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Evalu ation of Thrombotic Markers in Diabetic Septic Foot: A Study of Coagulation and Hematological Parameters in Khartoum State

Anwar S. ALhussan[1]*, Sahar Elbagir[2], Sarah O. Alsawmhi[1], Hassn Pyar[1,3]*

[1]College of Medicine and Health Science, Seiyun University, Yemen
[2]Faculty of Medical Laboratories, University of Medical Sciences and Technology, Khartoum, Sudan
[3]Faculty of Environmental Science and Marine Biology, Hadhramout University, Yemen.
*Corresponding author: anwaralhussain2020@gmail.com, *hassanpyar@yahoo.com

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Abstract: Diabetes mellitus is a globally prevalent chronic disease. It is characterized by a metabolic dysregulation in insulin secretion, resulting in persistent hyperglycemia. Uncontrolled HbA1c levels may lead to various complications, including diabetic Septic foot (DSF), which in severe cases can progress to lower limb amputation. Therefore, this study aimed to evaluate coagulation profiles and hematological parameters as potential thrombotic and inflammatory markers associated with diabetic foot infections. Preventive measures, patient education, and proper diabetic foot care remain the cornerstone strategies for reducing the risk and progression of such complications. The Total of 120 participants were divided into three groups by 40 patients, diabetic septic foot, without foot complications and healthy individuals (control). Coagulation and hematological parameters were assessed. Our results PT, INR, MCV, MCH, and PDW were significantly elevated in the DSF group with control group. Males were more affected than females. A moderate positive correlation was observed between HbA1c and both RBC count and PDW. Patients with diabetic septic foot exhibit significantly higher coagulation and hematological markers, particularly PT, INR, MCV, MCH, and PDW. These markers, along with HbA1c levels, may serve as potential indicators of thrombotic risk in DSF patients, especially among males.

Keywords: diabetic septic foot, diabetes mellitus, coagulation profile, hematological parameters, thrombotic markers

Abstrak: *Diabetes mellitus adalah penyakit kronis yang prevalensinya tinggi secara global. Penyakit ini ditandai oleh disregulasi metabolik pada sekresi insulin yang menyebabkan hiperglikemia persisten. Kadar HbA1c yang tidak terkontrol dapat menyebabkan berbagai komplikasi, termasuk kaki diabetik septik (DSF), yang pada kondisi berat dapat berkembang menjadi amputasi ekstremitas bawah. Oleh karena itu, penelitian ini bertujuan untuk mengevaluasi profil koagulasi dan parameter hematologi sebagai penanda potensial trombotik dan inflamasi yang berhubungan dengan infeksi kaki diabetik. Upaya pencegahan, edukasi pasien, dan perawatan kaki diabetik yang tepat tetap menjadi strategi utama untuk mengurangi risiko dan perkembangan komplikasi tersebut. Sebanyak 120 peserta dibagi menjadi tiga kelompok masing-masing terdiri atas 40 pasien, yaitu kelompok kaki diabetes septik, kelompok tanpa komplikasi kaki, dan kelompok individu sehat (kontrol). Parameter koagulasi dan hematologi dianalisis.. Hasil penelitian menunjukkan bahwa PT, INR, MCV, MCH, dan PDW secara signifikan lebih tinggi pada kelompok DSF dibandingkan dengan kelompok kontrol. Laki-laki lebih banyak terpengaruh dibandingkan perempuan. Korelasi positif sedang diamati antara HbA1c dan baik hitung sel darah merah (RBC) maupun PDW. Pasien dengan kaki diabetik septik menunjukkan penanda koagulasi dan hematologi yang secara signifikan lebih tinggi, terutama PT, INR, MCV, MCH, dan PDW. Penanda-penanda ini, bersama dengan tingkat HbA1c, berpotensi menjadi indikator risiko trombosis pada pasien DSF, terutama di kalangan laki-laki..*

Kata kunci: *kaki diabetik septik, diabetes mellitus, profil koagulasi, parameter hematologi, penanda trombosis*

INTRODUCTION

Diabetes is a serious, chronic disease that occurs either when the pancreas does not produce enough insulin (a hormone that regulates blood sugar, or glucose), or when the body cannot effectively use the insulin, it produces. Diabetes is an important public health problem. Raised blood glucose, a common effect of uncontrolled diabetes, may, over time, lead to serious damage to the heart, blood vessels, eyes, kidneys and nerves. More than 400 million people

live with diabetes. diabetes can damage the heart, blood vessels, eyes, kidneys and nerves, and increase the risk of heart disease and stroke. Such damage can result in reduced blood flow, which – combined with nerve damage (neuropathy) in the feet – increases the chance of foot ulcers, infection and the eventual need for limb amputation (WHO 2016).

Diabetes mellitus can be divided into two broad categories type 1, insulin -dependent diabetes mellitus (IDDM) and type 2, non-insulin-dependent diabetes mellitus (IDDM). In 1995, the international expert committee was given another category by the adoption of arabic numerals instead of roman numerals. Classification of diabetes mellitus type 1 DM the pathogenesis was B-cell destruction, absolute insulin deficiency and autoantibodies (Ekoé *et al* 2008). Type 1 diabetes is a chronic autoimmune disease characterized by insulin deficiency and resultant hyperglycemia. Knowledge of type 1 diabetes increased, resulting in a broad understanding about many aspects of the disease, including its genetics, epidemiology, immune and β-cell phenotypes, and disease burden. Interventions to preserve β cells have been tested, and several methods to improve clinical disease management have been assessed (DiMeglio *et al*. 2018).

Since 1980, the number of people with type 2 diabetes mellitus (T2DM) has tripled in just three decades, impacting 422 million adults in 2016. It continues to be the primary risk factor for cardiovascular illnesses globally and one of the most prevalent chronic noncommunicable diseases (Phasha *et al.* 2019).

In Type 2 DM, the pathogenesis was insulin resistance with an insulin secretory defect and relative insulin deficiency. Gestational DM (GDM) is the pathogenesis wear glucose intolerance during pregnancy metabolic and hormonal changes. the others classifications the associated with secondary conditions genetic defects of B-cells and pancreatic disease, endocrine disease, drug or chemical induced, insulin receptor abnormalities. Septic foot is a significant complication of diabetes mellitus and often precedes lower-extremity amputation. The most frequent underlying etiologies are neuropathy, trauma, deformity, high plantar pressures, and peripheral arterial disease (Frykberg 2002).

The primary role of platelets is to oversee thrombosis and hemostasis. Normally inactive, platelets engage with the subendothelial matrix to manage adhesion, activation, and aggregation when vascular injury occurs. This process subsequently initiates the coagulation cascade, leading to thrombus formation. Additionally, platelets contain highly organized pro- and anti-angiogenic proteins that are actively stored within α-granules. (Hoffbrand & Moss 2011; Walsh *et al*. 2015).

Endogenous vascular-protective and antithrombotic substances are released by peripheral arteries under healthy conditions (Vanhoutte *et al*. 2016). Vasoactive mediators, which control platelet reactivity and vascular tone and hence prevent thrombosis, are actively synthesised by endothelial cells. By inducing pro-thrombotic reactions in the arteries, platelet activation, aggregation, and vasoconstriction, atherosclerosis upsets homeostasis and promotes thrombosis. These events ultimately result in symptomatic lumen limitation or total occlusion (Habib *et al.* 2020).

Factor XII (FXII) is activated upon contact with negatively charged surfaces. Early studies showed that substances such as dextran sulfate and silica could induce its autoactivation. Later, it was shown that physiological surfaces such as RNA, DNA, and polyphosphates play a similar role, and activated platelet membranes may also provide a suitable surface for this activation. FXII is a key component of the contact system, along with prekallikrein (PKK) and high-molecular-weight kininogen (HK). Upon contact, FXII is partially activated to produce FXIIa, which in turn activates PKK to α-kallikrein (αKK). This enzyme reactivates FXII, creating a positive feedback loop that promotes coagulation. FXII activation is 30 times more efficient than autoactivation. HK also acts as a cofactor that increases this activity, and it is believed that the non-fissile form of FXII has mild activity that can also activate PKK, especially in the presence of polyphosphate (Grover & Mackman 2019).

Atherothrombosis in type 2 diabetes mellitus (T2DM) is largely caused by platelet activation, and even in the preclinical and early stages of the disease, patients with impaired glucose metabolism have been shown to have increased in vivo platelet activation with enhanced thromboxane (TX) biosynthesis (Santilli *et al.* 2015).

One of the leading causes of morbidity and hospitalisation among diabetic patients is diabetic foot, a common and dangerous limb-threatening condition. Approximately 4% to 10% of diabetics get foot ulcers (Boulton *et al.* 2008) One There have been reports of an 8–21% lower extremity amputation (LEA) rate after foot ulceration. 2, 3 Diabetic foot illness has a substantial psychological impact in addition to a substantial financial burden. Foot ulcers are frequently caused by peripheral vascular disease, neuropathy intensity, structural foot deformity, concurrent infection, high plantar pressure, poor glycaemic control, diabetes duration, male gender, and the presence of additional micro and macrovascular problems (Shareef *et al.* 2019).

Diabetic septic foot (DSF) is one of many complications that accompany fifteen percent of patients with diabetes mellitus. Amputation is recurrently the final event of a serious diabetic septic foot. The prone of DSF to frequent chronic infection affects the psychological health of the patient. Disease of the peripheral nerves is known in diabetic patients, and the management relies upon which nerve(s) is/are predisposed, this may include the

peripheral nerves, the cranial and the autonomic nerves, leading to numbness in the legs and may promote ulcer formation. When this problem is untreated, gangrene and amputation of the infected leg are provoked. Diabetic nephropathy and retinopathy were associated with anemia for some time (Salman *et al.* 2017).

Globally, diabetes mellitus is rising the prevalence is steadily increasing everywhere, mostly in the middle-income countries. The prevalence in the rural Sudan population is about 3.9%, which in turn leads to an increase in the rate of admission. Diabetic septic foot (DSF) is a common complication of diabetes, with an estimated that every 30 seconds a lower limb is lost somewhere as a consequence of the complication of DSF. Eighty percent of diabetic mortality rates is due to thrombotic events. While 75% of these mortalities belonged to cardiovascular problems, and 25% remainder due to peripheral vascular events as well as cerebrovascular complications (Bashir & Ali 2018).

The incidence of diabetes mellitus is increasing across Sub-Saharan Africa (SSA); a parallel increase in the number of septic feet in these populations has been documented. Although most published reports from SSA suggest that septic foot generally is associated with underlying peripheral neuropathy, recent data establish that peripheral arterial diseases are playing a more substantial role in ulcer causation than was previously thought. Diabetic foot infections usually begin in ulcers that are sequelae of existing neuropathy, macro-vascular disease, or certain metabolic disturbances. Such infections are the immediate cause of foot or leg amputation in 25–50 percent of patients with diabetes and may result in death. Gangrene and infection appear to be the most commonly cited indications for foot amputation in patients with diabetes. The most important intervention for the prevention of diabetic foot complication is the education of the patient about proper foot care (Boulton *et al*. 2006). Diabetic septic foot is a major health problem because it leads to long been a prevalent disease with complications such as diabetic retinopathy, kidney failure, and cardiovascular disease that reduce the life expectancy of patients. investigate the characteristics of thrombosis markers in diabetic septic foot through patient-specific predictive simulations that are informed by companion experiments. The aim of this study was to compare the coagulation profile (PT, APTT, platelet count) and hematological parameters of diabetic patients with those of healthy individuals, as well as to compare diabetic patients with and without diabetic septic foot. Finally, a correlation between coagulation profiles and diabetic septic foot HbA1c was to be established.

MATERIALS AND METHOD

Materials

The materials and instruments used in this study included A laboratory centrifuge, a water bath kept at 37 °C, micropipettes and disposable tips, standard laboratory consumables, a thromboplastin reagent, calcium chloride reagent, EDTA vacutainer tubes for hematological analysis, an automated hematology analyzer (Sysmex XP-300, Sysmex Corporation, Japan) for complete blood count (CBC) analysis, and commercial reagents for prothrombin time (PTT) and activated partial thromboplastin time (aPTT) assays were among the tools and materials used in this study. The medical records of the patients provided the HbA1c data.

Study design

This study was designed as case and control study.

Study area

The Study was conducted in Zenam Specialized Center, yastapshiroon Hospital and Al Muallem Medical City Hospital in Khartoum states.

Study population

The study was carried out in Forty (40) patients with diabetic septic foot and Forty (40) without diabetic septic foot as cases and Forty (40) Health person as control.

Inclusion Criteria:

Aged more than 18 years Diabetes irrespective of duration of the disease Ability and willingness will be participate based on information given to patient and to health facility.

Exclusion Criteria

The anticoagulant drugs and anemia and severe illnesses will be excluded.

Sample Size

This study included 120 samples and forty (40) samples from these samples were collected from diabetic septic foot patients, forty (40) samples from people without diabetic foot as cases and forty (40) samples from Healthy people as a control group.

The sample size was recorded in this study according to Equation (1)

$$n = \frac{z^2 pq}{d^2} \ldots (1)$$

N = sample size
Z = strength (1.96)
P = prevalence of disease
D = standing deviation (0.05)
X = 1 p

Sample Technique

Simple Random Selection was used as the sample technique.

Data collection

The laboratory data were obtained from reports generated by the Sysmex XP-300 device, which measured hematology parameters including RBC, HB, PCV, MCV, MCH, MCHC, RDW, WBC, and platelet count. For this purpose, 5 ml of blood was drawn from each patient and placed into a new test tube for analysis. Additionally, secondary data were gathered through interviews using a questionnaire that collected information such as age, gender, HbA1c control status, duration of illness, use of antibiotics, use of anticoagulant medications, presence of diabetes complications, and hypertension.

Blood Collection Method

Five milliliters of the blood were extracted and put into a tube containing 3.2% sodium citrate. After that, the sample was centrifuged right away to separate the serum.

Prothrombin Time (PT)

Prothrombin Time (PT) is a coagulation test that assesses the extrinsic and common pathways of blood clotting by measuring the time required for a fibrin clot to form in citrated plasma upon addition of tissue thromboplastin and calcium, which triggers stage 2 of the coagulation cascade in the presence of factor VII; since factors XII, XI, VIII, and platelets are bypassed, the test primarily depends on the activity of factors I, II, V, VII, and X, with deficiencies in any of these factors leading to prolongation of clot formation time. The procedure involves collecting 2.7 mL of venous blood in a 3.2% trisodium citrate vacutainer, followed by centrifugation at 4000 rpm for 15 minutes to obtain plasma. The water bath and PT reagent are pre-warmed to 37°C, after which 0.1 mL of the test plasma is pipetted into a test tube, incubated, and then 0.2 mL of pre-warmed thromboplastin reagent is added. A stopwatch is started simultaneously, and the time taken for clot formation is recorded once a solid clot appears, with the entire process ensuring standardized conditions for accurate measurement of coagulation function (Ciesla 2018).

Activated partial thromboplastin time (APTT)

The activated partial thromboplastin time (APTT) is a coagulation test based on the principle that sodium citrate, an anticoagulant, binds calcium in whole blood to prevent coagulation, resulting in plasma that contains all intrinsic coagulation factors except calcium and platelets; when calcium and a phospholipid substitute for platelets, along with an activator, are added to the plasma, the time required for clot formation, known as PTT, is measured. The procedure involves collecting 2.7 mL of venous blood in a 3.2% trisodium citrate vacutainer, followed by centrifugation at 4000 rpm for 15 minutes to obtain plasma. The water bath and calcium chloride reagent are pre-warmed to 37°C, with the calcium chloride warmed for at least 10 minutes. Then, 0.1 mL of test plasma and 0.1 mL of aPTT reagent are placed into a reaction tube and incubated together at 37°C for exactly 3 minutes. Subsequently, 0.1 mL of warmed calcium chloride reagent is added to the mixture, and the stopwatch is started immediately while mixing the tube thoroughly. The clotting time is recorded when a clot forms, typically within 20 seconds after calcium addition, providing a measure of the intrinsic pathway of coagulation (Bain *et al.* 2016).

Hematology Analyzer Device: Complete Blood Counts to Cell (CBC)

For each blood sample, the following hematimetric parameters are assessed: red blood cell count (RBC), hematocrit (PCV), hemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), white blood cell count (WBC), differential count, platelet count, and platelet indices.

Principle of Hematology Analyzers— Sysmex XP-300

The Sysmex XP-300 (XP-300) is a state-of-the-art, fully automated hematology analyzer engineered to deliver complete blood counts (CBC) with a 3-part differential. The process for determining the full blood count using the Sysmex XP-300 was carried out as follows: EDTA blood samples were first placed in a blood mixer for five minutes to ensure proper mixing. Subsequently, the samples were loaded into the analyzer, where blood cells were automatically counted via an integrated probe. Within approximately one minute, the blood cell count results appeared on the machine's-colored LCD screen (Dacie & Lewis 1999).

Hydrodynamic Focusing (Dc) Detection Method

Hydrodynamic Focusing (DC Detection): Within the detector, the sample nozzle is strategically positioned in front of the aperture and aligned with its center (Cahn *et al.* 2016). When the diluted sample is propelled from the sample nozzle into the conical chamber, it is enveloped by the front sheath reagent and flows through the center of the aperture.

Hemoglobin method

Most automated counters determine hemoglobin (Hb) levels using a modified version of the manual Hemoglobin Cyanide (HiCN) method. This involves diluting blood in a solution containing potassium cyanide and potassium ferricyanide, which convert hemoglobin, methemoglobin (Hi), and carboxyhemoglobin (HbCO) into HiCN. Some

manufacturers have replaced cyanide with non-toxic chemicals such as sodium lauryl sulfate or imidazole. For example, the Sysmex XP-300 employs a cyanide-free method using sodium lauryl sulfate (SLS). In this method, the reagent lyses red and white blood cells in the sample. The resulting hemoglobin concentration is then measured by a photodetector, with absorbance directly proportional to the hemoglobin level in the sample (Ebrahim *et al.* 2021).

Red blood cell count

Blood cells, including red blood cells, can be quickly and accurately counted using electronic systems that employ impedance or light-scattering technology. This has improved the clinical usefulness of measurements like MCV and MCH compared to manual methods, with counts typically performed on diluted blood using impedance to distinguish between different cell types.

Packed cell volume and Hemoglobin

The RBC count is reflected by the number of pulses generated, and the MCV is indicated by the mean size (height) of these pulses in the RBC histogram. Hematocrit (Hct) can be calculated using Equation (2).

$$\text{Hct (\%)} = \frac{(\text{RBC} \times 10^{12}/\text{L}) \times \text{MCV}}{10} \quad ...(2)$$

Summing the pulse heights also gives the Hct, and the MCV can be derived by dividing Hct by the RBC count. Variations in MCV and PCV may result from cell shape and flexibility, known as the shape factor. In impedance methods, normal cells elongate under shear force, but cells with low hemoglobin (Hb) or rigid membranes deform differently, causing under- or overestimation of MCV. Light scattering methods can also underestimate cell volume in low-Hb cells due to shape and internal reflective properties. When Hb concentration is directly measured via light scatter, it is called Cellular Hemoglobin Concentration Mean (Imoru *et al.* 2020)

Distribution of RCB volume

Automated hematology analyzers produce volume histograms to identify different red cell populations, assess the percentage of microcytes or macrocytes, and flag abnormalities. They also measure RDW, which indicates variability in red cell size, expressed as either standard deviation in femtoliters or coefficient of variation.

Total white cells and Automated differential count

Red blood cells are lysed with a reagent to facilitate white blood cell (WBC) counting using impedance or light scattering methods; thresholds are set to exclude platelets from the WBC count, but white cell clumping (agglutination) can cause falsely low WBC results. Instruments can perform 3- or 5-part WBC differentials on diluted blood where red cells are lysed or transparent; the 3-part count categorizes cells based on volume differences, while 5–7-part counts utilize multiple channels and measurement techniques to analyze additional cell characteristics.

Platelet's count

Platelet count is typically performed on the same diluted whole blood sample used for red blood cell analysis, using impedance or optical methods with specific thresholds to distinguish platelets from red cells and noise; impedance methods set thresholds above 2fL and below 20fL, while optical methods differentiate based on light scatter patterns and pulse area, fitting data to a log-normal distribution. Key platelet indices include MPV, which measures average platelet size and tends to increase as platelet count decreases; PDW, indicating the variability in platelet size or anisocytosis; and plateletcrit, representing the total volume of circulating platelets, calculated as the product of MPV and platelet count. These parameters are largely instrument-specific and may not be directly comparable across different devices. Blood samples are typically collected from veins into EDTA (ethylenediaminetetraacetic acid) tubes because EDTA acts as an anticoagulant by chelating calcium ions, which are essential for clotting. This prevents the blood from clotting and preserves cell components for accurate testing. Automated hematology analyzers such as Sysmex use methods like optical (flow cytometry with light scatter and fluorescence) or impedance techniques (electrical resistance changes as cells pass through an aperture) to precisely measure platelet count and other blood cell parameters. These technologies enable rapid, reliable, and reproducible blood analysis in clinical laboratories (Lippi *et al.* 2019).

Ethical consideration

The study received ethical approval and permission to assess coagulation and hematological parameters in patients with diabetic septic foot ulcers in Khartoum State, 2021. Participation was voluntary, confidential, and posed no risks. The research aimed to evaluate coagulation levels, explore correlations with HbA1c, and examine the effects of demographic factors. Results were promptly shared with patients' doctors, and questionnaires were completed during patients' rest.

RESULT AND DISSCUSION

In this study, a total of 120 participants were enrolled, divided into three groups: 40 patients with diabetic septic foot, 40 diabetic patients without septic foot, and 40 healthy controls. The ages of all participants ranged from 40 to 80 years, with a mean age of 55.6 ± 9.8 years, as shown in Table 1. The results indicated that the mean age in the case group (patients with septic foot) was higher than in the

control groups, with mean ages of 57.45 ± 10.46, 53.90 ± 8.96, and 53.30 ± 6.78 years, respectively. Regarding gender distribution, males outnumbered females in all groups, with counts of 31/9, 23/17, and 26/14 in the control, diabetic without septic foot, and diabetic septic foot groups, respectively.

In this study, the assessment of PT, APTT, platelet count, and hematological parameters in diabetic septic foot (DSF) patients revealed that the mean PT level in DSF patients was significantly higher than in both healthy individuals and diabetic mellitus (DM) patients (13.02 ± 2.42 vs. 11.81 ± 1.14 and 11.61 ± 1.44; $P = 0.00$). Similarly, the mean INR was significantly elevated in DSF patients compared to DM and healthy groups (1.22 ± 0.23 vs. 1.06 ± 0.14 and 1.05 ± 0.20 respectivally; $P = 0.00$). Although the mean APTT was slightly higher in DM patients (33.65 ± 4.88) than in DSF and healthy individuals (32.85 ± 4.48 and 31.65 ± 2.13 respectivally), this difference was not statistically significant (Table 2). When comparing coagulation profiles (PT, INR, APTT, platelet count, and hematological parameters) between DSF and DM groups (Table 3), the results confirmed that DSF patients had significantly prolonged PT and elevated INR compared with DM patients (13.02 ± 2.42 vs. 11.61 ± 1.44; $P = 0.00$ and 1.22 ± 0.23 vs. 1.06 ± 0.14; $P = 0.00$, respectively). However, no significant difference was found in APTT values between the two groups (32.85 ± 4.48 vs. 33.65 ± 4.88). These findings indicate that the mean levels of PT and INR were significantly higher in DSF patients than in the control group, suggesting a state of altered coagulation associated with diabetic foot infection. The present results are consistent with those reported by Gopalakrishna *et al*. (2020) in India, who studied 60 patients with diabetic foot ulcers and 60 diabetic controls without DSF. They found a significantly prolonged PT among DSF cases (16.68 ± 4.2 sec) compared to controls (12.5 ± 1.6 sec; $P = 0.0001$). Conversely, Bashir *et al*. (2018) in Sudan, who examined 57 diabetic patients with septic foot,

Table 1. Demographic Data mean ± SD of age and gender in case and control in DSF (**Mean ± SD)**

Type	**DSF (Case study)**		**DM (Case study)**		**Health person (Control study)**	
Age	**57.45 ± 10.46**		**53.90 ± 8.96**		**53.30 ± 6.78**	
Gender	Male	Female	Male	Female	Male	Female
	6	**4**	**3**	**7**	**1**	**9**

Table 2. Assessment the mean ± SD of PT, APTT, Platelet count and Hematological parameters in healthy, DM and DSF patients

Type	**Group Control Healthy person**	**Group Case DM**	**Group Case DSF**	**p value**
	Mean ± SD	Mean ± SD	Mean ± SD	
PT	11.81 ± 1.14	11.61 ± 1.44	13.02 ± 2.42	0.00
INR	1.05 ± 0.20	1.06 ± 0.14	1.22 ± 0.23	0.00
APTT	31.65 ± 2.13	33.65 ± 4.88	32.85 ± 4.48	0.08
Hb	13.11 ± 1.26	13.67 ± 1.79	13.02 ± 1.72	0.15
RBC	4.65 ± 0.48	5.00 ± 0.69	4.95 ± 0.52	0.01
PCV %	37.66 ± 11.48	41.09 ± 5.56	39.95 ± 3.88	0.13
MCV	86.64 ± 7.09	81.80 ± 5.11	78.21 ± 7.82	0.00
MCH	28.45 ± 2.27	27.50 ± 2.21	26.40 ± 2.40	0.00
MCHC	32.60 ± 1.16	33.24 ± 1.34	32.88 ± 1.48	0.10
RDW-CV	11.83 ± 2.87	13.19 ± 1.60	13.26 ± 1.11	0.00
T-WBC	6.41 ± 1.75	6.23 ± 2.10	6.65 ± 2.79	0.71
LYM	2.65 ± 1.67	2.44 ± 0.72	2.67 ± 1.02	0.64
NEUT	3.39 ± 1.56	3.45 ± 1.75	4.62 ± 1.28	0.38
PLT	286.10 ± 84.65	271.40 ± 51.80	265.68 ± 90.20	0.48
MPV	8.85 ± 0.94	9.76 ± 1.00	9.33 ± 1.09	0.00
Pct-Plat	0.20 ± 0.08	0.23 ± 0.06	1.19 ± 4.39	0.14
PDW-CV	14.14 ± 2.94	12.58 ± 1.71	14.05 ± 3.20	0.02

Table 3. Comparison the coagulation profiles PT, APTT, Platelet count and Hematology parameters between DSF and DM

Type	DSF	DM	p value
	Mean ± SD	Mean ± SD	
PT	13.02 ± 2.42	11.61 ± 1.44	0.00
INR	1.22 ± 0.23	1.06 ± 0.14	0.00
APTT	32.85 ± 4.48	33.65 ± 4.88	0.44
Hb	13.02 ± 1.72	13.67 ± 1.79	0.09
RBC	4.95 ± 0.52	5.00 ± 0.69	0.71
PCV %	39.95 ± 3.88	41.09 ± 5.56	0.29
MCV	78.21 ± 7.82	81.80 ± 5.11	0.01
MCH	26.40 ± 2.40	27.50 ± 2.21	0.03
MCHC	32.88 ± 1.48	33.24 ± 1.24	0.25
RDW-CV	13.26 ± 1.11	13.19 ± 1.60	0.81
T-WBC	6.65 ± 2.79	6.23 ± 2.10	0.44
LYM	2.67 ± 1.02	2.44 ± 0.72	0.25
NEUT	4.62 ± .1.28	3.45 ± 1.75	0.32
PLT	265.68 ± 9.20	271.40 ± 51.80	0.72
MPV	9.33 ± 1.09	9.76 ± 1.0	0.06
Pct-Plat	1.19 ± 4.39	0.23 ± 0.60	0.17
PDW-CV	14.05 ± 3.20	12.58 ± 1.71	0.01

reported a significantly shorter PT in DSF patients compared to controls ($P < 0.009$). Regarding APTT, the current study showed a mild, non-significant reduction in DSF patients compared to the control group. This observation agrees with Gopalakrishnan *et al*. (2020), who found that the mean APTT was 36.2 ± 7.07 sec among DSF cases and 34 ± 7.3 sec among diabetic controls, with no statistically significant difference ($P = 0.24$). In this study, the comparison of hematological parameters between diabetic septic foot (DSF) and diabetic mellitus (DM) patients showed no significant difference in hemoglobin (Hb) levels (13.02 ± 1.72 vs. 13.67 ± 1.79). Similarly, red blood cell (RBC) counts were comparable between the two groups (4.95 ± 0.52 vs. 5.00 ± 0.69), while hematocrit (PCV) levels were slightly lower in DSF patients (39.95 ± 3.88) than in DM patients (41.09 ± 5.56). When comparing all three groups (healthy, DM, and DSF), the study found that Hb levels did not significantly differ among them (13.67 ± 1.79, 13.11 ± 1.26, and 13.02 ± 1.72, respectively). However, the mean RBC count was significantly higher in DM patients compared to DSF and healthy groups (5.00 ± 0.69 vs. 4.95 ± 0.52 and 4.65 ± 0.48; P = 0.01), and PCV followed a similar pattern, being higher in DM patients (41.09 ± 5.56) than in DSF (39.95 ± 3.88) and healthy subjects (37.66 ± 11.48). Red cell indices showed notable differences among the groups. The mean corpuscular volume (MCV) was significantly lower in DSF compared to DM (78.21 ± 7.82 vs. 81.80 ± 5.11; p = 0.01), and both were lower than in healthy individuals (86.64 ± 7.09; $P = 0.00$). Likewise, mean corpuscular hemoglobin (MCH) was significantly reduced in DSF compared to DM (26.40 ± 2.40 vs. 27.50 ± 2.21; p = 0.03) and healthy individuals (28.45 ± 2.27; $P = 0.00$). Although mean corpuscular hemoglobin concentration (MCHC) was slightly higher in DM patients (33.24 ± 1.34) than in DSF (32.88 ± 1.48) and healthy groups (32.60 ± 1.16), this difference was not statistically significant. These findings suggest that DSF patients exhibit a mild decline in red cell indices (MCV and MCH), possibly indicating anemia or iron deficiency. This observation is consistent with the results of Wright *et al*. (2014) in London, who reported decreased Hb, MCV, and MCH in patients with diabetic foot syndrome (DSF), commonly associated with anemia and iron deficiency. Similarly, Cahn *et al*. (2016) in Palestine reported that RBC counts were significantly reduced in diabetic foot patients compared to diabetic patients without complications. In contrast, the present findings differ from those of Isam Noori Salman *et al*. (2017) in Iraq, who found a high incidence of anemia among patients with severe DSF. This discrepancy may be explained by variations in nutritional status, infection severity, and geographical or population characteristics between the studies conducted in Iraq and Sudan. Regarding other hematological parameters, red cell distribution width (RDW) was significantly higher in DSF patients (13.26 ± 1.11) compared to DM (13.19 ± 1.60) and healthy groups (11.83 ± 2.87; p = 0.00). However, no significant differences were observed in mean WBC

count (6.65 ± 2.79, 6.41 ± 1.75, and 6.23 ± 2.10 for DSF, DM, and healthy groups, respectively) or in lymphocyte counts (2.67 ± 1.02, 2.65 ± 1.67, and 2.44 ± 0.72). Neutrophil counts were significantly higher in DSF patients compared to DM and healthy individuals (4.62 ± 1.28 vs. 3.45 ± 1.75 and 3.39 ± 1.56), reflecting an inflammatory response to infection. Nevertheless, the overall WBC, lymphocyte, and RDW levels did not differ significantly between cases and controls. These findings contrast with the study by Goksugur *et al*. (2020)**,** who reported that neutrophil, lymphocyte, and RDW levels were significantly elevated in 250 adult patients with diabetic septic foot, suggesting that these parameters could serve as useful predictors for diagnosis and follow-up of DSF. The disparity may be due to differences in sample size, patient age, and the severity of infection among study populations (Arican *et al*. 2020). Platelet counts were higher in healthy individuals compared to DM and DSF patients (286.10 ± 84.65 vs. 271.40 ± 51.80 and 265.68 ± 90.20). However, the difference between the DSF and DM groups was not statistically significant (265.68 ± 90.20 vs. 271.40 ± 51.80). Mean platelet volume (MPV) was significantly higher in DM patients than in DSF and healthy groups (9.76 ± 1.00 vs. 9.33 ± 1.09 and 8.85 ± 0.94; p = 0.00), while no significant difference was observed between DSF and DM patients (9.33 ± 1.09 vs. 9.76 ± 1.00). Plateletcrit (PCT) was markedly elevated in DSF patients compared to both DM and healthy individuals (1.19 ± 4.39 vs. 0.23 ± 0.06 and 0.20 ± 0.08), showing a significant rise between DSF and DM groups. In contrast, platelet distribution width (PDW) was significantly higher in healthy individuals than in DSF and DM patients (14.14 ± 2.94 vs. 14.05 ± 3.20 and 12.58 ± 1.71; P = 0.02). Nonetheless, PDW was notably increased in DSF patients compared to DM patients (14.05 ± 3.20 vs. 12.58 ± 1.71; P = 0.01). According to the current findings, diabetic and DSF patients exhibited lower platelet counts, MPV, PDW, and PCT compared to healthy controls. In contrast, a study by Mardia et al. (2018) reported higher levels of platelet count, MPV, PDW, and PCT in 40 individuals with diabetic foot syndrome compared to controls. These discrepancies may be attributed to geographical variations and differences in sample size among study population.

Correlation Between HbA1c Levels and Coagulation Profiles in Diabetic Septic Foot

The current study observed no significant association between HbA1c levels and coagulation parameters (PT, APTT, and platelet count) in patients with diabetic septic foot (DSF) (Figure 1). Additionally, there was no correlation identified between RBC count and HbA1c in DSF patients.

Correlation of HbA1c with Hematological Parameters in Diabetic Septic Foot Patients

A moderate positive correlation was identified between HbA1c and RBC count (r = 0.356, P = 0.02), as well as between HbA1c and PDW (r = 0.380, P = 0.01). Additionally, HbA1c levels were significantly elevated in DSF patients compared to healthy controls (Figure 2). There was also a notable correlation between PDW and HbA1c in DSF patients.

This finding is consistent with the results of Farooque *et al.* (2020), who investigated 88 patients with diabetic foot syndrome (DFS) and demonstrated a significant association between elevated HbA1c levels and the occurrence of DFS. These results suggest that monitoring HbA1c may serve as a useful indicator for predicting the development of diabetic foot complications (Armstrong *et al.* 2017). Based on. the current findings, it is recommended that individuals with diabetic septic foot undergo regular monitoring of HbA1c, complete blood count, peripheral blood film, and coagulation tests.

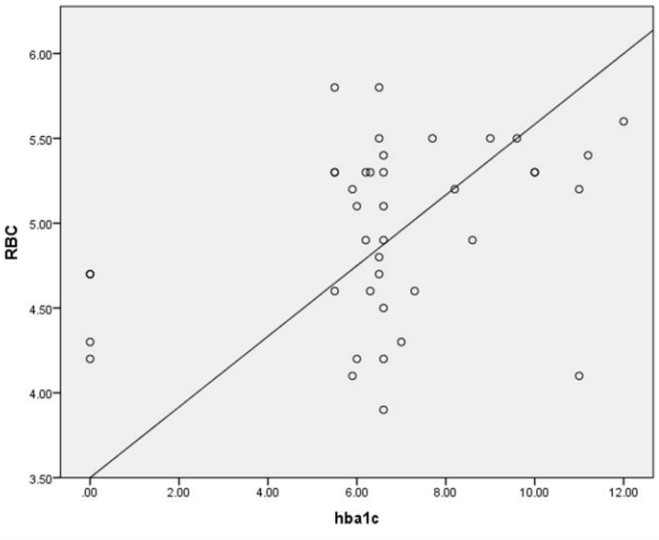

Figure 1. RBC and DSF HbA1c have a somewhat positive connection that is significant at the 0.05 level

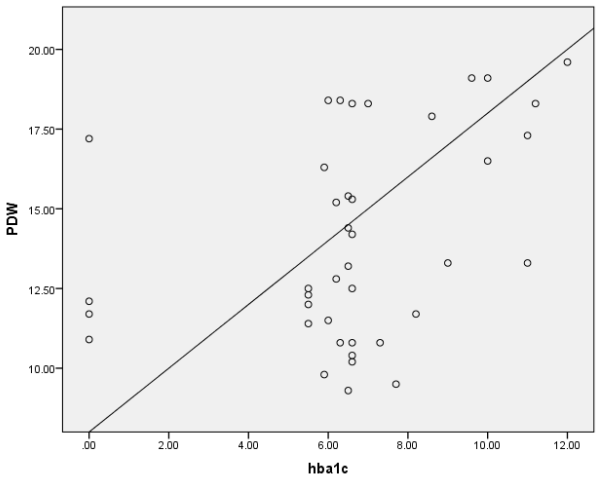

Figure 2. PDW and DSF's HbA1c have a somewhat favorable connection that is significant at the 0.05 level

Furthermore, hemostatic alterations observed in diabetic patients should be closely monitored and managed through appropriate clinical and pharmacological interventions.

CONCLUSION

The study found that PT and INR were significantly higher in patients with diabetic septic foot (DSF) compared to those with diabetes mellitus (DM) and healthy individuals, while APTT was also significantly elevated in DSF patients. Additionally, MCV, MCH, and PDW were significantly higher in the cases than in controls. There was a moderate positive correlation between HbA1c and RBC count, as well as between HbA1c and PDW. These results suggest that thrombotic markers play an important role in the treatment and prognosis of patients with diabetic septic foot.

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