St. Louis, MO: Elsevier. 37(1): 1-12.

- **Paredes S, Fonseca L, Ribeiro L, Ramos H, Oliveira JC, Palma I. (2019).** Novel and traditional lipid profiles in Metabolic Syndrome reveal a high atherogenicity. Scientific reports, 9(1): 11-79.
- **Regensteiner JG, Reusch JE. (2022).** Sex differences in cardiovascular consequences of hypertension, obesity, and diabetes: JACC focus seminar 4/7. Journal of the American College of Cardiology, 79(15): 1492-1505.
- **Rownak N, Akhter S, Khatun M, Baksh S, Rafiq S, Rahman M. (2017).** Study of osmotic fragility status of red blood cell in type II diabetes mellitus patients. European Journal of Environment and Public Health, 1(2): 6-12.
- **Rupasinghe S, Jayasinghe IK. (2024)**. Prevalence and associated factors of anaemia in patients with type 2 diabetes mellitus: a cross-sectional study in a tertiary care medical unit, Sri Lanka. BMC endocrine disorders, 24(1): 156-171.
- **Russo G, Pintaudi B, Giorda C, Lucisano G, Nicolucci A, Cristofaro MR, et al. (2015).** Age-and gender-related differences in LDL-cholesterol management in outpatients with type 2 diabetes mellitus. International journal of endocrinology, 15(1): 57-105.
- **Salazar-Vazquez BY, Intaglietta M, Rodríguez-Morán M, Guerrero-Romero F. (2006).** Blood pressure and hematocrit in diabetes and the role of endothelial responses in the variability of blood viscosity. Diabetes Care, 29(7):1523-1528.
- **Scott RA, Langenberg C, Sharp SJ, Franks PW, Rolandsson O, Drogan D, van der Schouw YT, et al. (2013).** The link between family history and risk of type 2 diabetes is not explained by anthropometric, lifestyle or genetic risk factors: the EPIC-InterAct study. Diabetologia. 56(1):60-9. Shaheen E-S. (2019). Prevalence of anemia in patients with type 2 diabetes. Journal of Medicine in Scientific Research, 2(2): 114-114.
- **Stamouli M, Pouliakis A, Mourtzikou A, Skliris A, Panagiotou I, Mournianakis E, et al. (2014).** Evaluation of the lipid profile in type 2 diabetes mellitus patients in Greece. Clinical laboratory, 60(10): 1593-1600.
- **Tarquini R, Lazzeri C, Pala L, Rotella CM, Gensini GF. (2011).** The diabetic cardiomyopathy. Acta Diabetologica, 48(1): 173-181.
- **Tikki KA, Jaber HH, Mahdi AA. (2022).** Estimation of Serum Uric Acid in Type II Diabetic Patients and Relationship with Anemia. HIV Nursing, 22(2): 1523-1526.
- **Tsimihodimos V, Gonzalez-Villalpando C, Meigs JB, Ferrannini E. (2018).** Hypertension and diabetes mellitus: coprediction and time trajectories. Hypertension, 71(3): 422-428.
- **Tujara, Z, Reta W, Tadesse E, Dereje I, Tesfa M. (2024).** Assessment of Erythrocyte Osmotic Fragility and Its Determinants, and Comparison of Hematological Indices Among Type 2 Diabetes Mellitus Patients on Follow-Up at Jimma Medical Center, Southwest Ethiopia. Journal of Blood Medicine. 1(1): 9-19.
- **Vlacho B, Rossell-Rusiñol J, Granado-Casas M, Mauricio D, Julve J. (2024).** Overview on chronic complications of diabetes mellitus. In

Chronic Complications of Diabetes Mellitus. Elsevier. 1(1): 1-10.

- **Voigt M, Schmidt S, Lehmann T, Köhler B, Kloos C, Voigt UA, et al. (2018).** Prevalence and progression rate of diabetic retinopathy in type 2 diabetes patients in correlation with the duration of diabetes. Experimental and Clinical Endocrinology & Diabetes, 126(9): 570-576.
- **Wang G-R, Li L, Pan Y-H, Tian G-D, Lin W-L, Li Z, et al. (2013).** Prevalence of metabolic syndrome among urban community residents in China. BMC public health, 13(1): 1-9.
- **Wang W, Ji Q, Ran X, Li C, Kuang H, Yu X, et al. (2023).** Prevalence and risk factors of diabetic peripheral neuropathy: A population-based cross-sectional study in China. Diabetes/metabolism research and reviews, 39(8): 2-37.
- **Wang Y, Ming J, Guo Z, Zhang W, Li X, Zhou S, et al. (2023).** Association of serum uric acid with anemia in US adults: a cross-sectional study using secondary data. BMC Cardiovascular Disorders, 23(1): 291-315.
- **Wu M, Wen J, Qin Y, Zhao H, Pan X, Su J, et al. (2017).** Familial history of diabetes is associated with poor glycaemic control in type 2 diabetics: a cross-sectional study. Scientific reports, 7(1): 14-32.
- **Yameny AA. (2024).** Diabetes Mellitus Overview 2024. Journal of Bioscience and Applied Research, 10(3): 641-645.
- **Yang H, Gao J, Li S, Xia H, Chen Z, Zhu S, et al. (2021).** Gender differences in the association between serum uric acid and arteriosclerotic cardiovascular risk among Chinese type 2 diabetes mellitus patients. International Journal of General Medicine, 1(1): 687-695.