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Original Article

Significance of Hematological Parameters in Patients with Type-2 Diabetes Mellitus and Its Relationship with Disease Complications

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ABSTRACT

Objective: To determine the association of haematological parameters with disease complications in patients with type 2 Diabetes Mellitus.

Study Design: Cross-sectional analytical study.

Place and Duration of Study: Department of Hematology, Armed Forces Institute of Pathology, Rawalpindi Pakistan from Feb to Aug 2019.

Methodology: In this study, 200 Patients were selected and divided into four groups, 1) Anaemia without Diabetes 2) Diabetes with Anaemia 3) Diabetes without Anaemia 4) Healthy Control Group. All the patients were assessed because of their clinical history and laboratory evidence. The patients' clinical details, type of anaemia, laboratory investigations and complications related to diabetes were recorded on a specially designed proforma.

Results: Diabetes-related complications were highest in diabetes with anaemia Group. It was recorded that diabetes with anaemia Group, 36 patients (50.0%) had microvascular complications and 32 patients (47.8%) had macrovascular complications. In the healthy control group, 8 patients (11.1%) had microvascular complications, and nine patients (13.4 %) had macrovascular complications.

Conclusion: Patients with type 2 Diabetes Mellitus should be evaluated and treated for anaemia routinely to prevent complications

Keywords: Anaemia, Diabetes mellitus, Microvascular complications, Macrovascular complications.

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INTRODUCTION

Diabetes is predicted to become the seventh-highest cause of death worldwide by 2030. Its global prevalence is very high, and almost 150 million people worldwide are suffering from it, and it is expected that this number will double in the next 20 years.[1,2] The second National Diabetes Survey of Pakistan demonstrated that the overall prevalence of diabetes in Pakistan was 26.3%, of which 19.2% were known patients with diabetes and 7.1% were newly diagnosed patie-nts.[3,4] Several haematological indices, including white blood cells, red blood cells, and coagul-ation factors, directly relate to Diabetes Mellitus.[5]

Hyperglycemia causes changes at the cellular level with enhanced production of reactive oxygen molecules, which alter cellular structure and function, and advanced glycation end products.[6,7] Another significant indicator for platelet function and activation is Mean platelet volume (MPV). It is shown that altered platelet activity is a risk factor for macro-vascular and microvascular disorders.[8,9] Studies have shown that insulin resistance is related to raised inflammatory indicators. A recent study has demonstrated that WBC counts and metabolic syndrome has a close link. Patients with Diabetes Mellitus have increased blood viscosity affecting microcirculation and leading to microangiopathy. Studies have demonstrated that a high WBC count is an important component of the inflammatory process, contributing to atherosclerosis and cerebrovascular diseases.[10] The increasing prevalence of diabetes in both developed and developing countries has challenged scientists to conduct further research for the treatment and management of diabetes. In Pakistan, little work has been done to reduce complications in diabetic patients with modified interventions. There is a dire need to study the correlation between anaemia and diabetes complications to develop better prevention techniques. Therefore, the present study was conducted to determine the association of haematological parameters with disease complications in patients with type-2 Diabetes Mellitus.

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METHODOLOGY

The cross-sectional analytical study was carried out at the Department of Hematology, AFIP, from

Pakistan, February to August 2019. After the ethical approval from Institutional Review Committee, (FC-HEM18-10/READ-IRB/20/364) and informed consent, patients were selected by consecutive sampling technique.

Inclusion Criteria: Patients of either gender, aged 25 to 70 years with type 2 Diabetes Mellitus were included in the study.

Exclusion Criteria: Seriously ill patients requiring critical care, patients having active bleeding, pregnancy, evidence of acute renal or liver impairment and the patients who had any recent history of cardiac dysfunctions and any hemoglobinopathy were excluded.

Patients were divided into four groups, 1) Anaemia without Diabetes, 2) Diabetes with Anaemia, 3) Diabetes without Anaemia, 4) Healthy Control Group.

Upon admission, all patients were assessed for diabetes related complications. People with diabetes were defined according to the World Health Organization (WHO) classification of Diabetes and Glycosylated haemoglobin (HBA1c) as >7 %.[11] Diabetic retinopathy was defined with the presence of at least two micro-aneurysms and/or retinal haemorrhages. Diabetic nephropathy was defined with microalbuminuria (30-300mg/24hrs), urinary excretion or macroalbuminuria. Diabetic neuropathy was defined as clinical symptoms of hyperesthesia/paraesthesia/motor weakness or polyradiculopathy.[12,13] Cardiovascular complications were considered present if the patient had an ischemic history or electrocardiographic signal ischemia, such as T waves spiking before ST elevation perturbations. CVD was diagnosed based on the presence of either transient ischemic attack or stroke. The peripheral arterial disease was diagnosed with a plaque on the carotid or lower limb arteries wall using ultrasonography. Diabetic Retinopathy, Diabetic Neuropathy and Diabetic peripheral Neuropathy were considered diabetic microvascular complications. In contrast, cardiovascular heart disease related to diabetes, Cerebrovascular Disease and Peripheral Artery diseases were considered diabetic macrovascular complications.[14] The demographic details were collected. Height, weight and Body Mass Index (BMI); weight(kg)/height(m^2) were measured. Detailed clinical history was obtained. A history of comorbid conditions was documented. Duration of diabetes and history of diabetes-related complications were taken. Patients were asked for dietary preferences, gastrointestinal disorders (i.e., acid peptic disease, gastro-oesophagal reflux disease, altered bowel habits) and history of blood loss. Treatment history and list of medications used by patients were recorded. Patients were also asked about using Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), corti-costeroids, anti-platelets, anticoagulants, proton pump inhibitors and antacids. Patients were then investigated for the presence of anaemia. Complete blood counts (CBC) were obtained, including red cell indices, white cell indices, platelet, Total lymphocyte count (TLC), HbA1c, and Plasma Glucose Fasting were recorded. Anaemia was diagnosed based on WHO criteria. Those with iron deficiency were further inves-tigated for the source of blood loss. Urea and creatinine levels were obtained, and a urine routine examination was performed for albuminuria. ECG was done for all patients. Anaemia was defined as Hemoglobin <13 g/dl in males and <12g/dL in females, as recommended by the WHO. The cut-off values for TLC were 4-11x10^3/mm, platelets were 140-440x10^3/mm and Mean Platelet Volume as 9.4-12.3fl.[15]

Data were analyzed using version 21 of the Statistical Package for Social Sciences (SPSS). Means were estimated and presented as Mean±SD. Analysis of variance technique was applied to see the significance level (α=0.05). Means were compared through the Least Significance Difference Test. Logistic regression analysis was applied to examine the association of complications with variables.

RESULTS

A total of 200 patients were analyzed in this study. Ninety-nine patients (49.5%) were males, and 101 (50.5%) were females in this study. The results showed that the systolic and diastolic blood pressure was higher in patients with diabetes along with anaemia and patients with diabetes without anaemia in comparison to the other groups. The BMI was highest in the diabetes with Anaemia Group, i.e. 27.16±1.99 (Table-I). In patients with diabetes and anaemia, TLC (12.16±2.00µL) and MPV (10.62±1.25µL) were slightly higher (P>0.05) in comparison to the other groups and control group (Table-II). The average haemoglobin was 9.50±1.40 (g/dL) for patients with diabetes along with anaemia and 9.55±1.20 (g/dL) for patients with anaemia having no diabetes respectively. The creatinine levels recorded in patients with diabetes along with anaemia were significantly higher at 1.70±0.79(mg/dL) when compared to the other groups. The mean systolic and diastolic blood pressure was higher in patients with microvascular and macrovascular complications compared to the control.

Table-I: Comparison of Hematological Indices in the Study Groups (n=200)

Parameters	Groups				*p*-value
	Group-1: Anaemia Without Diabetes	Group-2: Diabetes with Anaemia	Group-3: Diabetes without Anaemia	Group-4: Healthy Control	
	(n=50)	(n=50)	(n=50)	(n=50)	
Age (years)	45.66±9.57	44.22±8.41	50.24±7.32	45.32±11.15	0.007
Body Mass Index	26.10±4.52	27.16±1.99	26.75±2.18	26.20±4.70	0.412
Systolic BP (mmHg)	130.22±18.52	137.50±13.48	135.12±12.43	128.00±17.11	0.009
Diastolic BP (mmHg)	84.60±10.83	85.00±6.06	85.80±4.99	82.60±8.94	0.234
Plasma Glucose Fasting (mg/dL)	101.74±7.83	157.60±30.26	142.78±19.72	98.38±7.50	<0.001
HbA1c (%)	6.32±0.72	7.93±0.63	7.87±0.67	5.91±0.57	<0.001
Hb (g/dL)	9.55±1.20	9.50±1.40	13.76±1.05	13.74±1.28	<0.001
Total Lymphocyte Count (µL)	10.67±1.58	12.16±2.00	10.94±2.01	9.96±1.34	<0.001
Platelets (µL)	259.00±50.29	286.76±60.49	284.32±44.54	261.94±38.19	0.005
Mean Platelet Volume (µL)	10.25±0.74	10.62±1.25	10.40±0.99	10.56±0.79	0.230
Creatinine (mg/dL)	1.49±0.81	1.70±0.79	1.39±0.65	1.14±0.43	0.001

Table-II: Inter-Group Comparison of Hematological Indices (n=200)

Parameters	Group-1 vs Group-2	Group-1 vs Group-3	Group-1 vs Group-4	Group-2 vs Group-3	Group-2 vs Group-4	Group-3 vs Group-4
Age (years)	0.435	0.013	0.853	0.001	0.551	0.008
Body Mass Index	0.139	0.363	0.886	0.567	0.181	0.443
Systolic BP (mmHg)	0.020	0.117	0.477	0.446	0.002	0.023
Diastolic BP (mmHg)	0.803	0.456	0.215	0.619	0.137	0.048
Plasma glucose fasting (mg/dL)	<0.001	<0.001	0.374	0.001	<0.001	<0.001
HbA1c (%)	<0.001	<0.001	0.001	0.645	<0.001	<0.001
Hb (g/dL)	0.840	<0.001	<0.001	<0.001	<0.001	0.935
Total Lymphocyte count (µL)	<0.001	0.452	0.045	0.006	<0.001	0.006
Platelets (µL)	0.005	0.010	0.764	0.803	0.012	0.023
Mean Platelet Volume (µL)	0.059	0.431	0.116	0.268	0.748	0.431
Creatinine (mg/dL)	0.121	0.486	0.013	0.025	0.0001	0.073

The mean recorded systolic blood pressure was 143.47±11.70(mmHg), and diastolic blood pressure was 88.54±7.09(mmHg) in patients with microvascular complications. The mean plasma glucose fasting levels were higher in patients with microvascular and macrovascular complications when compared with patients without these complications. It was observed that the mean TLC was higher with both macro-vascular and microvascular complications at 12.21± 1.92(µL). It was observed that percentages of micro-vascular (50%) and macrovascular (47.8%) complica-tions were highest in people with diabetes with anaemia and lowest in the healthy control group, 11.1% and 13.4 %, respectively (Table-III & IV).

DISCUSSION

This study was conducted to assess the associa-tion of haematological parameters in type 2 diabetes mellitus patients in Ethiopia, and it demons-trated that the patients have significantly higher MPV, Platelet Distribution Width Levels, absolute lymphocyte count, and absolute neutrophil count, TLC, Red Cell Distribution Width and BMI as compared to healthy controls.

In this study, the increased WBC indices observed in the Type-2 DM group compared with the control group might be due to the high oxidative stress induced by the elevated levels of hyperglycemia. Thus, WBC might be activated by advanced glycation end products and cytokines in hyperglycemia.[16] These results follow various studies that have shown higher vascular complications in patients with diabetes mellitus as compared to the healthy control group due to a large number of circulating platelets in diabetes. In diabetes patients, small vascular bleeds might be present due to the rupture of thrombotic plaques causing bone marrow stimulation to recruit large hyperactive platelets.[17,18]

The main aim of this study was to assess the complications in patients with diabetes mellitus and the correlation of anaemia with these complications. In this study, it was observed that the group of patients having diabetes with anaemia had a significantly higher percentage of macro and microvascular complications as compared to the other groups. It was seen that 50.0% of patients with diabetes with anaemia had microvascular complications, and 47.8% had

Table-III: Comparison of Microvascular Complications (n=200)

Factors	Study Parameter		Univariate Logistic Regression			Multivariate Logistic Regression		
	Present	Absent	*p*-value	Un-adjusted OR	95%CI for OR	*p*-value	Adjusted OR	95% CI for OR
Group			0.001			0.744		
Group-1	17(23.6)	33(25.8)	0.041	2.705	1.040-7.036	0.520	0.335	0.012-9.379
Group-2	36(50.0)	14(10.9)	0.001	13.500	5.087-385.830	0.663	0.446	0.012-16.722
Group-3	11(15.3)	39(30.5)	0.446	1.481	0.540-4.064	0.500	0.299	0.009-10.002
Group-4	8(11.1)	42(32.8)	-	-	-	-	-	-
Gender	-	-	-	-	-	-	-	-
Male	60(46.9)	39(54.2)	0.323	0.747	0.418-1.332	0.846	1.172	0.236-5.807
Female	68(53.1)	33(45.8)	-	-	-	-	-	-
Age (Mean±SD)	48.83±7.58	44.97±10.10	0.006	1.045	1.013-1.079	0.165	0.930	0.840-1.030
BMI (Mean±SD)	27.01±2.80	26.29±3.94	0.182	1.057	0.974-1.147	0.518	0.928	0.740-1.164
Systolic BP (Mean±SD)	143.47±11.70	126.66±14.77	0.001	1.092	1.063-1.123	0.105	1.070	0.986-1.160
Diastolic BP (Mean±SD)	88.54±7.09	82.23±7.71	0.001	1.133	1.077-1.193	0.116	1.114	0.974-1.275
Gluco Fasting(Mean±SD)	143.64±34.94	114.71±24.45	0.001	1.033	1.021-1.045	0.179	1.037	0.984-1.093
HbA1c (Mean±SD)	7.56±0.92	6.70±1.10	0.001	2.192	1.609-2.986	0.686	0.756	0.195-2.936
Hb (Mean±SD)	10.48±2.21	12.29±2.34	0.001	0.717	0.626-0.821	0.180	0.585	0.267-1.282
TLC (Mean±SD)	12.21±1.92	10.21±1.50	0.001	1.942	1.578-2.39	0.000	2.786	1.757-4.418
Platelets (Mean±SD)	270.81±54.34	274.24±48.08	0.642	0.999	0.993-1.004	0.020	0.980	0.964-0.997
MPV (Mean±SD)	10.40±0.99	10.49±0.95	0.528	0.906	0.667-1.231	0.228	0.578	0.237-1.408
Creatinine (Mean±SD)	2.03±0.84	1.09±0.29	0.001	26.991	8.552-.85.186	0.000	12.848	3.858-42.785

Table-IV: Comparison of Macrovascular Complications (n=200)

Factors	Study Parameter		Univariate Logistic Regression			Multivariate Logistic Regression		
	Absent	Present	*p*-value	Un-Adjusted OR	95% CI for OR	*p*-value	Adjusted OR	95% CI for OR
Group			0.163			0.163		
Group-1	41 (30.8)	9 (13.4)	0.923	0.861	0.360-2.774	0.923	0.861	0.042-17.794
Group-2	18 (13.5)	32 (47.8)	0.808	1.584	3.214-20.406	0.808	1.584	0.039-64.738
Group-3	33 (24.8)	17 (25.4)	0.182	0.093	0.927-5.942	0.182	0.093	0.003-3.050
Group-4	41 (30.8)	9 (13.4)	-	-	-	-	-	-
Gender								
Male	53 (39.8)	46 (68.7)	0.289	2.232	1.775-6.159	0.289	2.232	0.507-9.832
Female	80 (60.2)	21 (31.3)	-	-	-	-	-	-
Age (Mean±SD)	48.83±7.58	44.97±10.10	0.001	1.185	1.087-1.180	0.001	1.185	1.073-1.308
BMI (Mean±SD)	27.01±2.80	26.29±3.94	0.292	1.106	1.133-1.432	0.292	1.106	0.917-1.334
Systolic BP (Mean±SD)	143.47±11.70	126.66±14.77	0.089	1.072	1.048-1.101	0.089	1.072	0.990-1.161
Diastolic BP (Mean±SD)	88.54±7.09	82.23±7.71	0.037	0.886	1.024-1.111	0.037	0.886	0.790-0.993
Glucose Fasting (Mean±SD)	143.64±34.94	114.71±24.45	0.410	1.020	1.027-1.054	0.410	1.020	0.973-1.069
HbA1c (Mean±SD)	7.56±0.92	6.70±1.10	0.008	6.588	2.396-5.255	0.008	6.588	1.631-26.606
Hb (Mean±SD)	10.48±2.21	12.29±2.34	0.584	0.823	0.810-1.032	0.584	0.823	0.410-1.651
TLC (Mean±SD)	12.21±1.92	10.21±1.50	0.559	1.097	1.334-1.910	0.559	1.097	0.803-1.499
Platelets (Mean±SD)	270.81±54.34	274.24±48.08	0.156	1.010	1.009-1.023	0.156	1.010	0.996-1.024
MPV (Mean±SD)	10.40±0.99	10.49±0.95	0.010	3.131	1.712-3.558	0.010	3.131	1.314-7.460
Creatinine (Mean±SD)	2.03±0.84	1.09±0.29	0.001	0.173	0.771-1.730	0.001	0.173	0.062-0.483

macrovascular complications. However, patients with diabetes without anaemia showed only 15.3% microvascular complications and 25.4% macrovascular complications, respectively.

In the present study, the percentage of macrovascular diseases in patients with diabetes and anaemia was much higher than the patients without anaemia. Furthermore, anaemia was associated with macrovascular disease by univariate logistic regression analysis, indicating that anaemia increased the risk of developing the macrovascular disease in patients with Type-2 Diabetes Mellitus.

Another important finding of the study was that a high frequency of nephropathy was noticed in the diabetic and anaemic group with high creatinine levels, i.e., 2.03(mg/dL), compared to the other groups.

This finding was probably because anaemia decreases oxygen delivery to the kidney tissue, causing a detrimental hypoxic state. In a study of anaemia patients with diabetes, EPO-stimulated increases in Hemoglobin in these patients were associated with slower progression of nephropathy.[19]

It was also noticed in the present study that total white cell count, Body Mass Indices, and mean platelet volume were significantly higher among patients with diabetes as compared to healthy controls. This was a consequence of an unhealthy lifestyle and low glycemic control.

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CONCLUSION

Patients with type 2 Diabetes Mellitus should be evaluated and treated for anaemia routinely to prevent complications

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

FAR & HMR: Data acquisition, critical review, approval of the final version to be published.

MI & AM: Conception, study design, drafting the manuscript, approval of the final version to be published.

MA & NK: Data analysis, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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