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HbA1c, Lipid profile disturbances, and ESR in diabetic foot ulcer patients

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Abstract

A diabetic foot ulcer is a problem that develops due to peripheral artery disease, neuropathy, and other complications. This study investigated the association of elevated glycated hemoglobin (HbA1c) levels and inflammatory markers, including erythrocyte sedimentation rate (ESR) and blood lipids, during exacerbation of diabetic foot ulcers, and evaluated the relationships among these biochemical variables. We compared patients with diabetic ulcers and apparently healthy controls.

This case-control analytical study was conducted to evaluate the relationship between HbA1c, lipid profile, and inflammatory markers (ESR) among patients. A sample of 106 patients with diabetic foot ulcers and 60 apparently healthy controls was collected between November 2025 and March 2026, in this study conducted at a private diabetic foot clinic and Al-Kindi Teaching Hospital.

The mean of glycated hemoglobin (HbA1c) in patients was 9.59 ± 1.88 %, erythrocyte sedimentation rate (ESR) 91.42 ± 23.01 mm/hr, cholesterol 198.93 ± 46.42 mg/dL, triglycerides 153.31 ± 80 mg/dL, low-density lipoprotein (LDL) cholesterol 78.02 ± 36.14 mg/dL, high-density lipoprotein (HDL) cholesterol 34.59 ± 12.78 mg/dL, and very-low-density lipoprotein (VLDL) cholesterol 32.73 ± 16.02 mg/dL. A significant positive correlation was observed between HbA1c and total cholesterol ($r=0.217$, $P=0.025$) as well as between total cholesterol and triglyceride levels ($r=0.343$, $P<0.001$). However, no significant correlation was found between ESR and the studied biochemical parameters ($P > 0.05$). Statistical analysis was performed using SPSS version 20, with statistical significance considered at $P \leq 0.05$.

The study concluded that an increase in HbA1C% and inflammatory marker (ESR) levels, accompanied by a noticeable decrease in HDL, can serve as an indicator for monitoring and preventing unwanted side effects in diabetic patients, such as foot ulcers.

Keywords: Diabetic foot ulcer, ESR, HbA1c, Lipid profile.

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Introduction

Diabetic foot ulcers are a common and sometimes fatal complication of this disease, and it is estimated that 19 to 34 percent of people with type 2 diabetes may develop diabetic foot ulcers during the course of their disease (1). Diabetic foot ulcers are associated with an increased risk of infection, hospitalization, and amputation, as well as a significant decrease in quality of life (2). It is believed that poor wound healing of diabetic foot ulcers is associated with disruption in the regulation of several biological processes involved in tissue repair (3). Consequently, diabetic foot significantly impacts patients and increases healthcare costs (4).

Chronic hyperglycemia significantly impacts the development of diabetic foot complications. When glucose levels are poorly controlled, wounds take longer to heal because it impairs cellular activity, the immune response, and blood flow to tissues. For this reason, it is very important to check blood sugar levels regularly to diagnose and treat diabetes (5). Glycated hemoglobin (HbA1c) is a widely used marker for assessing long-term glycemic control over the previous 8–12 weeks. Red blood cells, which live for about 120 days, help glucose attach to hemoglobin automatically, and this property is not affected by enzymes (6).

Elevated levels of HbA1c are strongly associated with the development of peripheral neuropathy and peripheral artery disease (PAD), both complications of microvascular and macrovascular blood vessels. This has been demonstrated in several reputable clinical trials, such as the Diabetes Control and Complications Trial (DCCT).

Due to the complications associated with diabetes, individuals with elevated levels of HbA1c are more prone to developing foot ulcers. The American Diabetes Association states that most adults with diabetes should aim for an HbA1c level of about 7% to reduce the risk of microvascular complications (7-10).

People with type 2 diabetes often suffer from dyslipidemia, a condition that occurs when blood sugar levels are significantly elevated. This dyslipidemia can also damage the arterial walls. There is a possibility of having small, dense low-density lipoprotein (LDL), low levels of high-density lipoprotein (HDL-C), and high triglyceride levels (11-13). LDL particles remain harmful to health even if LDL-C levels are normal. This point should be noted. Lipid-related problems can lead to atherosclerosis and heart disease. There is a consensus that dyslipidemia increases the risk of cardiovascular disease; however, the precise mechanism by which dyslipidemia contributes to the formation of diabetic foot ulcers is not yet fully understood (14,15).

A recent study demonstrated that regularly monitoring lipid levels, particularly triglycerides and high-density lipoprotein (HDL) cholesterol, is crucial for assessing an individual's risk of developing diabetic foot ulcers (16). The effectiveness of lipid biomarkers in predicting disease prognosis remains uncertain. The mechanism by which lipid abnormalities cause diabetic foot ulcers is also not fully understood. Treating diabetic foot ulcers may be more challenging in the presence of inflammation, oxidative stress, high blood sugar, or high blood lipids. One of the most important benefits of regular lipid biomarker testing is that it helps identify diabetic foot ulcer patients who would benefit most from improved diabetes care (17).

Prompt diagnosis of osteomyelitis is critical to prevent the spread of infection. If treatment is delayed, the patient may develop recurrent foot

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ulcers, require further surgery, and necessitate prolonged antibiotic use (18).

Inflammatory markers, such as erythrocyte sedimentation rate (ESR), are inexpensive and readily available, and for this reason, previous studies have shown that ESR is a more useful indicator of disease than modern biomarkers such as procalcitonin and interleukins (19).

This study aimed to evaluate lipid profile parameters, HbA1c, and ESR in patients with diabetic foot ulcers, as well as to assess the relationships among these biochemical variables.

Material and Methods:

This case-control study included 106 adult patients with type 2 diabetes who were clinically diagnosed with acute diabetic foot ulcers. Diabetic foot ulcers were diagnosed by specialists through clinical examination and medical history. Patients with chronic inflammatory diseases, autoimmune disorders, malignancies, or severe systemic diseases were excluded from the study.

This study was specifically designed to evaluate ESR, HbA1c, and lipid profile parameters in patients with diabetic foot ulcers; therefore, radiographic examinations and ulcer severity classification systems were not included in the study protocol.

Sixty apparently healthy individuals served as a control group. The study was conducted from November 2025 to March 2026 at the Diabetic Foot Clinic and Al-Kindi Teaching Hospital.

Sample Collection:

Three milliliters of venous blood were collected from each of the 166 participants and distributed into three tubes. One sample was placed in a plain gel tube for serum separation and lipid profile analysis. Another sample was collected in an EDTA tube for HbA1c measurement, while ESR was measured using blood collected in a sodium citrate tube according to the modified Westergren method. Serum was separated by centrifugation at 4000 rpm for 10 minutes.

Statistical analysis: An independent sample t-test was used to compare age and biochemical parameters between diabetic foot ulcer patients and healthy controls. Pearson correlation analysis was performed to evaluate the relationships among HbA1c, ESR, and lipid profile parameters. Results were expressed as mean ± standard deviation (SD). Values of $p > 0.05$ were considered statistically nonsignificant, while $p \leq 0.05$ was considered significant, and $p < 0.01$ was considered highly significant. Contingency table analysis was performed using SPSS (version 20).

Results:

Among the 106 patients with diabetic foot ulcers, 43 were females (40.6%), and 63 were males (59.4%), as shown in Figure 1.

Table 1: Descriptive Statistics: Age between individuals in the study.

Descriptive Statistics				
Age	N	Mean	Std. Deviation	P value
Patients	106	**57.01**	9.4	0.72
Control	60	**55.33**	2.8	

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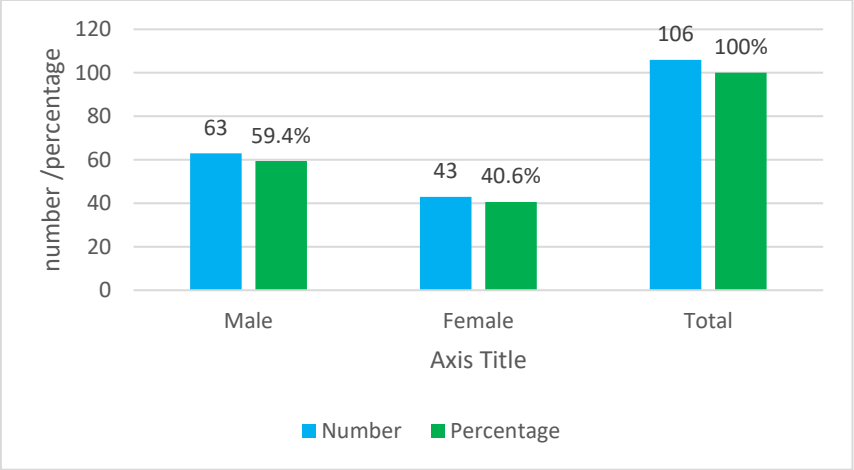

Figure 1: Distribution of DFU patients among sex groups in this study.

Male patients constituted a higher proportion of the study group. One hundred sixty-six participants were studied. Participants were divided into two groups: 106 patients with diabetic foot ulcers, and 60 controls. Age between 27 and 80 years old, the mean age of patients was 57.01±9.4, while the mean age of controls was 55.33±2.8, as shown in Table 1.

The mean value of HbA1c and ESR in the patient group was 9.59±1.88 (%) and 91.42±23.01 (mm/hr), respectively, while the cholesterol level was 198.93±46.42 (mg/dl), triglyceride 153.31±80 (mg/dl), LDL 78.02±36.14 (mg/dl), HDL 34.59±12.78 (mg/dl), and VLDL levels were 32.73±16.02 (mg/dl). Table 2.

The correlation analysis was performed only within the diabetic foot ulcer patient cohort to assess relationships among HbA1c, ESR, and blood lipid level parameters. A significant positive correlation was found between HbA1c and Cholesterol (r=0.217, P=0.025). Additionally, Cholesterol and Triglyceride showed a significant positive correlation (r=0.343, P <0.001), while no significant correlation was found between ESR and biochemical parameters in the study (P>0.05), as shown in Table 3.

Table 2: The results of the test factors between the patient and the control.

Tested factors	Patients N=106		Control N=60		P value
	Mean	Std. Deviation	**Mean**	Std. Deviation	
HbA1C (%)	**9.59**	1.88	**4.81**	0.61	**0.01**
ESR (mm/hr)	**91.42**	23.01	**8.5**	1.4	**0.001**
Cholesterol (mg/dl)	**198.93**	46.42	**187.31**	13.9	**0.01**
Triglyceride (mg/dl)	**153.31**	80.00	**111.58**	7.33	**0.001**
LDL (mg/dl)	**78.02**	36.14	**63.2**	9.4	**0.002**
HDL (mg/dl)	**34.59**	12.78	**48.3**	4.9	**0.01**
VLDL (mg/dl)	**32.73**	16.02	**25.33**	5.11	**0.05**

A p-value ≤ 0.05 was considered statistically significant, while p < 0.01 was considered highly significant

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Table 3: Correlation between factors HbA1c, ESR, Cholesterol, and Triglyceride in diabetic foot ulcer patients

Correlation between factors		**HbA1c**	**ESR**	**Cholesterol**	**Triglyceride**
HbA1c	Pearson Correlation	**1**	0.002	.217*	0.128
	Sig. (2-tailed)		0.983	**0.025**	0.191
ESR	Pearson Correlation	0.002	**1**	-0.085	0.105
	Sig. (2-tailed)	0.983		0.385	0.286
Cholesterol	Pearson Correlation	.217*	-0.085	**1**	.343**
	Sig. (2-tailed)	0.025	0.385		**< 0.001**
Triglyceride	Pearson Correlation	0.128	0.105	.343**	**1**
	Sig. (2-tailed)	0.191	0.286	**< 0.001**	

Discussion

The findings of this study are consistent with previous research highlighting the role of lipid abnormalities in patients with diabetic foot ulcers. Parhofer *et al*. reported that individuals with infected diabetic foot ulcers tend to have significantly lower levels of high-density lipoprotein (HDL) compared to healthy controls.

Reduced HDL concentrations are also commonly observed in patients with metabolic syndrome and diabetes (20). In addition, factors such as smoking, chronic inflammatory conditions, and renal impairment contribute to systemic inflammation, which is closely associated with decreased HDL levels (21). In more severe cases, markedly low HDL may also indicate underlying atypical conditions, including malignancy or an increased susceptibility to infections such as peritonitis (22).

Patients with diabetic foot ulcers often suffer from other health problems, such as kidney problems that can be exacerbated by diabetes and systemic infections. Furthermore, these patients have an increased risk of developing sepsis. In this case, low HDL levels may be a strong indicator of underlying metabolic and inflammatory conditions (23). HDL cholesterol is known to help reduce inflammation, acts as an antioxidant, and helps cholesterol return to its normal state. It also protects the lining of blood vessels by preventing monocytes from adhering to them, thus accelerating blood vessel healing. HDL cholesterol is composed of many different molecules, including enzymes, acute-phase proteins, complement factors, and protease inhibitors (24). Furthermore, HDL prevents and dissolves blood clots and has a positive effect on blood vessels (25). It also appears to protect cells from damage, such as necrosis and apoptosis, particularly in pancreatic beta cells. These protective mechanisms suggest that HDL may help maintain insulin secretion and reduce the risk of developing diabetes (26,27).

However, Cho *et al*. and Tran *et al*. have found that the vascular benefits of HDL cholesterol may not be directly related to blood HDL concentrations, particularly in individuals with diabetes, coronary artery disease, chronic kidney disease, and other cardiovascular risk factors. It remains unclear whether HDL functions optimally (28,29).

Furthermore, it is a key component of the innate immune system due to its ability to regulate inflammation, maintain cell health, and accelerate

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wound healing. HDL is believed to be an essential part of both the innate and adaptive immune systems (30).

Our study showed that patients with diabetic foot ulcers had one of the lowest HDL levels (34.59 ± 12.78 mg/dL). Unlike previously published data, only two trials showed worse results (31). The results of the investigation varied considerably. Ulloque-Badaracco *et al*. study showed HDL levels exceeding 50 mg/dL (16). The observed differences may be attributable to variations in blood lipid levels by location (31). Previous studies have indicated an association between changes in blood lipid levels and complications of diabetic foot ulcers. In this study, most lipid profiles remained within normal ranges; however, a decrease in HDL levels was observed in diabetic foot ulcer patients compared to healthy individuals. HDL plays an important role in protecting blood vessels and combating inflammation, and its reduced levels may be associated with impaired wound healing and inflammatory responses in diabetic foot ulcer patients (32,33).

Although triglyceride levels were within normal ranges in the current study, previous reports have indicated that elevated triglyceride levels may contribute to oxidative stress and inflammatory pathways associated with diabetes complications (34,35).

Glycated hemoglobin (HbA1c) reflects long-term glycemic control and has a significant impact on the development of foot problems in people with diabetes. The mean HbA1c level in the participants in this study was 9.59 ± 1.88, indicating poor glycemic control. Elevated HbA1c levels are strongly associated with an increased risk of amputation, infection, and tissue damage. Several studies have shown that high HbA1c levels are associated with an increased risk of diabetic foot ulcers and their worsening. Meta-analyses indicate that the likelihood of limb loss increases significantly when HbA1c levels exceed 8%. HbA1c is a reliable measure of long-term glycemic control and is strongly associated with the risk of diabetic complications (36,37). Diabetic patients with hyperglycemia experience higher oxidative stress, which can damage both small and large arteries. Alterations in hyperglycemia and glucose metabolism in individuals with diabetic foot ulcers are associated with peripheral artery disease (PAD), atherosclerosis, endothelial dysfunction, hyperlipidemia, increased viscosity, and increased platelet activity. PAD affects between 10% and 20% of individuals with diabetic foot ulcers (38).

The ESR may be a useful supportive marker rather than a reliable diagnostic tool alone for diabetic foot ulcers associated with osteomyelitis. Patients with diabetic foot ulcers who also have osteomyelitis have a worse prognosis, increasing the likelihood of surgery or leg amputation. This also increases the likelihood of treatment failure, which can lead to serious consequences, including antibiotic resistance, kidney damage, and catheterization problems. This makes treatment more difficult and reduces the patient's chances of recovery (39). Yapıcı *et al* also demonstrated that ESR can predict the progression of osteomyelitis in diabetic foot and the likelihood of amputation (40).

It is important to note that the correlation between HbA1c and total cholesterol (TC) suggests an association between glycemic control and lipid profile alterations in diabetic patients, which agrees with a previous study (41).

Albert *et al* found that this correlation between total cholesterol and triglycerides may suggest metabolic dysfunction in diabetic patients, that agreement with our study (42). Metabolic markers were not significantly correlated with ESR, suggesting an inflammatory state unrelated to changes in glucose and lipid concentrations.

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Limitations of the study:

One limitation of this study was the lack of a control group of diabetic patients without foot ulcers, which would have provided additional comparative insights. The study lacked ulcer severity classification and radiological assessment.

Conclusion

An increase in HbA1c % and inflammatory marker (ESR) levels, accompanied by a noticeable decrease in HDL, can be considered an indicator to monitor and prevent unwanted side effects in diabetic patients, such as foot ulcers.

Recommendations

Further research requires larger, more diverse patient cohorts to elucidate the potential clinical significance of changes in HbA1c, ESR, and blood lipid levels in patients with diabetic foot ulcers. It is recommended that future studies include diabetic patients without foot ulcers as a control group to improve comparability. Future studies incorporating standardized ulcer severity classification and radiographic assessment may contribute to a more comprehensive understanding of the clinical and biochemical characteristics of diabetic foot ulcer patients.

Ethical considerations:

The research was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. This procedure was carried out after obtaining both oral and written informed consent from the patients before sample collection. Approval was also obtained from the local ethics committee at the College of Science/ Al-Mustansiriyah University, as detailed in document BCSMU/10025/00077M dated September 15, 2025.

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Author contributions

All authors contributed to the collection of data and the preparation of the draft, and read and approved the final version of the manuscript.

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