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Original Research Article

Evaluating the Role of some Hematological Parameters in Patients with Diabetic Foot Ulcers

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Abstract: Diabetic foot ulcers (DFUs) are among the most serious complications of diabetes mellitus, greatly reducing patients' quality of life and frequently leading to chronic infections and possible limb amputation. DFUs arise from a multifaceted interaction involving peripheral neuropathy, insufficient blood flow, and immune system impairments. This research focuses on examining specific cytokines and hematological indicators in individuals with DFUs to gain deeper insight into the reasons behind impaired wound healing. The study as well as complete blood count (CBC) C-reactive protein (CRP), 90participants took part in the study, categorized into three groups: 30 diabetic patients with DFUs, 30 diabetic patients without foot ulcers, and 30 healthy individuals. Those who reviewed the Diabetes Centers at Al-Hashimiyah General Hospital and Al-Qassim General Hospital in Babylon Province between September 2024 and February 2025 were included in the study. Each patient was diagnosed with DFU by a specialist, with confirmation provided through X-ray imaging. Blood samples were collected CBC. Biochemical tests were carried out to measure CRP. Statistical analysis was performed to compare findings across the. The comparison of some blood parameters (WBC, RBC and platelets) "A comparative analysis was carried out between the patient groups and the healthy controls. The mean white blood cell (WBC) count was 7.48 ± 2.21 in patients with ulcers, 8.41 ± 2.18 in diabetic (DM) patients, and 7.25 ± 2.01 in the control group. Despite DM patients showing higher average WBC counts than the other groups, the difference between ulcer and DM patients was not statistically significant ($P > 0.05$). For red blood cell (RBC) counts, the averages were 3.93 ± 0.81 for ulcer patients, 4.00 ± 0.76 for DM patients, and 4.38 ± 0.41 in the control group. Although both patient groups had lower RBC counts compared to the controls, the difference between ulcer and DM patients was again not statistically significant ($P > 0.05$). Furthermore, platelet counts did not significantly differ between patients and healthy individuals ($P > 0.05$). The mean C-reactive protein (CRP) levels were 128.4 ± 13.3 in ulcer patients, 47.78 ± 12.7 in DM patients, and 7.03 ± 1.3 in the healthy controls. Mean levels of C-reactive protein (CRP) were and the difference was significant ($P< 0.05$) in Ulcer patients, DM patients and healthy control group. We conclude from our current study a chronic inflammatory environment in DFU patients WBC count alone may not be a reliable marker for systemic inflammation or disease severity in diabetic individuals. More accurate and specific biomarkers such as C-reactive protein (CRP) are necessary for a precise evaluation of inflammatory status Elevated

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CRP levels highlight the underlying metabolic challenges that impair wound healing. The reduced RBC levels may indicate mild anemia, which impairs erythropoietin production a platelet levels could be attributed to small sample size or considerable inter-individual variability these biomarkers point to a complex interplay of immune and metabolic dysfunction, underscoring the need for comprehensive treatment strategies that include blood glucose control, immune regulation, and angiogenesis support. The study promotes the use of these biomarkers for diagnostic purposes.

Keywords: fibroblast growth factor, Cytokines, Diabetic foot ulcers, TNF-α Diabetes mellitus.

INTRODUCTION

Diabetes mellitus is a long-term metabolic disease characterized by consistently high levels of glucose in the blood, stemming from either insufficient insulin production, reduced sensitivity of cells to insulin, or a combination of both factors (Seidu *et al*., 2022). This condition has harmful effects on multiple critical organs such as the kidneys, eyes, nerves, heart, and blood vessels due to imbalances in carbohydrate, protein, and lipid metabolism (Liu *et al*., 2022). A common complication linked to diabetes is peripheral neuropathy, which diminishes blood circulation to nerve tissues and leads to sensory impairments, particularly in areas like the metatarsophalangeal joints and heels, thereby heightening the risk of ulcer formation (Pallela *et al*., 2017). At the core of this condition is a dysfunction in the pancreatic islet cells, where beta cells are tasked with producing insulin and alpha cells with secreting glucagon. A hormonal imbalance between these leads to chronic hyperglycemia (Lenzen, 2021). Among the gravest complications are diabetic foot ulcers (DFUs), which frequently result in persistent infections, tissue death (gangrene), and even the need for limb amputation (Petersen *et al*., 2022; Rawaan, 2022). The development of these ulcers is primarily attributed to the interplay of peripheral neuropathy, arterial disease in the extremities, inadequate glycemic control, and structural abnormalities in the foot (Al-Rubeaan *et al*., 2015). Long-standing high blood sugar levels in diabetic individuals exacerbate oxidative stress and impair the function of blood vessel linings, which in turn hinders the body's natural ability to heal wounds (Al-Salih & Ali, 2021). The research examines various physiological and biochemical indicators in diabetic patients with and without foot ulcers.

Aim of the Study

This study aims to assess the significance of hematological parameters and inflammatory markers in individuals with diabetic foot ulcers.

1. It examines various physiological and biochemical parameters among three groups: diabetic patients with foot ulcers, diabetic patients without foot ulcers, and healthy individuals serving as controls. These parameters include red blood cell (RBC) count, white blood cell (WBC) count, and platelet (PLT) count.
2. It also involves measuring the levels of C-reactive protein (CRP).

METHODS

Training Desing and sample Gathering

Individuals with diabetes and diabetic foot ulcers (DFU) who attended the Diabetes Centers at Al-Hashimiyah General Hospital and Al-Qassim General Hospital in Babylon Province between September 2024 and February 2025 were included in the study. Each patient was diagnosed with DFU by a specialist, with confirmation provided through X-ray imaging. A total of 90 patients with diabetes and confirmed DFU consistently attended follow-up appointments and received standard wound care (SWO) throughout the study period.

Ethics Approval

Permission to conduct the study was obtained from the Babil Health Directorate, and verbal consent was secured from the patients during the sample collection process.

Data Collection

Demographic and Clinical Information Was Gathered by Conducting Interviews with Patients Using a Structured Questionnaire

Questionnaires

They were developed at Al-Hashimiyah General Hospital, Al-Qassim General Hospital in Babylon, and in private clinics to record the number of individuals diagnosed with diabetic foot ulcers (DFU). These questionnaires gathered data on: Biological sex, age group, time since diabetes diagnosis, reliance on insulin, ulcer features (such as their duration, location, and type), blood pressure readings, and HbA1c levels&smoking status.

Blood Samples Collection

Approximately 5 ml of venous blood was drawn from the participant after cleaning the cubital fossa with 70% ethanol. A tourniquet was applied, and venipuncture was carried out using disposable syringes. For hematological testing, 2 ml of the blood was placed in an EDTA tube. The remaining 3 ml was transferred to a gel tube, left to clot, and then centrifuged at 4000 RPM for 10 minutes to extract the serum. The serum was then moved to an Eppendorf tube and stored at -20°C for immunological analysis.

Complete Blood Count (CBC)

A 2 mL sample of venous blood was drawn into a tube containing EDTA to prevent clotting (Henry, 2011). The tube was gently inverted 8 to 10 times to mix the blood evenly (Henry, 2011). To preserve accuracy, the samples were examined within two hours of collection (Hoffbrand & Moss, 2016). Testing was carried out using the Swelab Alfa automated hematology analyzer, which uses the impedance method to count blood cells (Bain, 2021). The measured parameters included White Blood Cell count (WBC), Red Blood Cell count (RBC), and Platelet count (PLT). The results were interpreted using standard reference ranges that take into account the participant's age, sex, and clinical condition (Hoffbrand & Moss, 2016).

Biochemical Tests

Three milliliters of blood were collected in a gel tube and allowed to clot at room temperature (20–25 °C) for 15 minutes. The samples were then centrifuged at 4000 rpm for approximately 10 minutes to separate the serum. The obtained serum was divided into three aliquots of 0.5 ml each and stored in tightly sealed Eppendorf tubes.

Conduct the C - reactive protein (CRP) Test

We perform the C-reactive protein (CRP) test using the ichroma™ II system by following these steps: First, use an empty sample collector to puncture the seal of the detection solution container. Next, draw 10 microliters of the sample—this can be whole blood, serum, plasma, or a control—using the same collector. Mix the collected sample with the detection solution in a single container. Stir the mixture at least ten times to ensure the sample is completely released from the collector. It's important to use this mixture within 30 seconds. After that, remove the cap from the mixed tube and discard the first two drops before applying the remaining sample to the test cartridge. Then, dispense exactly two drops of the mixture into the cartridge's sample well. Let the cartridge sit at room temperature for three minutes before placing it into the ichroma™ device holder. Insert the cartridge into the holder, then press the 'Select' button or tap 'Start' on the device to begin the scanning process. The device will automatically scan the cartridge and display the test results on its screen. (Boditech Med Inc. 2022).

RESULTS AND DISCUSSION

Results of Some Blood Parameters (WBC, RBC and platelets) in Patients and Healthy Controls

The comparison of certain blood parameters (WBC, RBC, and platelets) between patient groups and the control group is presented in Table (4-8) and Figures (4-4), (4-5), and (4-6). The average white blood cell (WBC) counts were 7.48 ± 2.21 in ulcer patients, 8.41 ± 2.18 in diabetic (DM) patients, and 7.25 ± 2.01 in the healthy control group. WBC levels were higher in DM patients compared to the other groups; however, the difference between ulcer and DM patients was not statistically significant ($P < 0.05$). As for red blood cell (RBC) counts, the means were 3.93 ± 0.81, 4.00 ± 0.76, and 4.38 ± 0.41 in ulcer patients, DM patients, and the control group, respectively. RBC levels were lower in both patient groups compared to the control group, though the difference between ulcer and DM patients was also not statistically significant ($P < 0.05$). Additionally, there was no significant difference in platelet counts between patients and the control group ($P < 0.05$).

Table 3-1: Comparison of some blood parameters (WBC, RBC and platelets) in patients and healthy controls

Groups		WBC	RBC	Platelets
Ulcer patients	**Mean ± SD**	**7.48 ± 2.21^{A}**	**3.93 ±** 0.81^{A}	**253.9 ±** 33.6^{A}
	Range	3.80-12.40	2.20-5.11	135.0-471.0
DM patients	**Mean ± SD**	**8.41 ±** 2.18^{A}	**4.00 ±** 0.76^{A}	**238.4 ±** 30.9^{A}
	Range	5.30-14.60	2.60-5.39	135.0-402.00
Control	**Mean ± SD**	**7.25 ±** 2.01^{A}	**4.38 ±** 0.41^{A}	**218.9 ±** 21.8^{A}
	Range	3.56-11.20	3.85-5.49	130.0-310.0
p-value		**0.431**	**0.139**	**0.115**
Different latters denote to the significant differences at p< 0.05				

SD: standard deviation; †: one way ANOVA; **: significant at P <0.05

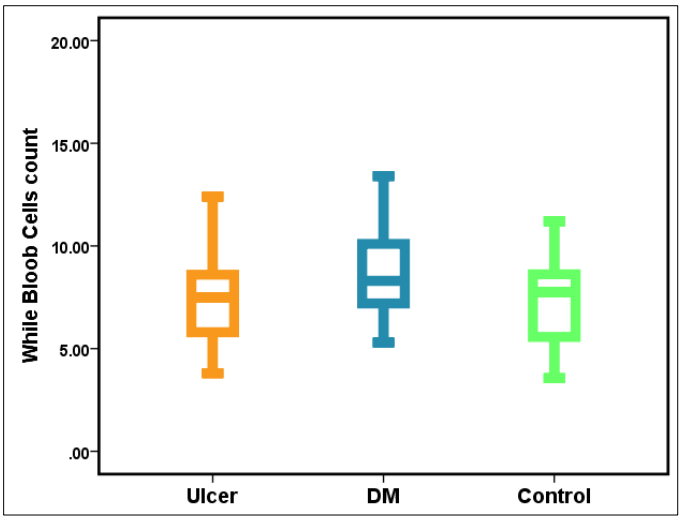

Figure 3-1: The means of WBC count in patients and control groups

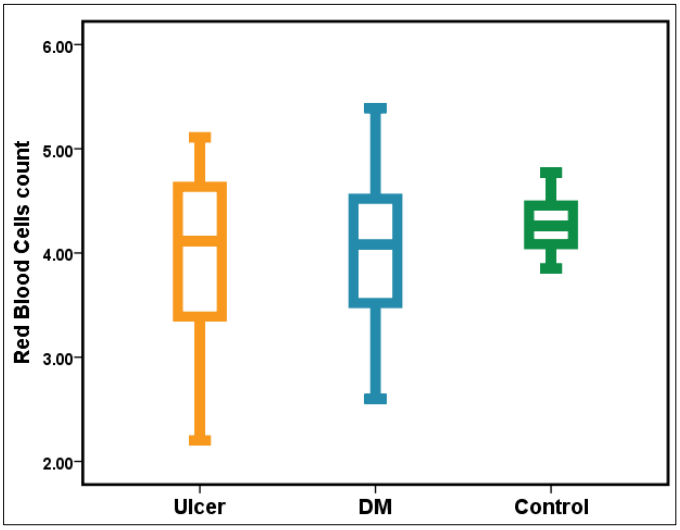

Figure 3-2: The means of RBC counts in patients and control groups

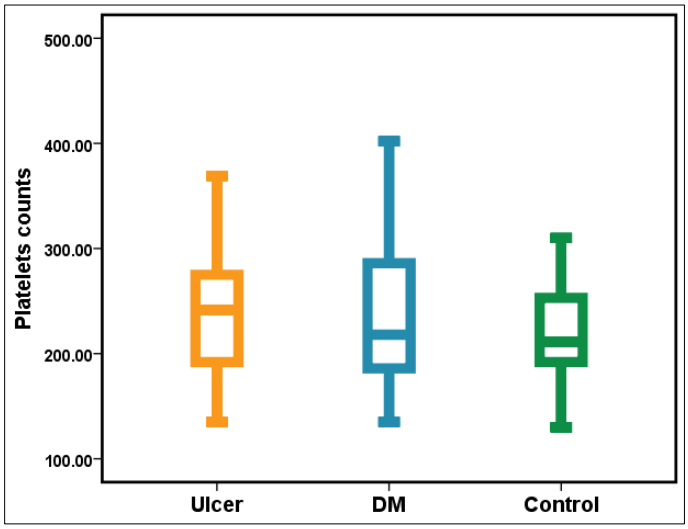

Figure 3-3: The means of platelets count in patients and control groups

Shown in Table (3-1), Figure (3-1), (3-2), and (3-3), the average white blood cell (WBC) count was found to be higher in diabetic patients (8.41 ± 2.18 $\times 10^3/\mu L$) compared to those with diabetic foot ulcers

($7.48 \pm 2.21 \times 10^3/\mu L$) and healthy individuals ($7.25 \pm 2.01 \times 10^3/\mu L$). This elevation may reflect a mild inflammatory response in diabetic patients; however, the differences between the groups were not statistically significant ($p = 0.431$), suggesting that the observed variations are likely within normal physiological boundaries. Our study revealed that although WBC counts were elevated in diabetic subjects, they still fell within the normal reference range, implying that WBC count alone may not be a reliable indicator for assessing systemic inflammation or disease severity. Thus, relying solely on WBC as a diagnostic tool may be insufficient, and integrating more accurate and specific biomarkers, such as C-reactive protein (CRP), is essential for a more thorough evaluation of the inflammatory state. These findings align with those of(Wang *et al.,* (2021), who also reported no significant difference in WBC levels between diabetic individuals and those with diabetic foot ulcers, highlighting the limited diagnostic utility of WBC in these cases. Similarly, (Alavi *et al*., 2019) noted that WBC variations, while potentially influenced by metabolic abnormalities, often do not correlate with the presence or severity of ulcers. On the other hand, some studies have reported contrasting findings.(Goh *et al*. 2020) observed a markedly higher WBC count in patients with infected diabetic foot ulcers compared to both non-infected cases and healthy controls, indicating that WBC may still serve as a useful marker for detecting acute infections rather than chronic inflammatory states. The inconsistent findings regarding WBC elevations across different studies underscore the need to employ a more comprehensive panel of inflammatory markers when evaluating patients with diabetes and diabetic foot complications.

As for RBC counts, the means were lower in ulcer patients ($3.93 \pm 0.81 \times 10^6/\mu L$) and diabetic patients ($4.00 \pm 0.76 \times 10^6/\mu L$) compared to healthy controls ($4.38 \pm 0.41 \times 10^6/\mu L$). This reduction could reflect mild anemia in the patient groups, possibly due to chronic inflammation or diabetes-related complications; however, the differences were not statistically significant either ($p = 0.139$). Anemia is a common complication in diabetic patients, particularly those with nephropathy. Renal impairment leads to reduced erythropoietin production and increased oxidative stress, both contributing to lower red blod cell counts (Thomas *et al.,* 2003). Regarding platelet counts, the results showed a slightly higher mean in ulcer patients ($253.9 \pm 33.6 \times 10^3/\mu L$) than in diabetic patients ($238.4 \pm 30.9 \times 10^3/\mu L$) and healthy controls ($218.9 \pm 21.8 \times 10^3/\mu L$). Although there was some variation, the differences between the groups were not statistically significant ($p = 0.115$).

The absence of statistically significant results in the present study may be due to a small sample size or considerable individual variability within groups, which could obscure real differences. Moreover, various external factors, including medication intake, secondary infections, or pre-existing health conditions, can affect platelet levels, potentially weakening the observed association between platelet count and diabetic foot ulcer status. These findings align with those of (Demirtas, *et al*., 2016) A mild rise in platelet levels is commonly observed in chronic inflammatory or infectious conditions, as the bone marrow becomes more active in response to widespread inflammation (Kaser *et al*., 2001). This reaction is probably triggered by pro-inflammatory cytokines like interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), which both contribute to increasing platelet production. (Koupenova *et al*., 2015).

Results of C - reactive protein (CRP) in Patients and Healthy Controls

The comparison of C-reactive protein (CRP) between patient and control groups was conducted, and the findings are presented in Table (3-2) and Figure (3-4). The mean CRP levels were recorded as 128.4 ± 13.3 in Ulcer patients, 47.78 ± 12.7 in DM patients, and 7.03 ± 1.3 in the healthy control group. Both patient groups exhibited significantly higher mean CRP levels compared to the healthy controls ($P > 0.05$). Furthermore, a significant difference was also observed between the Ulcer and DM patient groups themselves ($P > 0.05$).

Table 3:2 :Comparison of C-reactive protein (CRP) in patients and healthy controls

Groups		**C-reactive protein (CRP) levels**
Ulcer patients	**Mean ± SE**	**128.4 ± 13.3^A**
	Range	16.0-295.0
DM patients	**Mean ± SE**	**47.78 ±** 12.7^B
	Range	1.20-293.0
Control	**Mean ± SE**	**7.03 ±** 1.3^C
	Range	1.00-41.00
p-value		**0.001***
Different latters denote to the significant differences at p< 0.05		

SD: standard deviation; †: one way ANOVA; **: significant at P <0.05

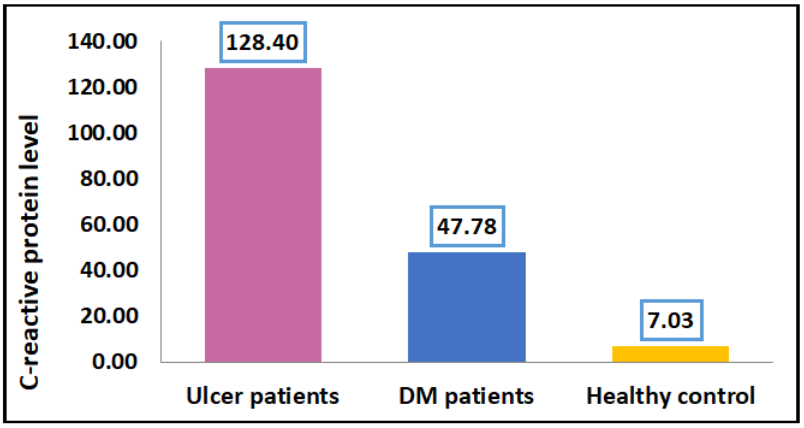

Figure 3-4: The means level of CRP in patients and control groups

C-reactive protein (CRP) is a protein made by the liver that increases in the bloodstream when there's inflammation somewhere in the body. This inflammation can result from infections, injuries, or chronic diseases. CRP is considered one of the most sensitive and early indicators of widespread inflammation**.** CRP levels start to increase within a few hours after the onset of inflammation and usually peak within 24 to 48 hours. Its production is mainly controlled by the inflammatory molecule interleukin-6 (IL-6). CRP plays a role in the body's initial defense mechanism, referred to as the innate immune response, by helping activate the complement system and aiding in the removal of pathogens and damaged cells (Pepys & Hirschfield, 2003). As explained in table (3-2), Figure (3-4): the average serum levels of C-reactive protein (CRP) were 128.4 ± 13.3 mg/L in diabetic patients with foot ulcers, 47.78 ± 12.7 mg/L in diabetic patients without ulcers, and 7.03 ± 1.3 mg/L the study observed a notably higher level of CRP in both groups of diabetic patients compared to the healthy control group ($P < 0.05$), with a significant distinction also found between the two diabetic groups ($P < 0.05$). These results are consistent with earlier studies that reported markedly increased serum CRP levels in individuals suffering from diabetic foot ulcers in comparison to healthy subjects. CRP is a well-established marker of systemic inflammation and is frequently linked to tissue damage or infection—conditions that are commonly seen in diabetic foot cases. (Shrestha *et al.,* 2021; Herder *et al*., 2019).

CONCLUSIONS

WBC count alone may not be a reliable marker for systemic inflammation or disease severity in diabetic individuals. More accurate and specific biomarkers such as C-reactive protein (CRP) are necessary for a precise evaluation of inflammatory status, the reduced RBC levels may indicate mild anemia, possibly due to chronic inflammation or diabetes-related complications such as nephropathy, which impairs erythropoietin production and promotes oxidative stress platelet levels could be attributed to small sample size or considerable inter-individual variability, external factors such as medications, coexisting infections, or underlying health conditions may influence, commonly observed in chronic inflammatory or infectious conditions due to bone marrow stimulation by pro-inflammatory cytokines like interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) & Metabolism Journal, 45(2), 245–254.

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