

## Relationship between Peripheral Blood Cytopenia and Type 2 Diabetic Patients in Benha University Hospital

Mostafa S.Banhawy<sup>1</sup>, Hiam A.Eleleimy<sup>1</sup>, Ahmed M. abdefattah<sup>1</sup>, Walied A.Abd –Elhaliem<sup>2</sup> and Mohamed A.Mohamed<sup>1</sup>

<sup>1</sup> Internal Medicine Dept., Faculty of Medicine Benha University, Egypt

<sup>2</sup> Clinical Pathology Dept., Faculty of Medicine Benha University, Egypt

E-mail : mbanhaw05@gmail.com

### Abstract

**Background:** Type 2 diabetes mellitus (T2DM) is a rapidly growing health problem affecting about 10.2% of adults worldwide. In Egypt, the prevalence of type 2 diabetes is around 15.6% of all adults aged 20 to 79. The aim of this work is to detect the hematological abnormalities that may occur with diabetic patients and to assess the relationship between hematological abnormalities and diabetic complications.

**Methods:** This cross-sectional study was carried out on 100 T2DM patients were age between 30- 65 years old, diabetic patients diagnosed by FBG, 2hPP and HbA1c. All the diabetic patients are under treatment in all units of Internal medicine department, Benha University Hospital.

**Results:** According to Relation between (HbA1C) and Complete Blood Count, there was a statistically significant difference between Controlled group (n= 38) and Uncontrolled group (n= 62) regarding RBCs count, Hb concentration, HCT, MCV and PLT count (P <0.001, 0.002, <0.001, 0.066, <0.001 respectively). According to Relation between HbA1C and different parameters, there was a statistically significant difference between Controlled group (n= 38) and Uncontrolled group (n= 62) regarding Neutrophil (P=0.005), Lymphocytes (p <0.001) and Monocyte (p=0.26) while no statistically significant difference was found regarding eosinophils and basophils counts.

**Conclusions:** T2DM disrupts the hematological parameters and results in a mild form of cytopenia.

**Keywords:** Peripheral Blood Cytopenia, Type 2 Diabetic Patients.

### Introduction

Type 2 diabetes mellitus (T2DM) is a rapidly growing health problem affecting about 10.2% of adults worldwide. In Egypt, the prevalence of T2DM is around 15.6% of all adults aged 20 to 79.<sup>[1]</sup>

It is a chronic serious disease which can cause micro and macro vascular complications in the form of nephropathy, retinopathy neuropathy as well as metabolic complications. T2DM occurs when a combination of low insulin production from Beta cells of pancreas and increased peripheral resistance to secreted insulin occurs.<sup>[2]</sup>

Cytopenia is defined as a decrease in of the elements of the produced blood cells. The Erythropoiesis system is affected by DM because of the hyperglycemic state that leads to protein glycation.<sup>[3]</sup> Anemia is the most common form of cytopenia that occurs in T2DM. Anemia can be caused by systemic inflammation which will influence iron metabolism and release of multiple inflammatory cytokines and free radicles that will lead to increase of hepcidin, leading to anemia. All these changes will affect the blood cell count, especially RBCs count.<sup>[4]</sup>

T2DM and its medications can also affect the WBCs count and platelets. The immune mediated mechanism is the commonest cause of thrombocytopenia. Dysfunction of the platelets is associated with micro and macro vascular complications.<sup>[5]</sup>

The aim of this work was to detect the hematological abnormalities that may occur with diabetic patients and to assess the relationship between hematological abnormalities and diabetic complications.

### Patients and Methods

This cross-sectional study was carried out on 100 T2DM patients were age between 30- 65 years old, diabetic patients diagnosed by FBG, 2hPP and HbA1c. All the diabetic patients are under treatment in all units of Internal medicine department, Benha University Hospital.

Informed written consent was obtained from the patients. The study was done after approval from the Ethics Committee of the Faculty of Medicine, Benha University (approval code :).

Exclusion criteria were type 1 DM, patient with other chronic diseases and patients with auto immune diseases.

All patients underwent complete history taking, physical examination, the following investigation was performed to every patient (fasting blood glucose, 2hPP, HbA1c, CBC, S. Creatinine, 24 h urinary protein, fundus examination, neurological examination and monofilament test).

### Blood sample collection

The vacutainer collected 3 mL of venous blood. A tube containing tri-potassium Ethylene Diamine Tetraacetic Acid received the blood. Blood was utilized for CBC testing. Standard operating procedures were followed to take the blood sample aseptically.

### Complete blood cell count determination

Results were obtained using the Beckman Coulter UniCel DxH 800 fully automated hematology analyzer. The DxH 800 CBC analysis uses the coulter principle to transport a blood cell solution through a tiny hole with an electric current. Blood cells moving through the orifice alter impedance based on their size.

Cell size distribution and counting are provided by the system. WBC differential technology was developed employing coulter volume, conductivity, and scatter measurements of cell volume, high-frequency conductivity, and laser-light scatter.

### Data quality control measures

Removing hemolysis, clotting, blood to anticoagulant proportion, and delaying laboratory analysis maintained sample quality. Blood was also discharged to the EDTA test tube wall to eliminate hemolysis.

CBC, peripheral morphology, and blood film reagents were also examined for expiry dates and prepared according to manufacturer instructions. Before testing samples, the commercial Beckman Coulter UniCel® DxH 800 hematological cell controls (low, normal, and high) were performed

### Results

The mean age of studied group was  $47.01 \pm 9.92$  ranged from 38 to 56 years and 54% of them were females. (Table 1)

**Table (1) Distribution of the studied cases according to demographic data**

		No.	%
Sex	Male	46	46.0
	Female	54	54.0
Age	Range	30.0 – 64.0	
	Mean $\pm$ SD.	$47.01 \pm 9.92$	
	Median (IQR)	48.0 (38.0 – 56.0)	

Regarding distribution of the studied cases according to CBC, 12 patients (12%) had abnormal RBCs count either decrease in 9 cases (9%) or increase in 3 cases (3%). The mean of RBCs count in all patients was  $4.83 \pm 0.54$  m/dl ranged from 3.50 to 5.90 m/dl. Hb concentration was abnormal in 21 cases (21%) either decrease in 15 cases (15%) or increase in 6 cases (6%). The mean of Hb concentration was  $14.29 \pm 1.73$  g/dl ranged from 4.80 to 17.50 g/dl which was abnormal in 21 cases (21%) either decreased in 15 case (15%) or increased in 6 cases .(%)

The mean of HCT was  $43.97 \pm 6.45$  ranged from 24.0 to 58.0 which was abnormal in 36 case (36%) either decreased in 13 cases (13%) or increased in 23 cases (23%). The mean of MCV was  $85.49 \pm 7.30$  ranged from 70.0 to 118.0 which was Microcytic in 10 case (10%), Normocytic in 86 case (86%) and Macrocytic in 4 cases (4%). PLT count was  $239.7 *10^3$ /dl in average ranged from 130.0 to  $367.0 *10^3$ /dl which was normal in all cases except 2 cases of thrombocytopenia (2%), Regarding distribution of the studied cases

daily. Malaria positive and negative slides were used to evaluate the smear and Giemsa stain.

### Urine analysis

An nocturnal first-voided urine sample was measured. Urine albumin concentration (mg/l) and albumin/creatinine ratio (mg/mmol) measure excretion. Men with a urine albumin/creatinine ratio of  $2.5-25$  mg/mmol and women with  $3.5-35$  mg/mmol have microalbuminuria. The ratio provides a more accurate representation of albuminuric patients than absolute urine albumin concentration.

### Statistical analysis:

Statistical analysis was conducted using IBM SPSS v27 (Armonk, NY, USA). Shapiro-Wilks and histograms assessed data normality. Parametric quantitative data were given as mean and SD and examined using unpaired student t-test. Non-parametric quantitative data were provided as median and IQR and examined using Mann Whitney-test. When applicable, the Chi-square test or Fisher's exact test was used to examine qualitative variables like frequency and percentage (%). A two-tailed P value  $< 0.05$  indicated significance.

according to WBCs counts, Neutrophil counts was normal in all cases with Mean of  $3.84 \pm 0.80$  ranged from 2.10 to 6.80 and Median (IQR) of 3.85 (3.40 – 4.41) while Lymphocytes counts was abnormal (decreased) in 2 cases (2%) with Mean of  $2.27 \pm 0.40$  ranged from 0.90 to 3.50 and Median (IQR) of 2.30 (2.10 – 2.41). Monocyte was abnormal count in 18 case (18%) either decreased in 11 case (11%) or increased in 7 cases (7%) with Mean of  $0.43 \pm 0.24$  ranged from 0.0 – 0.95 and Median (IQR) of 0.40 (0.25 – 0.60). Eosinophils decreased in 62 case (62%) and increased in 10 cases (10%) with Mean of  $0.11 \pm 0.22$  ranged from 0.0 to 0.90 and Median (IQR) of 0.0 (0.0 – 0.10). Basophils was increased in 20 cases (20%) with Mean of  $0.03 \pm 0.07$  ranged from 0.0 to 0.30 and Median (IQR) of 0.0 (0.0 – 0.0), According to Distribution of the studied cases according to HbA1C, FBS and 2hpp, 38 cases (38%) were controlled (HbA1C  $<6.8$ ) and 53% (20 cases) of them were females while uncontrolled patients was 62% (62 cases) and 55% (34 cases) of them were females. The mean of FBS was  $161.3 \pm 46.82$

mg/dl and mean of 2hpp was  $256.43 \pm 61.71$  mg/dl, and According to Distribution of the studied cases according to 24 urinary collection protein and S. Create, no case was found to have Normal (<30) proteinuria. Microalbuminuria (30 – 300) was

found in 56 case (56%) and Macroalbuminuria (>300) was founded in 44 case (44%). S. Create was found to be normal (<1.3) in 88 cases (88%) and normal (>1.3) in 12 cases (12%) with mean of  $0.96 \pm 0.31$  ranged from 0.07 to 2.70. (Table 2)

**Table (2) Distribution of the studied cases according to CBC, different parameters, HbA1C, FBS, 2hpp, 24 urinary collection protein and S. Create**

		No.	%
<b>CBC</b>	<b>Normal</b>	88	88.0
	<b>Abnormal</b>	12	12.0
<b>RBCs</b>	<b>Decrease</b>	9	9.0
	<b>Increase</b>	3	3.0
	<b>Range</b>	3.50 – 5.90	
	<b>Mean ± SD.</b>	$4.83 \pm 0.54$	
	<b>Median (IQR)</b>	4.80 (4.60 – 5.20)	
<b>Hb</b>	<b>Normal</b>	79	79.0
	<b>Abnormal</b>	21	21.0
	<b>Decrease</b>	15	15.0
	<b>Increase</b>	6	6.0
	<b>Range</b>	4.80 – 17.50	
<b>HCT</b>	<b>Mean ± SD.</b>	$14.29 \pm 1.73$	
	<b>Median (IQR)</b>	14.50 (13.55 – 15.40)	
	<b>Normal</b>	64	64.0
	<b>Abnormal</b>	36	36.0
	<b>Decrease</b>	13	13.0
<b>MCV</b>	<b>Increase</b>	23	23.0
	<b>Range</b>	24.0 – 58.0	
	<b>Mean ± SD.</b>	$43.97 \pm 6.45$	
	<b>Median (IQR)</b>	43.70 (41.60 – 47.0)	
	<b>Microcytic</b>	10	10.0
<b>PLT</b>	<b>Normocytic</b>	86	86.0
	<b>Macrocytic</b>	4	4.0
	<b>Range</b>	70.0 – 118.0	
	<b>Mean ± SD.</b>	$85.49 \pm 7.30$	
	<b>Median (IQR)</b>	85.0 (82.0 – 87.0)	
<b>Different parameters</b>	<b>Thrombocytopenia</b>	2	2.0
	<b>Normal</b>	98	98.0
	<b>Thrombocytosis</b>	0	0.0
	<b>Range</b>	130.0 – 367.0	
	<b>Mean ± SD.</b>	$239.7 \pm 53.68$	
<b>Neutrophil</b>	<b>Median (IQR)</b>	238.0 (197.5 – 264.5)	
	<b>Normal</b>	100	100.0
	<b>Abnormal</b>	0	0.0
	<b>Range</b>	2.10 – 6.80	
	<b>Mean ± SD.</b>	$3.84 \pm 0.80$	
<b>Lymphocytes</b>	<b>Median (IQR)</b>	3.85 (3.40 – 4.41)	
	<b>Normal</b>	98	98.0
	<b>Abnormal</b>	2	2.0
	<b>Decrease</b>	2	2.0
	<b>Increase</b>	0	0.0
<b>Monocyte</b>	<b>Range</b>	0.90 – 3.50	
	<b>Mean ± SD.</b>	$2.27 \pm 0.40$	
	<b>Median (IQR)</b>	2.30 (2.10 – 2.41)	
	<b>Normal</b>	82	82.0
	<b>Abnormal</b>	18	18.0

	<b>Range</b>	0.0 – 0.95	
	<b>Mean ± SD.</b>	0.43 ± 0.24	
	<b>Median (IQR)</b>	0.40 (0.25 – 0.60)	
	<b>Normal</b>	28	28.0
	<b>Abnormal</b>	72	72.0
	<b>Decrease</b>	62	62.0
	<b>Increase</b>	10	10.0
<b>Eosinophils</b>	<b>Range</b>	0.0 – 0.90	
	<b>Mean ± SD.</b>	0.11 ± 0.22	
	<b>Median (IQR)</b>	0.0 (0.0 – 0.10)	
	<b>Normal</b>	80	80.0
	<b>Abnormal</b>	20	20.0
	<b>Decrease</b>	0	0.0
	<b>Increase</b>	20	20.0
<b>Basophils</b>	<b>Range</b>	0.0 – 0.30	
	<b>Mean ± SD.</b>	0.03 ± 0.07	
	<b>Median (IQR)</b>	0.0 (0.0 – 0.0)	
	<b>Controlled (&lt;6.8)</b>	38	38.0
	<b>Male</b>	18	18.0
	<b>Female</b>	20	20.0
	<b>Uncontrolled (≥6.8)</b>	62	62.0
	<b>Male</b>	28	28.0
	<b>Female</b>	34	34.0
<b>HbA1C</b>	<b>Range</b>	5.50 – 13.50	
	<b>Mean ± SD.</b>	8.11 ± 2.24	
	<b>Median (IQR)</b>	7.60 (6.30 – 9.70)	
	<b>Range</b>	78.0 – 278.0	
<b>FBS</b>	<b>Mean ± SD.</b>	161.3 ± 46.82	
	<b>Median (IQR)</b>	173.5 (122.0 – 189.0)	
	<b>Range</b>	145.0 – 400.0	
<b>2hpp</b>	<b>Mean ± SD.</b>	256.43 ± 61.71	
	<b>Median (IQR)</b>	273.5 (193.5 – 296.5)	
	<b>Normal (&lt;30)</b>	0	0.0
	<b>Microalbuminuria (30 – 300)</b>	56	56.0
	<b>Macroalbuminuria (&gt;300)</b>	44	44.0
<b>24 urinary collection protein</b>	<b>Range</b>	50.0 – 14200.0	
	<b>Mean ± SD.</b>	930.5 ± 1623.2	
	<b>Median (IQR)</b>	183.5 (110.0 – 1770.5)	
	<b>Normal (&lt;1.3)</b>	88	88.0
	<b>Abnormal</b>	12	12.0
<b>S. Create</b>	<b>Range</b>	0.07 – 2.70	
	<b>Mean ± SD.</b>	0.96 ± 0.31	
	<b>Median (IQR)</b>	0.89 (0.80 – 1.10)	

IQR: Inter quartile range, SD: Standard deviation

According to Distribution of the studied cases regarding fundus exam, 43 cases (43%) were normal retina while 57 case (57%) showed a degree of Diabetic retinopathy. According to Distribution

of the studied cases regarding monofilament test, 38 case (38%) showed normal test while 62 case (62%) showed abnormal test. (Table 3)

**Table (3) Distribution of the studied cases according to fundus exam monofilament test (n = 100)**

	No.	%
<b>Fundus exam</b>		
<b>Normal</b>	43	43.0
<b>Diabetic retinopathy</b>	57	57.0
<b>Monofilament test</b>		
<b>Normal</b>	38	38.0
<b>Abnormal</b>	62	62.0

According to Relation between HbA1C and CBC, there was a statistically significant difference between Controlled group (n= 38) and Uncontrolled group (n= 62) regarding RBCs count,

Hb concentration, HCT, MCV and PLT count (P <0.001, 0.002, <0.001, 0.066, <0.001 respectively). According to Relation between HbA1C and different parameters, there was a statistically

significant difference between Controlled group (n= 38) and Uncontrolled group (n= 62) regarding Neutrophil (P=0.005), Lymphocytes (p <0.001) and Monocyte (p=0.26) while no statistically significant difference was found regarding eosinophils and basophils counts. (Table 4)

**Table (4) Relation between HbA1Cand CBC, and between HbA1C and different parameters (n = 100)**

	HbA1C		t	p
	Controlled (n = 38)	Uncontrolled (n = 62)		
<b>RBCs</b>				
Mean ± SD.	5.17 ± 0.54	4.63 ± 0.43	5.457*	<0.001*
Median (Range)	5.40 (3.50 – 5.90)	4.70 (3.50 – 5.40)		
<b>Hb</b>				
Mean ± SD.	15.07 ± 2.21	13.82 ± 1.13	3.227*	0.002*
Median (Range)	15.55 (4.80 – 17.50)	13.95 (10.80 – 15.60)		
<b>HCT</b>				
Mean ± SD.	47.94 ± 6.50	41.61 ± 5.25	5.457*	<0.001*
Median (Range)	47.0 (28.0 – 58.0)	43.0 (24.0 – 49.50)		
<b>MCV</b>				
Mean ± SD.	84.0 ± 4.34	86.40 ± 8.53	1.859	0.066
Median (Range)	84.0 (70.0 – 98.0)	85.0 (72.0 – 118.0)		
<b>PLT</b>				
Mean ± SD.	279.3 ± 48.79	215.4 ± 40.73	6.752*	<0.001*
Median (Range)	284.0 (190.0 – 367.0)	210.0 (130.0 – 343.0)		
<b>Neutrophil</b>				
Mean ± SD.	3.52 ± 0.97	4.03 ± 0.61	t=2.904*	0.005*
Median (Range)	3.50 (2.10 – 6.80)	4.10 (2.42 – 5.10)		
<b>Lymphocytes</b>				
Mean ± SD.	2.46 ± 0.35	2.15 ± 0.38	U=608.50*	<0.001*
Median (Range)	2.40 (1.58 – 3.50)	2.20 (0.90 – 3.30)		
<b>Monocyte</b>				
Mean ± SD.	0.36 ± 0.23	0.47 ± 0.24	U=865.0*	0.026*
Median (Range)	0.30 (0.0 – 0.95)	0.40 (0.10 – 0.92)		
<b>Eosinophiles</b>				
Mean ± SD.	0.06 ± 0.09	0.15 ± 0.27	U=1120.0	0.635
Median (Range)	0.0 (0.0 – 0.40)	0.0 (0.0 – 0.90)		
<b>Basophils</b>				
Mean ± SD.	0.03 ± 0.07	0.03 ± 0.07	U=	0.686
Median (Range)	0.0 (0.0 – 0.30)	0.0 (0.0 – 0.20)		

t: Student t-testp: p value for comparison between the studied categories \*: Statistically significant at p ≤ 0.05

According to Relation between 24 urinary collection protein and HbA1C, there was a statistically significant difference between Microalbuminuria group (n= 56) and Macroalbuminuria group (n= 44) regarding HbA1C (P <0.001), According to Relation between 24 urinary collection protein and CBC, there was a statistically significant difference between Microalbuminuria group (n= 56) and

Macroalbuminuria group (n= 44) regarding RBCs count, Hb concentration, HCT, MCV and PLT count (P <0.001), and According to Relation between 24 urinary collection protein and different parameters, there was no statistically significant difference between Microalbuminuria group (n= 56) and Macroalbuminuria group (n= 44) regarding WBCs counts (Neutrophil, Lymphocytes, Monocyte, Eosinophils and Basophils). (Table 5)

**Table (5) Relation between 24 urinary collection protein and (HbA1C, CBC, and different parameters) (n = 100)**

	24 urinary collection protein				□□	p
	Microalbuminuria (30 – 300) (n= 56)		Macroalbuminuria (>300) (n= 44)			
	No.	%	No.	%		
<b>HbA1C</b>						
Controlled	32	57.1	6	13.6	19.796	<0.001*
Un controlled	24	42.9	38	86.4		
<b>RBCs</b>						
Mean ± SD.	5.06 ± 0.45		4.55 ± 0.51		5.338*	<0.001*
Median (Range)	5.10 (3.50 – 5.90)		4.70 (3.50 – 5.60)			
<b>Hb</b>						

<b>Mean ± SD.</b>	14.79 ± 1.82	13.66 ± 1.39	3.419*	0.001*
<b>Median (Range)</b>	15.0 (4.80 – 17.50)	13.70 (10.80 – 16.80)		
<b>HCT</b>				
<b>Mean ± SD.</b>	46.11 ± 5.59	41.35 ± 6.67	3.879*	<0.001*
<b>Median (Range)</b>	45.0 (28.0 – 58.0)	42.75 (24.0 – 55.0)		
<b>MCV</b>				
<b>Mean ± SD.</b>	84.03 ± 4.0	87.34 ± 9.79	2.111*	0.039*
<b>Median (Range)</b>	84.50 (70.0 – 91.80)	85.0 (72.0 – 118.0)		
<b>PLT</b>				
<b>Mean ± SD.</b>	257.2 ± 54.37	217.4 ± 44.13	3.937*	<0.001*
<b>Median (Range)</b>	255.0 (130.0 – 367.0)	210.5 (134.0 – 340.0)		
<b>Neutrophil</b>				
<b>Mean ± SD.</b>	<b>3.73 ± 0.81</b>	3.98 ± 0.77	t=1.569	0.120
<b>Median (Range)</b>	<b>3.70 (2.10 – 6.80)</b>	4.15 (2.20 – 5.10)		
<b>Lymphocytes</b>				
<b>Mean ± SD.</b>	<b>2.34 ± 0.39</b>	2.18 ± 0.39	U=989.50	0.091
<b>Median (Range)</b>	<b>2.30 (0.90 – 3.50)</b>	2.30 (0.95 – 3.10)		
<b>Monocyte</b>				
<b>Mean ± SD.</b>	<b>0.39 ± 0.23</b>	0.47 ± 0.24	U=989.0	0.090
<b>Median (Range)</b>	<b>0.30 (0.0 – 0.95)</b>	0.43 (0.10 – 0.90)		
<b>Eosinophils</b>				
<b>Mean ± SD.</b>	<b>0.06 ± 0.13</b>	0.18 ± 0.29	U=	0.205
<b>Median (Range)</b>	<b>0.0 (0.0 – 0.70)</b>	0.0 (0.0 – 0.90)	1073.50	
<b>Basophils</b>				
<b>Mean ± SD.</b>	<b>0.03 ± 0.06</b>	0.04 ± 0.08	U=1168.0	0.532
<b>Median (Range)</b>	<b>0.0 (0.0 – 0.30)</b>	0.0 (0.0 – 0.20)		

$\chi^2$ : Chi square test p: p value for comparison between the studied categories \*: Statistically significant at  $p \leq 0.05$ , t: Student t-test, U: Mann Whitney test.

### Discussion

Cytopenia, conversely, refers to a reduction in the production of one of the cellular components. Diabetes mellitus (DM) affects the process of erythropoiesis by triggering a state of high blood sugar, which leads to the glycation of proteins.<sup>[6]</sup> Therefore, cytopenia can occur as a consequence in this particular situation. Anemia is the most prevalent form of disorder in T2DM among various types of cytopenia. Anemia can result from reduced production of erythropoietin, which is associated with microvascular complications and kidney damage, systemic inflammation affecting iron metabolism, and the release of various inflammatory cytokines and free radicals that elevate hepcidin levels (causing degradation of ferroproteins and resulting in iron deficiency anemia).<sup>[7]</sup>

In the present study, the mean age of studied group was  $47.01 \pm 9.92$  ranged from 38 to 56 years and 54% of them were females. Regarding distribution of the studied cases according to CBC, 12 patients (12%) had abnormal RBCs count either decrease in 9 cases (9%) or increase in 3 cases (3%). The mean of RBCs count in all patients was  $4.83 \pm 0.54$  m/dl ranged from 3.50 to 5.90 m/dl. Hb concentration was abnormal in 21 cases (21%) either decreased in 15 cases (15%) or increased in 6 cases (6%). The mean of Hb concentration was  $14.29 \pm 1.73$  g/dl ranged from 4.80 to 17.50 g/dl which was abnormal in 21 case (21%) either decreased in 15 case (15%) or increased in 6 cases (6%).

The results of this study were consistent with a prior study conducted in Gondar by Kebede et al.,<sup>[8]</sup> which reported an anemia prevalence rate of 8.06%. Nevertheless, the prevalence of anemia in the current study is lower compared to the studies conducted by Taderegew et al.,<sup>[9]</sup> (20.1%) and Engidaw et al.,<sup>[10]</sup> (29.81%), which reported a higher incidence of anemia.

In the present study, the mean of HCT was  $43.97\% \pm 6.45$  ranged from 24.0% to 58.0 which was abnormal in 36 case (36%) either decreased in 13 case (13%) or increased in 23 cases (23%). The mean of MCV was  $85.49 \pm 7.30$  ranged from 70.0 to 118.0 which was Microcytic in 10 case (10%), Normocytic in 86 case (86%) and Macrocytic in 4 cases (4%). PLT count was  $239.7 *10^3$ /dl in average ranged from 130.0 to 367.0  $*10^3$ /dl which was normal in all cases except 2 cases of thrombocytopenia (2%).

In the present study, according to distribution of the studied cases according to HbA1C, FBS and 2hpp, 38 cases (38%) were controlled (HbA1C <6.8) and 53% (20 cases) of them were females while uncontrolled patients were 62% (62 cases) and 55% (34 cases) of them were females. The mean of FBS was  $161.3 \pm 46.82$  mg/dl and mean of 2hpp was  $256.43 \pm 61.71$  mg/dl. According to Distribution of the studied cases according to 24 urinary collection protein and S. Create, no case was found to have Normal (<30) proteinuria. Microalbuminuria (30 – 300) was found in 56 case

(56%) and Macroalbuminuria (>300) was founded in 44 case (44%). S. Creatinine was found to be normal (<1.3) in 88 cases (88%) and abnormal (>1.3) in 12 cases (12%) with mean of  $0.96 \pm 0.31$  ranged from 0.07 to 2.70. According to Relation between 24 urinary collection protein and HbA1C, there was a statistically significant difference between Microalbuminuria group (n= 56) and macroalbuminuria group (n= 44) regarding HbA1C ( $P < 0.001$ )

In the Ahmad et al. [11] research, 404 (31.56%) individuals had microalbuminuria. Most patients (78.4%) were obese with BMIs above 25. The research participants had diabetes for an average of  $9.7 \pm 7.8$  years, with 63.3% having it for over 5 years.

In the present study, According to Relation between 24 urinary collection protein and different parameters, there was no statistically significant difference between Microalbuminuria group (n= 56) and macroalbuminuric group (n= 44) regarding WBCs counts (Neutrophil, Lymphocytes, Monocyte, Eosinophils and Basophils)

Also, in Aynalem et al., [6] study, Leukopenia and leukocytosis were detected in 10.9% (95% CI: 8.09, 14.59) and 4.8% (95% CI: 2.99, 7.49) of T2DM patients, respectively.

In the current study, according to the relation between HbA1C and CBC, there was a statistically significant difference between the Controlled group (n= 38) and uncontrolled group (n= 62) regarding RBCs count, Hb concentration, HCT, MCV, and PLT count ( $P < 0.001, 0.002, < 0.001, 0.066, < 0.001$  respectively). There was a statistically significant difference between the controlled group (n= 38) and the uncontrolled group (n= 62) regarding neutrophils ( $P=0.005$ ), lymphocytes ( $p < 0.001$ ), and monocyte ( $p=0.26$ ) while no statistically significant difference was found regarding eosinophils and basophils counts.

In same line with us, Essawi et al., [12] investigated the association of HbA1C and demographic characteristics, CBC parameters, and CBC-derived parameters in 250 known diabetic patients along with 175 healthy adult controls. They reported that RBCs count, Hb concentration, HCT, MCV, and absolute neutrophil and monocyte counts were significantly different between T2DM and control groups ( $p < 0.0001$ ). PLT count and WBCs count were insignificantly different between T2DM and control groups ( $p > 0.05$ ).

According to our findings, Al-Ghareebawi and Ali [13] carried out a study to ascertain the utility of complete blood count (CBC) parameters as a useful tool in monitoring Diabetes Mellitus (DM) control in diabetic patients and to identify potential alterations in CBC parameters as indicators in the identification and management of DM. 30 males (aged 35 to 50) were chosen, 10 of whom were non-diabetic, 10 of whom had type 1 and 10 of type

2 diabetes, based on a random sugar test, each subject's case history, blood samples from each subject, and CBC parameters for every specimen. When comparing type 2 diabetic individuals to males without diabetes, the findings showed a substantial drop in WBC, RBC, HCT%, and RDW-SD, as well as a significant increase in MCHC and MPV. There were no significant ( $p > 0.05$ ) differences in the percentages of lymphocytes, monocytes, or granulocytes among the groups under study.

In line with our findings, Milosevic and Panin [2] conducted research on 178 individuals with Type 2 diabetes mellitus (T2DM) to ascertain potential alterations in the complete blood count (CBC) parameters based on glycemic management. based on the HbA1c (%) level. Two groups of participants—one regulated ( $HbA1c \leq 7$ ) and the other unregulated ( $HbA1c > 7$ )—were created. The regulated group (n = 94) and the unregulated group (n = 84) differed statistically significantly in terms of RBC count, Hb concentration, HCT, MCV, WBC count, and PLT count.

Our results are at odds with those of Alodhayani et al. [14], who retrospectively examined 385 Saudi patients with T2DM who were at least 18 years old in order to determine the correlation between CBC values and HbA1c levels. They found that the WBC, RBC, Hb concentration, HCT, MCV, and PLT counts did not vary statistically significantly across various HbA1C levels.

We use Kizilgul et al. [15] to assess the counts of white blood cells, neutrophils, lymphocytes, monocytes, platelets, RDW, MPV, and PDW in 135 T2DM patients who, although receiving insulin treatment, had improper glycemic management ( $HbA1c > 7\%$ ), as well as 121 controls. They showed that the DM group had substantially increased WBC, neutrophil, lymphocyte, and monocyte counts than the control group ( $p < 0.0001$ ). Both groups' hemoglobin levels and platelet counts were comparable ( $p > 0.05$ ). The HbA1c level was positively linked ( $p < 0.05$ ) with the numbers of neutrophils and lymphocytes.

The current research found a statistically significant difference ( $P < 0.001$ ) in the RBC count, Hb concentration, HCT, MCV, and PLT count between the macroalbuminuria group (n = 44) and the microalbuminuria group (n = 56) based on the relationship between 24 urine collection proteins and CBC. Regarding WBC counts (neutrophils, lymphocytes, monocytes, eosinophils, and basophils), there was no statistically significant difference between the microalbuminuria group (n = 56) and the macroalbuminuria group (n = 44).

Alodhayani et al. [14] reported that in patients with nephropathy (defined as the presence of microalbuminuria, macroalbuminuria, or end stage renal disease), the counts of WBCs (neutrophils, lymphocytes, monocyte, eosinophils, and

basophils), RBCs, Hb concentration, HCT, and PLT were not significantly different. These findings are consistent with our findings.

As per our findings, Besada et al. [16] proposed that a higher platelet volume might be a significant contributing factor to the elevated risk of vascular problems. Fifty individuals with diabetes, fifty individuals with diabetic nephropathy, and fifty persons of healthy age and sex were included in the research as controls. When comparing diabetic individuals with nephropathy to those without nephropathy, mean platelet volume (MPV) was greater in the former group ( $P=0.001$ ), and there was a significant difference in MPV between the two groups ( $P$  value=0.004).

Concurrent with our findings, Fawwad et al. [17] conducted research to determine if type 2 diabetes patients' neutrophil-to-lymphocyte ratio (NLR) and diabetic microvascular problems are related. Of the 5620 individuals with type 2 diabetes, 3374 had one or more microvascular problems, whereas 2246 did not have any. In comparison to diabetic participants without any difficulties, the NLR was found to be 1.14 times higher in those with at least one microvascular issue ( $4.34 \pm 3.32$  vs.  $3.36 \pm 2.67$ ;  $P < 0.0001$ ). Compared to diabetic participants without nephropathy or any other microvascular diabetes problems, people with diabetic nephropathy had considerably greater NLR levels. Subjects with at least one microvascular problem showed substantially higher platelet, neutrophil, and total leukocyte counts. The groups also differed considerably in all other CBC measures.

The neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) have been investigated as new surrogate indicators of diabetic kidney disease (DKD), in contrast to our research, which was conducted by Kamrul-Hasan et al. [18]. Out of the 312 T2DM research participants, 150 (48.1%) developed DKD. Subjects with DKD compared to those without DKD had comparable levels of hemoglobin, total leukocyte count,

absolute lymphocyte count, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and red cell distribution width. The DKD group had elevated platelet counts and mean absolute neutrophil counts (ANC).

In contrast to us, Jaaban et al.'s research [19] examined the association between inflammatory markers—the platelet-to-lymphocyte and neutrophil-to-lymphocyte ratios—and diabetic nephropathy in patients from Syria. Based on the urine albumin-to-creatinine ratio, 158 individuals with type 2 diabetes mellitus were divided into three groups: Type 2 diabetic patients were divided into three groups: Group A had normoalbuminuria (urinary albumin-to-creatinine ratio  $<30$  mg/g); Group B had microalbuminuria (urinary albumin-to-creatinine ratio = 30-300 mg/g); and Group C had macroalbuminuria (urinary albumin-to-creatinine ratio  $\geq 300$  mg/g). PLT ( $p = 0.003$ ), Hb ( $p = 0.000$ ), and the absolute lymphocyte count ( $p = 0.000$ ) did not significantly vary across the groups. They came to the conclusion that there was a significant correlation between increased neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios and diabetic nephropathy. Furthermore, they suggested that high neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios could be used as prognostic risk markers and predictors of diabetic nephropathy.

#### Conclusions:

Type 2 diabetes mellitus (T2DM) disrupts the hematological parameters and results in a mild form of cytopenia. It is recommended that regular monitoring and control of hematological abnormalities, particularly cytopenia, be implemented in patients with type 2 diabetes mellitus (T2DM) to improve prognosis and quality of life.

**Financial support and sponsorship:** Nil

**Conflict of Interest:** Nil

#### References

- [1] Hegazi R, El-Gamal M, Abdel-Hady N, Hamdy O. Epidemiology of and Risk Factors for Type 2 Diabetes in Egypt. *Ann Glob Health*. 2015;81:814-20.
- [2] Milosevic D, Panin VL. Relationship Between Hematological Parameters and Glycemic Control in Type 2 Diabetes Mellitus Patients. *J Med Biochem*. 2019;38:164-71.
- [3] Panda AK, Ambade RA. Prevalence of anemia and its correlation with HBA1c of patients in type-II diabetes mellitus: a pilot study. *Natl J Physiol Pharm Pharmacol*. 2018;8:1409-13.
- [4] Antwi-Baffour S, Kyeremeh R, Boateng SO, Annison L, Seidu MA. Haematological parameters and lipid profile abnormalities among patients with Type-2 diabetes mellitus in Ghana. *Lipids Health Dis*. 2018;17:283-90.
- [5] Jain A, Naniwadekar M. An etiological reappraisal of pancytopenia-largest series reported to date from a single tertiary care teaching hospital. *BMC Blood Disorders*. 2013;13:1-9.
- [6] Aynalem M, Getu F, Adane T. Peripheral Cytopenia and Its Associated Factors in Type 2 Diabetes Mellitus Patients, Northwest Ethiopia. *J Blood Med*. 2022;13:373-83.



- [7] Park JM, Lee HS, Park JY, Jung DH, Lee JW. White Blood Cell Count as a Predictor of Incident Type 2 Diabetes Mellitus Among Non-Obese Adults: A Longitudinal 10-Year Analysis of the Korean Genome and Epidemiology Study. *J Inflamm Res.* 2021;14:1235-42.
- [8] Kebede SA, Tusa BS, Weldesenbet AB. Prevalence of Anaemia and Its Associated Factors among Type 2 Diabetes Mellitus Patients in University of Gondar Comprehensive Specialized Hospital. *Anemia.* 2021;2021:6-10.
- [9] Taderegew MM, Gebremariam T, Tareke AA, Woldeamanuel GG. Anemia and Its Associated Factors Among Type 2 Diabetes Mellitus Patients Attending Debre Berhan Referral Hospital, North-East Ethiopia: A Cross-Sectional Study. *J Blood Med.* 2020;11:47-58.
- [10] Engidaw MT, Feyisa MS. Prevalence of Anemia and Its Associated Factors Among Adult Diabetes Mellitus Patients at Debre Tabor General Hospital, Northcentral Ethiopia. *Diabetes Metab Syndr Obes.* 2020;13:5017-23.
- [11] Ahmad T, Ulhaq I, Mawani M, Islam N. Microalbuminuria in Type-2 Diabetes Mellitus; the tip of iceberg of diabetic complications. *Pak J Med Sci.* 2017;33:519-23.
- [12] Essawi K, Dobie G, Shaabi MF, Hakami W, Saboor M, Madkhali AM, et al. 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.* 2023;16:3123-32.
- [13] AL-Ghareebawi AMA, Ali SH. STUDY THE EFFECT OF DIABETES MELLITUS (TYPE 1 AND 2) ON COMPLETE BLOOD COUNT IN DIABETIC PATIENTS. *International Journal of Applied Sciences and Technology.* 2022.
- [14] Alodhayani A, Almansour A, Alotaibi J, Alghamdi G, Alageel M, Binabbad R. Relationship Between HbA1c and Complete Blood Count Parameters In Adult Patients With Type 2 Diabetes In Saudi Arabia. *International Journal of Advanced Research.* 2022;10:900-6.
- [15] Kizilgul M, Sencar E, Ucan B, Beysel S, Ozcelik O, Ozbek M, et al. Components of the complete blood count in type 2 diabetes mellitus with inadequate glycemc control. *Dicle Tip Dergisi.* 2018;45:113-20.
- [16] Besada MSD, Elsayed AA, Ali AE, Hashem AA. Platelet indices as an indicators of diabetic nephropathy. *SVU-International Journal of Medical Sciences.* 2021;4:41-8.
- [17] Fawwad A, Butt A, Siddiqui I, Khalid M, Sabir R, Basit A. Neutrophil-to-lymphocyte ratio and microvascular complications in subjects with type 2 diabetes: Pakistan's perspective. *TURKISH JOURNAL OF MEDICAL SCIENCES.* 2018;48:157-61.
- [18] Kamrul-Hasan ABM, Mustari M, Asaduzzaman M, Gaffar MAJ, Chanda PK, Rahman MM, et al. Evaluation of Neutrophil–lymphocyte Ratio and Platelet–lymphocyte Ratio as Markers of Diabetic Kidney Disease in Bangladeshi Patients with Type 2 Diabetes Mellitus. *Journal of Diabetology.* 2021;12.
- [19] Jaaban M, Zetoune AB, Hesenow S, Hesenow R. Neutrophil-lymphocyte ratio and platelet-lymphocyte ratio as novel risk markers for diabetic nephropathy in patients with type 2 diabetes. *Heliyon.* 2021;7.