Derna Academy Journal for Applied Sciences

E-ISSN: 3006-3159

DAJAS

Diagnostic and Prognostic Value of Inflammatory Markers (l IL-6) in Predicting Diabetic Foot Progression in Patients with Type 2 Diabetes at Al-Wahda Hospital

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القيمة التشخيصية والتنبؤية للعلامات الالتهابية (l IL-6) في التنبؤ بتطور القدم السكرية لدى مرضى السكري من النوع 2 في مستشفى الوحدة

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Volume : 8 **Issue: 1** **Page Number: 146 - 158**

Keywords:
Diabetic foot, Type 2 DM, Diagnostic biomarker, Prognostic biomarker, inflammatory marker, IL-6.

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Received: 25\09\2026
Accepted: 05\10\2026
Published: 20\10\2026

https://doi.org/10.71147/1qd60m39

ABSTRACT

Diabetic foot disease is a major complication of type 2 diabetes mellitus (T2DM), with inflammation contributing to tissue damage and delayed wound healing. This study evaluated serum interleukin-6 (IL-6) as a potential biomarker of diabetic foot disease and its progression. An observational study included 120 patients with T2DM, comprising 60 patients without diabetic foot disease and 60 with diabetic foot disease, who underwent clinical assessment and serum IL-6 measurement using ELISA. Patients with diabetic foot disease had significantly higher IL-6 levels than controls (19.01 ± 5.95 vs. 4.98 ± 2.00 pg/mL, $p < 0.001$). IL-6 was strongly correlated with diabetic foot disease (Spearman's $\rho = 0.864$, $p < 0.001$) and CRP ($r = 0.762$, $p < 0.001$), but did not differ significantly across Wagner grades ($p = 0.786$) or during 3–6 months of follow-up ($p = 0.631$). ROC analysis showed excellent diagnostic performance for IL-6 (AUC = 0.999), exceeding that of CRP (0.944), ESR (0.915), and WBC (0.851). Higher IL-6 levels were also associated with diabetic foot disease in logistic regression analysis (OR = 14.09, 95% CI: 1.29–153.88, $p = 0.030$). Serum IL-6 may therefore serve as a valuable biomarker for identifying patients with T2DM at increased risk of diabetic foot disease and may support early clinical risk stratification and management.

الملخص

يُعد مرض القدم السكري من المضاعفات الرئيسية لمرض السكري من النوع الثاني(T2DM) ، حيث يسهم الالتهاب في حدوث تلف الأنسجة وتأخر التئام الجروح. هدفت هذه الدراسة إلى تقييم مستوى الإنترلوكين-6 (IL-6) في مصل الدم باعتباره مؤشرًا حيويًا محتملًا لمرض القدم السكري وتطوره. شملت الدراسة الرصدية 120مريضًا مصابًا بداء السكري من النوع الثاني، منهم 60 مريضًا دون الإصابة بمرض القدم السكري و60 مريضًا مصابًا به، وخضع جميع المرضى للتقييم السريري وقياس مستوى IL-6في مصل الدم باستخدام تقنية .ELISA أظهرت النتائج أن المرضى المصابين بمرض القدم السكري لديهم مستويات أعلى بشكل ملحوظ من IL-6مقارنةً بمجموعة الضبط 5.95 ± 19.01) مقابل 4.98 ± 2.00 بيكوغرام/مل، .(0.001 > pكما وُجد ارتباط قوي بين مستوى IL-6ومرض القدم السكري(ρ = 0.864) ، (0.001 > pوبين IL-6 والبروتين المتفاعل (r = C (CRP) 0.762، .(0.001 > pفي المقابل، لم تُظهر مستويات IL-6 فروقًا ذات دلالة إحصائية بين درجات Wagnerالمختلفة (p = 0.786)أو خلال فترة المتابعة التي تراوحت بين 3و6 أشهر .(p = 0.631)وأظهر تحليل منحنى ROC أداءً تشخيصيًا ممتازًا لـ IL-6، حيث بلغت المساحة تحت المنحنى(AUC = 0.999) ، متفوقًا على كل من CRP (0.944)و ESR (0.915)وكريات الدم البيضاء .WBC (0.851) كما ارتبط ارتفاع مستويات IL-6 بوجود مرض القدم السكري في تحليل الانحدار اللوجستي (OR = 14.09، فاصل الثقة 95%: 1.29–153.88، .(p = 0.030 وبناءً على ذلك، قد يمثل IL-6في مصل الدم مؤشرًا حيويًا ذا قيمة للتعرف على مرضى السكري من النوع الثاني الأكثر عرضة للإصابة بمرض القدم السكري، كما قد يسهم في التقييم المبكر لمستوى الخطورة والمساعدة في توجيه التدبير السريري والعلاجي.

الكلمات المفتاحية: مرض القدم السكري ؛ الإنترلوكين؛ المؤشرات الحيوية؛ الالتهاب؛ البروتين المتفاعل .

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1. INTRODUCTION

Diabetic foot is considered one of the most serious and challenging complications of diabetes; it is clinically associated with chronic ulcers, infection, tissue damage, hospitalization, disability, and lower-limb amputation. The pathophysiology of diabetic foot is complex and multifactorial, influenced by chronic hyperglycemia, peripheral neuropathy, peripheral artery disease, impaired immune response, tissue ischemia, and delayed wound healing. Therefore, early detection of patients at risk of worsening diabetic foot conditions is crucial to mitigating the burden associated with this disease (Mohamed et al., 2024). Chronic low-grade inflammation plays a pivotal role in the pathogenesis and progression of diabetic foot disease. Chronic hyperglycemia acts as a key trigger for a cascade of processes, including inflammation, endothelial dysfunction, oxidative stress, and impaired tissue healing. Consequently, inflammatory biomarkers have garnered increasing attention, particularly regarding their role in predicting the severity of diabetic foot disease (Qin, & Deng, 2025). Despite the recognized importance of these biomarkers in predicting infection and disease severity, studies concerning their utility in diagnosis and the prediction of disease progression remain inconsistent and lack sufficient clarity. Interleukin-6 (IL-6) is a pro-inflammatory cytokine that mediates a variety of immune and inflammatory processes; findings regarding it vary, with evidence showing that blood levels of IL-6 correlate with the severity of peripheral neuropathy and diabetic foot disease, and that elevated baseline levels measured at the start of follow-up are associated with a poor clinical course (Zhou,et al,2025). Numerous studies have addressed the predictive role of inflammatory markers in diabetic foot disease. A study (Dmitriyeva et al., 2025). examining this role revealed that baseline serum Interleukin-6 (IL-6) concentrations were significantly higher in patients with advanced stages of the disease (according to the Wagner classification) and in those with poorer clinical outcomes; furthermore, multivariate analyses demonstrated that IL-6 serves as an independent predictor of the severity and progression of diabetic foot disease. These findings suggest that IL-6 levels could be utilized to determine the severity of diabetic foot disease and assess the quality of the immune response. More recently, the diagnostic role of inflammatory markers in diabetic foot disease has been evaluated more extensively, a fact corroborated by a study (Wang et al., 2025). More recently, another group of studies (Chen et al., 2024) has evaluated the diagnostic role of inflammatory biomarkers in diabetic foot disease on a broader scale. A systematic review and meta-analysis conducted by Chen et al. (2024) assessed the accuracy of inflammatory markers in diagnosing infected diabetic foot ulcers, demonstrating that these markers can provide clinically useful information for distinguishing between infected and non-infected ulcers.

Among the markers evaluated, C-reactive protein (CRP) exhibited the highest diagnostic accuracy, with an area under the curve (AUC) of 0.93, followed by procalcitonin, erythrocyte sedimentation rate (ESR), and white blood cell (WBC) count. These findings support the potential role of inflammatory biomarkers in the early diagnosis and clinical assessment of diabetic foot complications; a study by Shaikh et al. (2026) also supports this. Shaikh used a hospital-based case-control study of 250 subjects to determine the relationship between inflammatory molecular biomarkers and severity of DFU. They found that serum levels of TNF-, IL-6, and hs-CRP were significantly higher among subjects with DFU than among diabetic controls without ulcers ($P<0.001$), and a positive association with increasing Wagner grade of DFU in the inflammatory biomarkers ($P<0.001$) was observed. It appears that IL-6 in combination with TNF-α and hs-CRP would be among the biomarker candidates for clinical risk stratification of severity of disease in DFU. In a case-control study (Wu et al., 2023) evaluating inflammatory markers in diabetic patients, Interleukin-6 (IL-6) was identified as a significant marker for diabetic foot disease; the odds ratio for the association between IL-6 and diabetic foot disease was 1.434 (95% confidence interval: 1.142–1.802; $p=0.002$). Furthermore, reports indicated that the sensitivity of IL-6 for detecting diabetic foot disease was 70%, with an area under the receiver operating characteristic (ROC) curve of 0.728. The same study also identified C-reactive protein (CRP) and fasting blood glucose levels as significant predictors for the progression of diabetic foot disease.

2. METHOD

Patients and Methods

Study design and setting

The study utilized relevant demographic, clinical, and laboratory data, as well as longitudinal follow-up data, covering the period from May 2024 to January 2025. Study phases included patient identification, collection of clinical and demographic data, image acquisition, and the establishment of a reference diagnosis. Designed as an observational case-control study conducted at Al-Wahda Hospital, the research focused on patients diagnosed with type 2 diabetes mellitus. The study aimed to investigate the relationship between serum Interleukin-6 (IL-6) levels and the presence and severity of diabetic foot disease. A total of 120 patients meeting the eligibility criteria were enrolled and divided into a control group (patients without diabetic foot disease) and a study group (patients with diabetic foot complications). All patients underwent standardized clinical and laboratory assessments; serum IL-6 levels were measured upon admission, and the severity of diabetic foot disease was clinically evaluated. The study design enabled a comparison of inflammatory marker levels between patients with and without diabetic foot disease, thereby allowing for an assessment of the association between IL-6 levels and the severity of the condition.

Patient selection

The study sample consisted of 120 patients diagnosed with type 2 diabetes who met the pre-established eligibility criteria. The patients were divided into two groups: a control group ($n = 60$) comprising patients without diabetic foot, and an experimental group ($n = 60$) comprising patients with diabetic foot. All participants underwent a comprehensive clinical assessment, including demographic characteristics, duration of diabetes, glycemic control, and relevant comorbidities. In addition, venous blood samples were collected to determine serum interleukin-6 (IL-6) concentrations using an enzyme-linked immunosorbent assay (ELISA), while the severity of diabetic foot disease was assessed according to established clinical criteria, including the Wagner classification. The collected data were subsequently analyzed to evaluate the association between serum IL-6 levels and the presence and severity of diabetic foot disease, as well as its potential value in predicting disease progression.

Inclusion Criteria

To be included in the study, patients had to be adults aged 18 years and older with a diagnosis of type 2 diabetes mellitus and provide adequate clinical and laboratory information to satisfy study criteria for inclusion. In the closed diabetic foot group, patients needed to present with either a diabetic foot ulcer or a diabetic foot complication; while participants in the control group needed to have no diagnosis of diabetic foot disease or ulcers, either ever or at any period of time. All participants had to be able to fill out a detailed clinical form, including information on the duration of diabetes, how elevated the levels of glycemia were, and comorbid diseases, and provide a venous blood sample for serum measurement of IL-6. No patients were included without informed consent or who did not satisfy all eligibility criteria of the study (Al-Sharoofiet al., 2026).

Exclusion Criteria

Individuals were not part of the study if they suffered from type 1 diabetes, gestational diabetes, or some other types of diabetes, or were younger than 18 years. Those who had exacerbations of systemic illness of acute origin or chronic diseases of a malignant type along with liver and kidney ailments, or any other disorder affecting a person's inflammatory biomarkers, were not included in the study. Neither were people undergoing therapies involving corticosteroids or other medicines that change the level of one of the cytokines much, such as IL-6. (Wang et al., 2025).

Clinical Assessment

The evaluation of various participants was undertaken in a careful and standardized manner by the medical specialists. Hence, many records were documented, including clinical data such as age, gender, duration of diabetes, BMI, smoking status, glycemic level, and other illnesses suffered by the participants. In the case of the diabetic patients, ulcer assessment was done from various angles such as site of occurrence, number of ulcers, size, depth, the existence of necrotic tissue, wound characteristics, and infection caused by the ulcer. The degree of the disease was classified according to the levels in the Wagner classification system, and peripheral vascular inquiry was undertaken by investigation of peripheral pulses, skin changes, or capillary refill. The past occurrence of ulceration or complications of diabetic foot is also noted (Korkmaz,et al., 2018).

Imaging Assessment

Imaging examination of those who suffered from foot infection and osteomyelitis was performed according to what was clinically indicated. Standard radiography of the affected foot was done to assess for bone-related problems, soft-tissue alterations, foreign bodies, and other evidence of osteomyelitis. If needed, Doppler ultrasonography was also performed to check for peripheral arteries and determine whether the arteries suffered from disease. Imaging Assessment (Kaleli,. et al., 2019).

Laboratory Evaluation

Blood samples that are venous in nature were taken from every one of the individuals involved in the research. This was done under standard conditions (i.e. in a manner that allows for proper biochemical tests to be carried out). The tests done on a routine basis include complete blood count; glucose test via blood sample; tests for renal functions and cholesterol inspection. C-reactive protein, ESR, and serum interleukin-6 levels were also studied. The last-mentioned substances were evaluated using an enzyme-linked immunosorbent assay test. The data obtained is compared to findings associated with diabetic foot(Chen et al., 2020).

Statistical Package for the Social Sciences (SPSS) was used to perform the data analysis. Quantitative variables were summarized using mean values and standard deviations, while categorical variables were represented using frequency distributions and percentages (Mitrea et al., 2026).

The comparison of the three groups was done using suitable parametric or non-parametric tests depending on the distribution of the data. Correlation analysis, Receiver Operating Characteristic (ROC) curve analysis, and multivariate regression analysis were performed to find the relationship between Severity Index (SII) and radiological measurements, and the presence of liver and kidney injuries. The results were statistically significant, with p-values less than 0.05.

3. ETHICS APPROVAL

The study protocol was approved by the Research Ethics Committee of Al-Wahda Hospital / Faculty of Medicine, Menofia University (Approval no.: REC/2026/054). Informed written consent was obtained from all patients participating in this study, and the work was carried out in accordance with the ethical standards of the Declaration of Helsinki and its later amendments.

4. RESULT

Table 1: Demographic and Clinical Characteristics of the Study Participants

Variable	Control T2DM (n=60)	Diabetic Foot (n=60)	P-value
Age, years	58.87 ± 10.78	57.42 ± 9.93	0.445
BMI, kg/m²	28.76 ± 3.95	28.71 ± 3.70	0.943
Diabetes duration, years	11.52 ± 5.41	10.42 ± 4.82	0.246
Male sex, n (%)	33 (55.0)	37 (61.7)	0.579
Current smoker, n (%)	16 (26.7)	20 (33.3)	0.643
Hypertension, n (%)	39 (65.0)	37 (61.7)	0.85
Dyslipidemia, n (%)	41 (68.3)	40 (66.7)	1
Peripheral neuropathy, n (%)	25 (41.7)	28 (46.7)	0.713
Diabetic nephropathy, n (%)	11 (18.3)	20 (33.3)	0.095

Note:
M: mean value, (SD): standard deviation, P-values <0.05: statistically significant, BMI: body mass index.

According to Table 1, the two groups were broadly comparable in their demographic and clinical characteristics, with no statistically significant differences observed in age, BMI, diabetes duration, sex, smoking, hypertension, dyslipidemia, or peripheral neuropathy. Although diabetic nephropathy was more frequent in the diabetic foot group, the difference was not statistically significant.

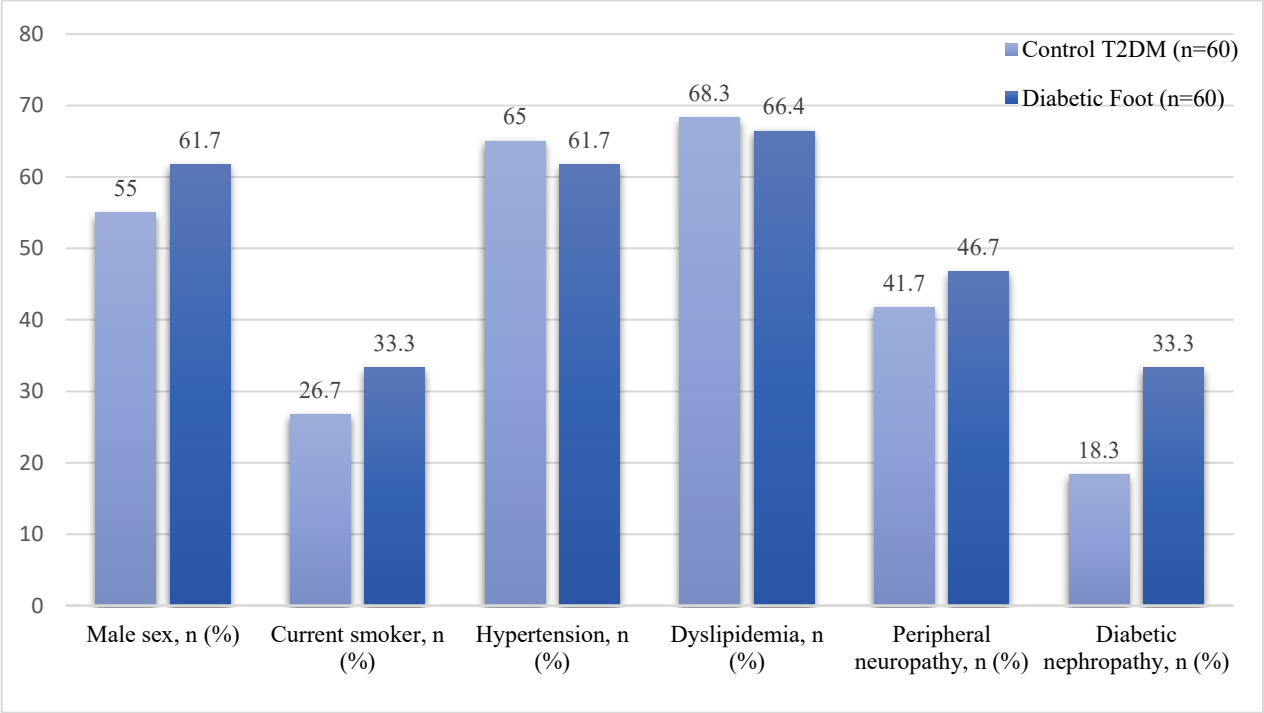


Figure 1 shows demographic characteristics of the Study Participants

Figure 2 illustrates that for the diabetic foot group, there was a relatively greater proportion of males, smokers, peripheral neuropathy, and diabetic nephropathy compared to the control group. On the other hand, there were greater occurrences of hypertension and dyslipidemia in the control group. Therefore, the differences between the baselines is actually limited except for diabetic nephropathy, which showed a considerably larger difference

Table 2: Glycemic and Inflammatory Laboratory Parameters

Parameter	Control T2DM (n=60)	Diabetic Foot (n=60)	P-value
WBC, ×10⁹/L	6.88 ± 1.48	9.75 ± 2.41	<0.001
ESR, mm/h	25.88 ± 11.59	53.05 ± 16.55	<0.001
CRP, mg/L	4.39 ± 1.96	17.41 ± 7.63	<0.001
HbA1c, %	8.16 ± 1.22	9.02 ± 1.53	<0.001
Fasting glucose, mg/dL	151.54 ± 34.18	172.09 ± 46.81	0.007
IL-6, pg/mL	**4.98 ± 2.00**	**19.01 ± 5.95**	**<0.001**

Note:
M: mean value, (SD): standard deviation, P-values <0.05: statistically significant., BMI: body mass index.

According to Table 2, Patients with diabetic foot demonstrated significantly higher WBC, ESR, CRP, HbA1c, fasting glucose, and particularly serum IL-6 concentrations compared with the control group. The marked difference in IL-6 levels supports its potential association with diabetic foot disease.

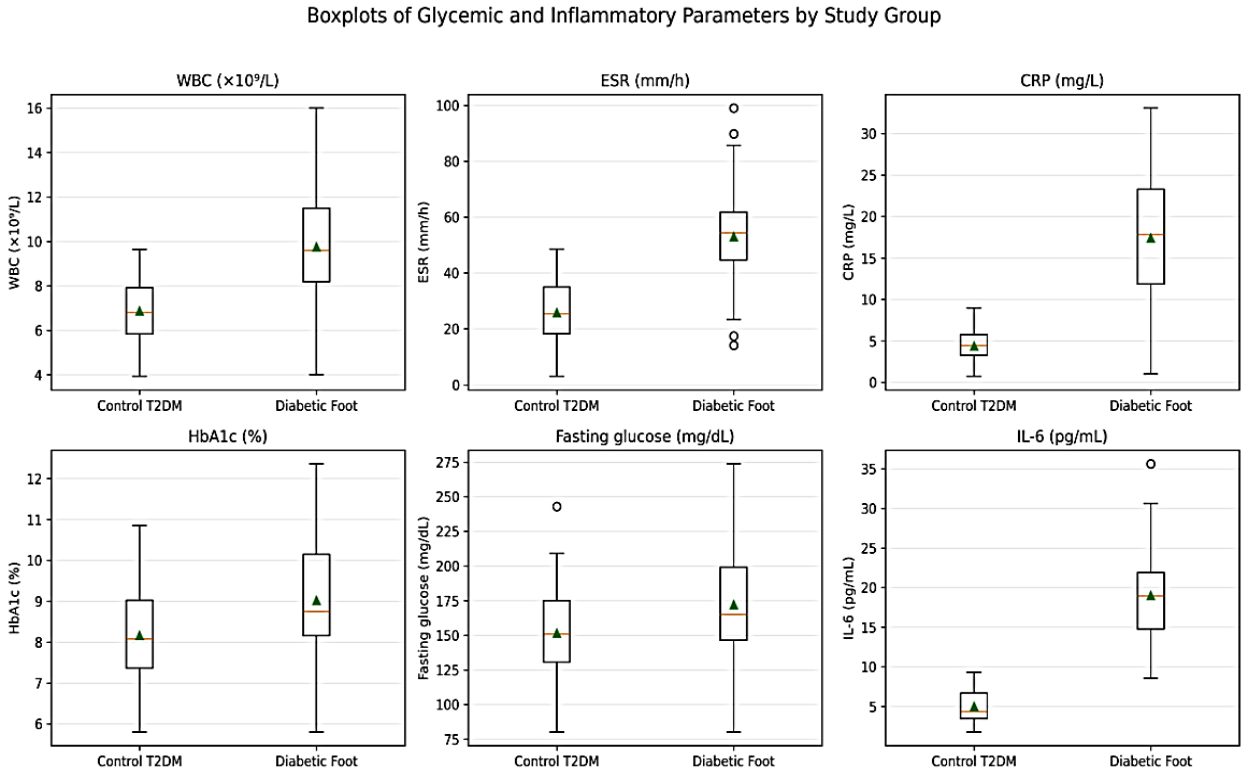


Figure 2 illustrates Combined Boxplots of Glycemic and Inflammatory Parameters

From the combined boxplots figure (2), it is evident that there is a distinct difference between the control and diabetic foot groups in relation to both aspects that have been discussed. There was a notable difference in the readings of WBC, ESR, CRP, HbA1c, fasting glucose, and IL-6 associated with patients diagnosed with diabetic foot syndrome, which is especially applicable to IL-6.

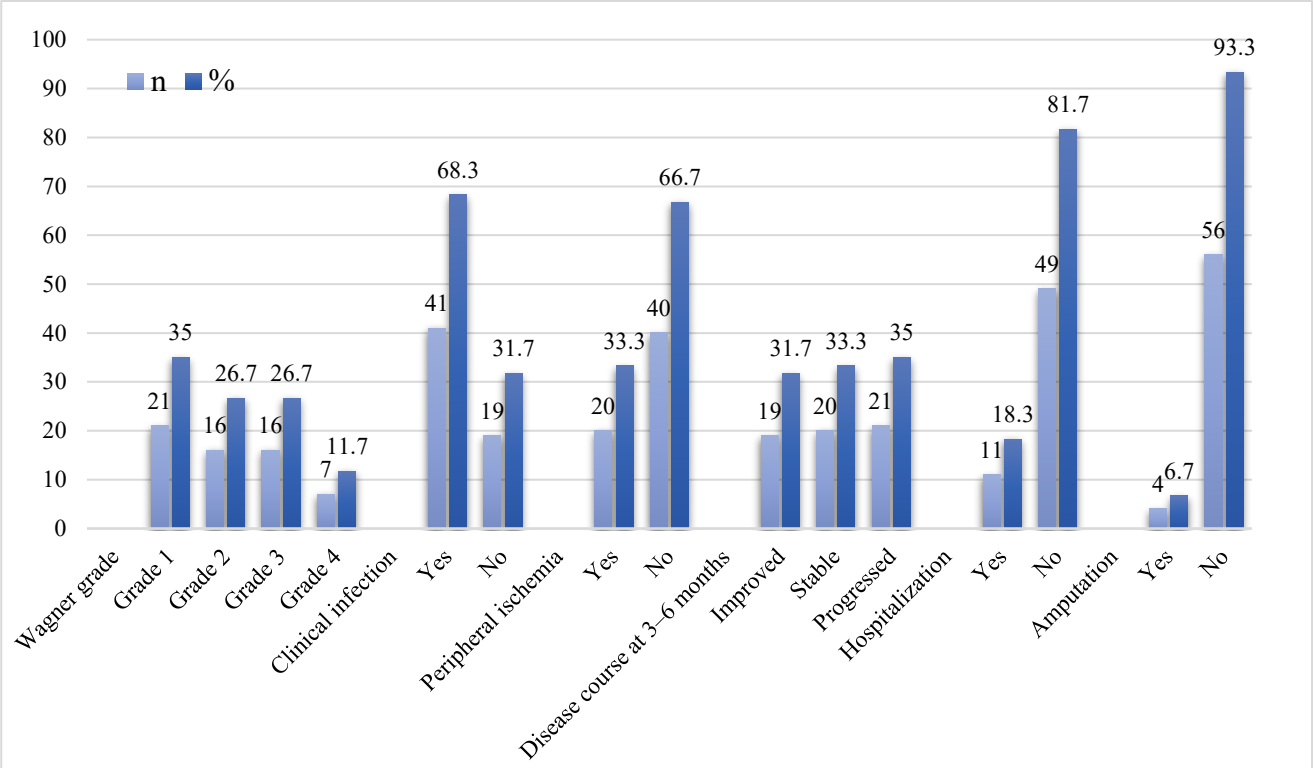


Figure 3: Clinical Characteristics of Patients with Diabetic Foot

Figure (3) presents information regarding the clinical features and results of the patients with diabetic foot disease. Most of the patients belonged to grade 1 Wagner classification (35.0%), then grades 2 and 3, which were present in 26.7% each. Grade 4 condition was present in 11.7% of the cases.

Among the included patients, infection was seen in 68.3% of cases, and peripheral ischemia was seen in 33.3% of cases. During the follow-up of 3 to 6 months, 35% of patients experienced clinical progression of the disease while 33.3% remained stable, whereas 31.7% of patients improved during this period. 18.3% of the patients were hospitalized, and 6.7% of the patients underwent amputation of limbs, which denotes the significant impact of diabetic foot problems on clinical care.

Table 3: Serum IL-6 According to Wagner Grade

Wagner Grade	n	IL-6, pg/mL (Mean ± SD)
Grade 1	21	18.85 ± 5.70
Grade 2	16	17.81 ± 4.49
Grade 3	16	19.89 ± 7.01
Grade 4	7	20.22 ± 7.71
Overall	60	19.01 ± 5.95

Note:
M: mean value, (SD): standard deviation, P-values <0.05: statistically significant., BMI: body mass index.

According to Table 3, Serum IL-6 levels varied across Wagner grades, with the highest mean level observed in Grade 4 (20.22 ± 7.71 pg/mL) and the lowest in Grade 2 (17.81 ± 4.49 pg/mL). However, the differences among Wagner grades were not statistically significant (P = 0.786).

Table 4: IL-6 According to Disease Course During Follow-up

Disease course	n	IL-6, pg/mL (Mean ± SD)
Improved/Stable	39	18.84 ± 6.21
Progressed	21	19.32 ± 5.57
P-value		0.631

Note:
M: mean value, (SD): standard deviation, P-values <0.05: statistically significant. BMI: body mass index.

According to Table 4, Patients who experienced disease progression had slightly higher mean IL-6 levels than those with an improved or stable course (**19.32 ± 5.57 vs. 18.84 ± 6.21 pg/mL**); however, this difference was **not statistically significant (P = 0.631)**.

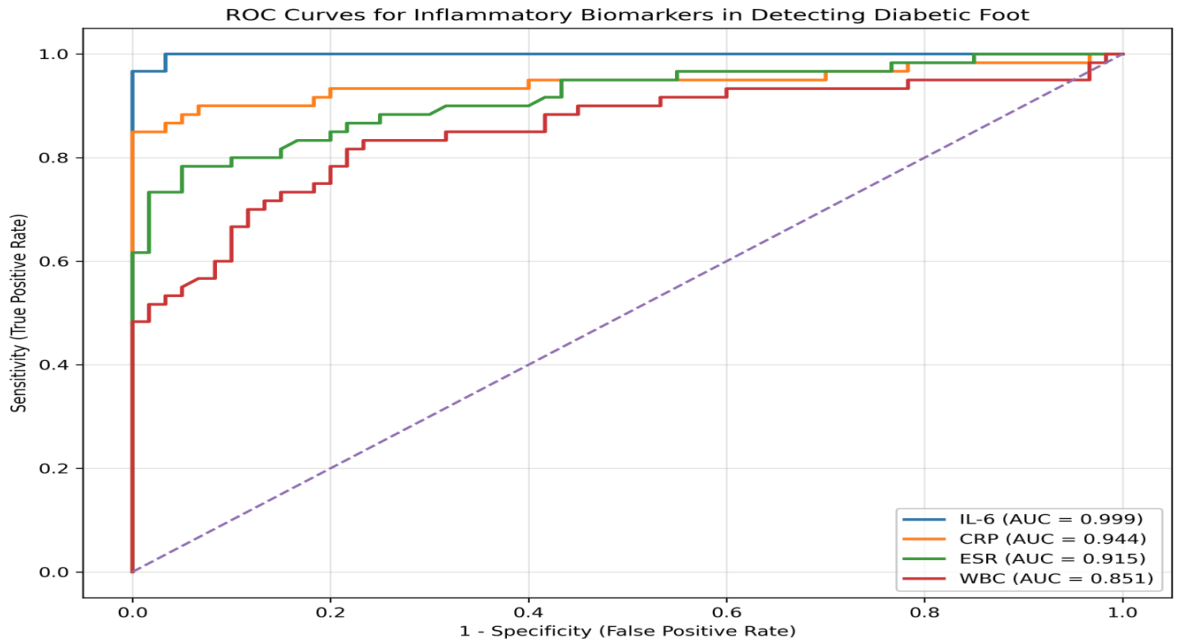


Figure 5 shows that the ROC analysis demonstrated excellent discriminatory performance

According to Figure 5) the outcomes of the analysis indicated an excellent ability of all of the tested inflammatory biomarkers to discriminate between the studied groups. The highest diagnostic performance was shown by IL-6 (AUC = 0.999), followed by CRP (AUC = 0.944), ESR (AUC = 0.915), and WBC (AUC = 0.851). Overall, the results showed that IL-6 appeared to be able to differentiate patients with diabetic foot from other diabetic patients. Inflammatory biomarkers for identifying diabetic foot disease.

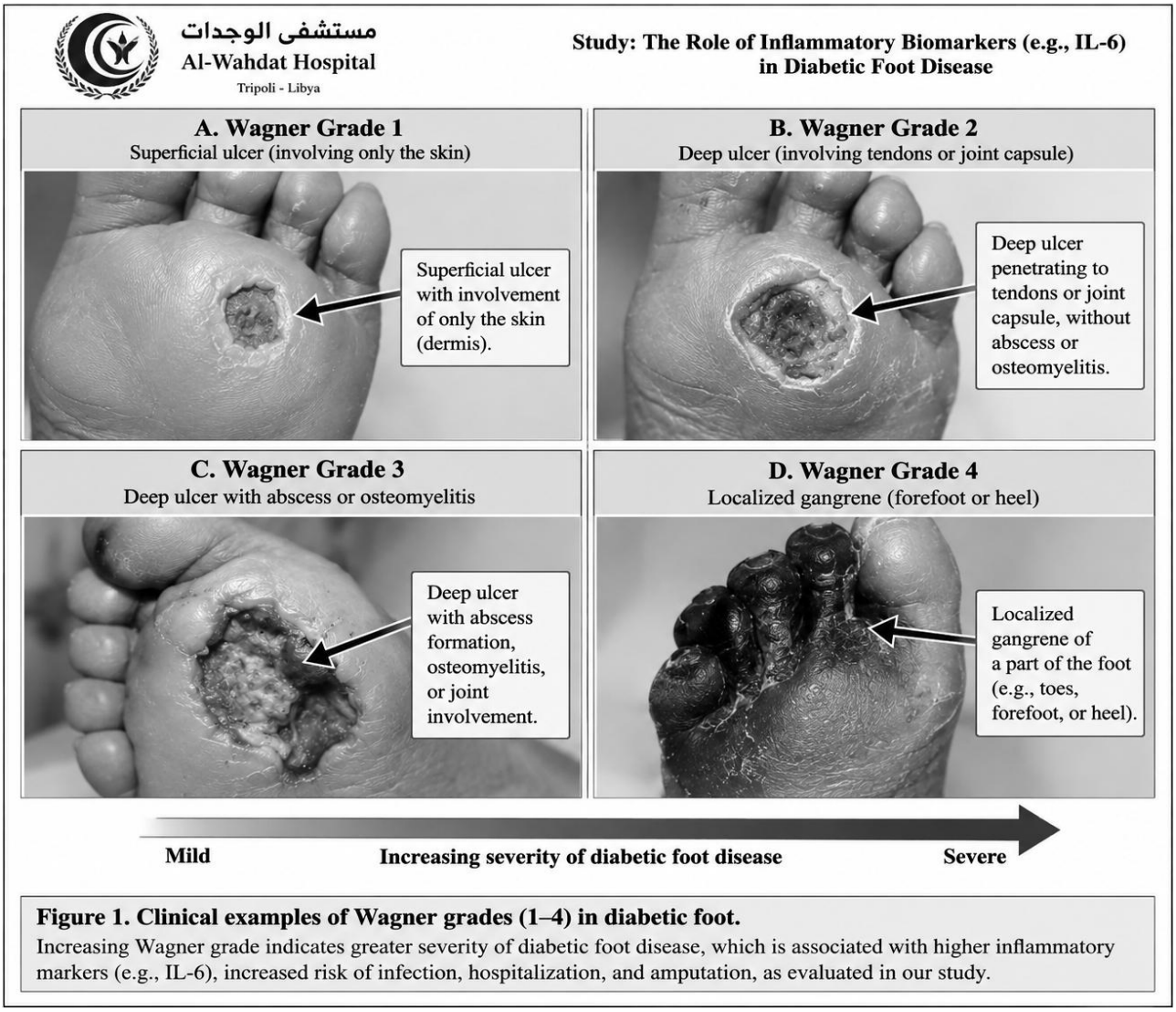


Figure 6: illustrates the progression of diabetic ulcers according to the Wagner classification, from grade 1 to grade 4.

Figure 6 shows the various levels of severity of diabetic foot disease as per the Wagner system, from Grade 1, which is a superficial ulcer, to Grade 4, which is localized necrosis of the tissue. The images show the different levels and depths of the damage seen in this disease. This classification was used by the authors of this paper in the study of their diabetic foot patients and its association with inflammatory mediators like serum IL-6

.Table 5. Association of Inflammatory Biomarkers with Diabetic Foot and Their Correlation with Serum IL-6

Inflammatory marker	Correlation with diabetic foot (Spearman ρ)	P-value	OR for diabetic foot	95% CI for OR	Correlation with IL-6 (Pearson r)	P-value
WBC	0.608	<0.001	2.124	1.606–2.809	0.498	<0.001
ESR	0.719	<0.001	1.153	1.098–1.212	0.591	<0.001
CRP	0.768	<0.001	1.815	1.407–2.340	0.762	<0.001
IL-6	**0.864**	**<0.001**	**14.085**	**1.289–153.880**	—	—

Note: Spearman's correlation coefficient (r) was used to evaluate associations between inflammatory biomarkers and diabetic foot status. Pearson's correlation coefficient (r) was used to evaluate the association between serum IL-6 levels and continuous inflammatory biomarkers. Odds ratios (ORs) were obtained from univariable logistic regression models with diabetic foot status as the dependent variable.

CI, confidence interval; WBC, white blood cell count; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; IL-6, interleukin-6.
$P < 0.05$ was considered statistically significant.

According to Table 5, A significant positive association was observed between all evaluated inflammatory biomarkers and diabetic foot disease. IL-6 demonstrated the strongest correlation with diabetic foot ($\rho = 0.864$, $P < 0.001$), followed by CRP ($\rho = 0.768$), ESR ($\rho = 0.719$), and WBC ($\rho = 0.608$). In addition, IL-6 was positively correlated with CRP, ESR, and WBC, with the strongest association observed between IL-6 and CRP ($r = 0.762$, $P < 0.001$).

5. DISCUSSION

The study carried out examines the relationship between serum inflammatory markers and diabetic foot condition in type 2 diabetic patients. The main outcome revealed that diabetic foot patients exhibited significantly higher IL-6 serum levels when compared with diabetic controls without foot condition. Meanwhile, WBC, ESR, CRP, HbA1c, and fasting glucose levels were also considerably elevated in the diabetic foot cohort. This gives further evidence for the assumption that diabetic foot condition is associated with an increase in systemic inflammatory processes, making IL-6 a good marker for differentiating diabetic patients with and without foot complications (Lee et al., 2026).
The significant increase in IL-6 levels confirmed in this work is in line with the findings of recent research connecting inflammatory process activation with the severity of diabetic foot condition. Wu et al. (2023) found out that IL-6 was associated with WBC, ESR, CRP, and procalcitonin in terms of increased levels among patients with severe Wagner grades, which means that IL-6, together with five other inflammatory markers, boosts the chances of developing diabetic foot condition among patients. This study conducted multivariable analysis and obtained the conclusion that a higher baseline level of IL-6 is positively associated with worse outcomes in ulcer cases, estimating OR as 1.008. Moreover, Shaikh et al. (2026) reported significantly higher serum IL-6, TNF-α, and hs-CRP concentrations in patients with diabetic foot ulcers compared with diabetic controls and described positive associations between these biomarkers and Wagner severity. Taken together, these findings provide external support for the substantially elevated IL-6 concentration observed in our diabetic foot cohort (Serban et al., 2024).
An important finding of this study was the association between inflammatory biomarkers and diabetic foot. Spearman correlation analyses revealed positive correlations between diabetic foot disease and WBC ($r = 0.608$, $P < 0.001$), ESR ($r = 0.719$, $P < 0.001$), CRP ($r = 0.768$, $P < 0.001$), and IL-6 ($r = 0.864$, $P < 0.001$).
Particularly strong correlations were observed for IL-6, which indicates that it more accurately reflects the inflammatory state of diabetic foot than the conventional indices seen in our data set(Pichu et al., 2017).
Furthermore, IL-6 correlated significantly with WBC, ESR, and CRP, with the strongest relationship with CRP ($r = 0.762$, $P < 0.001$). Although IL-6 is known to be a pro-inflammatory cytokine, biologically this significant association between IL-6 and CRP seems plausible because IL-6 is known to be a pro-inflammatory cytokine involved in the acute-phase response and has the capacity to promote hepatic CRP production. The combined findings of elevated IL-6 and CRP and their correlation appear to suggest an interconnected inflammatory pathway rather than two separate ones (Mohsin et al., 2024).
Further diagnostic analyses underscored the potential clinical relevance of IL-6. The ROC analysis revealed an excellent AUC of 0.999 for IL-6, compared with an AUC of 0.944 for CRP, 0.915 for ESR, and 0.851 for WBC. These results indicate good discrimination between diabetic foot patients and diabetic controls in our data se(Pan et al., 2025).
The findings generally align with what is already known about the diagnostic value of conventional inflammatory markers, although the magnitude of discrimination we observed for IL-6 in our sample was in fact greater than expected.
A 2024 systematic review and meta-analysis involving 10 studies and a total of 765 patients with infected diabetic foot ulcers reported that the pooled ROC-AUC of ESR was 0.93 (95% CI: 0.89-0.97), pooled sensitivity was 0.82 (95% CI: 0.76-0.88), pooled specificity was 0.83 (95% CI: 0.76-0.90), and pooled diagnostic odds ratio (OR) was 62.19 (95% CI: 36.77-105.17). The pooled sensitivity was 0.81 (95% CI: 0.63-0.94), pooled specificity was 0.91 (95% CI: 0.52-0.99), and pooled OR was 44.11 (95% CI: 24.05-94.43) for CRP, with 0.93 (95% CI: 0.89-0.97) as the pooled ROC-AUC for both markers combined. The pooled OR for procalcitonin was 75.29 (95% CI: 41.57-133.57) and that for WBC was 34.24 (95% CI: 19.68-59.21). Thus, comparisons of these pooled estimates from the literature with the present IL-6 AUC must be interpreted cautiously because they evaluated different diagnostic questions.

This study determined associations between biomarkers and baseline diabetic foot status, whereas the meta-analysis defined the diagnostic utility of each marker in the context of diagnosing active infection of a diabetic foot ulcer (Sangeeta et al., 2025).

Despite a strong correlation between IL-6 and diabetic foot presence, assessment of severity of diabetic foot based on Wagner grade (1–5) did not confirm this association. Levels of IL-6 were still higher in the presence of more severe diabetic foot (Wagner grade 4: 20.22 7.71 pg/mL, whereas it was lowest in grade 2: 17.81 4.49 pg/mL), but this difference was not significant (P = 0.786). The IL-6 level was also slightly higher in diabetic foot patients with disease progression than those with disease stabilization or regression (19.32 5.57 vs. 18.84 6.21 pg/mL; P = 0.631).
Taken together, these results indicate that baseline IL-6 was well correlated with the presence of diabetic foot, but a single baseline IL-6 level could not independently predict the degree of Wagner grade or disease progression in this context.
These results are in contrast to some literature which imply the ability of IL-6 to predict diabetic foot progression (Qin et al., 2024; Wu et al., 2024). The clinical characteristics of the participants are of relevance to the interpretation of our results. Although age, BMI, duration of diabetes, sex, smoking status, hypertension, dyslipidemia, and the presence of peripheral neuropathy were similar between groups, diabetic nephropathy was more frequent among patients with diabetic foot, although this difference was not statistically significant. In the diabetic foot group, 68.3% had infection, 33.3% had peripheral ischemia, 35.0% experienced progression during follow-up over 3-6 months, and 6.7% had to undergo amputation (Ding et al., 2026).
These results highlight the clinically diverse nature of diabetic foot and reinforce that serum biomarkers cannot replace consideration of clinical parameters, pressure and pulse assessments, diabetic control, and existing severity classifications, but should be integrated into the overall clinical picture (Mureșan et al., 2023).
The observation of higher HbA1c and fasting glucose levels in the diabetic foot group provides context; poor diabetic control increases the risk of impaired healing, poor infection control, micro- and macrovascular disease, and ongoing inflammatory activation. HbA1c was significantly higher in patients with diabetic foot (9.02 1.53%) versus controls (8.16 1.22%; P < 0.001). Therefore, the relationship between IL-6 and diabetic foot should not be interpreted as necessarily causal or independent of glycemic management. In future studies, multivariate analysis of several covariates including HbA1c, duration of diabetes, renal disease, neurological status, vascular findings, and other relevant parameters will help to determine whether IL-6 independently correlates with diabetic foot (Chen et al., 2026).

6. CONCLUSION

The outcome of this research will analyze whether serum interleukin-6 (IL-6) has a significant association with the development and severity of diabetic foot disease in patients diagnosed with type 2 diabetes. The increase in IL-6 levels might show the increase of inflammation associated with the development of diabetic foot disease, according to its severity; therefore, the IL-6 biomarker may provide a very useful approach for identifying patients at risk for severe diabetic foot disorder. Combined with other indicators such as clinical examination, glycemic status, and traditional inflammatory markers, IL-6 might be a great help in determining patients' condition. Further research is needed, though, to conclude how predictive this blood test is in terms of diabetic foot progression and other complications.

ACKNOWLEDGMENT

The authors are thankful to Al-Wahda Hospital administration and medical staff for their support and co-operation during the whole study. The authors are thankful to all the patients who cooperated in this study. diabetic foot disorder. Combined with other indicators such as clinical examination, glycemic status, and traditional inflammatory markers, IL-6 might be a great help in determining patients' condition. Further research is needed, though, to conclude how predictive this blood test is in terms of diabetic foot progression and other complications.

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