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# The Relationship between Growth Factors VEGF, PDGF and Pro-Inflammatory Cytokines in Diabetic Ulcers

**Hind AL-Hammami[1], Anfal Abdulhussain Jawad[2], Dhuha Abdullah Kadhim[3]**
[1]Faculty of Medical Sciences, Jabir Ibn Hayyan University for Medical and Pharmaceutical Sciences, Najaf, Iraq
[2,3]Faculty of Medicine, Jabir Ibn Hayyan University for Medical and Pharmaceutical Sciences, Najaf, Iraq



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**ABSTRACT**

***Objective:*** *The currenThe goal of research is to to test the blood levels in the peripheral areas of TNF-a, platelet-derived growth factor (PDGF), in addition vascular endothelial growth factor (VEGF) and examine their connection to the duration and severity of the infection, thus providing diagnostic proof for the prompt detection and management of diabetic patients.* ***Method:*** *Patients 50 involve men (n=25) and women (n=25) of both sexes, ages 31 to 71, with type 2 diabetes mellitus were included in this study. To act as controls, a cohort of 50 healthy persons involve men (n=25) and wemen (n=25) were matched by sex and age was chosen from the same population. Both patients and controls had around 3 milliliters of venous blood drawn. To separate the serum for the ELISA.* ***Results:*** *The results revealed the serum concentrations of TNF-a, was (49.85 ± 7.06) in infection group at p<0.05, while mean of TNF-a was (28.68 ± 6.44) in the non-infection group. The results show there were significantly higher in patients with Diabetic Ulcers contrasted to the non-infected team, at p<0.05. The serum levels of PDGF and VEGF in patients were (60.81 ± 6.82) and (9.81 ± 3.68) respectively showed significantly higher in patients compared to the non-infection group, at (P<0.05).* ***Novelty:*** *The concentration of these factors may serve as potential therapeutic targets and biomarkers for monitoring the treatment of diabetic foot ulcers.*

## INTRODUCTION

Diabetes is a type of metabolic disease associated with the body's metabolism. It among the most common glandular illnessesillness marked by high blood sugar levels brought on by deficiencies in insulin production, fun ction, or both [1]. High blood glucose levels (hyperglycemia) may lead to serious health problems. It can causes ulcers in diabetic patients. About 25% of people who endure the consequences of diabetes show ulcers on the feet during their lifetime. Ulcers and other complications are responsible for the hospitalization of 20% of the approximately three million people who are referred to hospitals for diabetes treatment every year [2]. The increase in blood glucose results in a rise in oxidative stress and a decline in the insulin-like growth factor-1 expression, which in turn affects thegrowth of both keratinocytes and fibroblastsand the epithelial tissue renewal and the mechanism of wound repair. The decrease in endothelial insulin/insulin-like growth factor-1 signaling is a key factor that delays the wound healing process [3]

The vascular endothelial growth factor (VEGF) family represents key Facilitators of Experiments have shown that angioplasty and vessel development involvingmouse with deletion genesmodels [4]. VEGF-A was initially recognized as a vascular The

component of penetration and later identified for its significant role affecting the formation of vascular cells inducing vasodilation, and preventing endothelial cellCell death. Additionally, VEGF-A plays a pivotal function for maintaining of balance of the vascular system in various tissues, and its participation in the etiology of several diseases including tumor development and metastasis, as well as diabetic and hypertensive retinopathy [5]. VEGF is a cytokine that is responsible for inducing angiogenesis, cell migration, proliferation, and synthesis of extracellular fluid proteins [6]. Fibroblast growth factors (FGFs) provokes angiogenesis and proliferation of fibroblasts, resulting in granulation tissue.During the initial phases of wound recovery process, newly formed tissue gradually fills the wound space and occupies the wound cavity [7].Platelet-derived growth factor (PDGF) represents a family of dimeric isoforms that have regulatory effects on connective tissue cells and several other cell types. PDGF was initially discovered as a platelet-derived constituent released into the serum in conjunction with the blood coagulation process [8].TNF-α The interleukin is multifaceted formed by cells including macrophages, keratinocytes and mast cells [9], TNF-α plays a beneficial role in the wound healing processplays an significant role in the production of collagen [10]. Chronic diabetic wounds are closely related to the state of permanent inflammation, increased pro-inflammatory cytokines, and defects in the expression of growth factors [11].

## RESEARCH METHOD

In 2025, this case-control research was completed.Patients and healthy individuals who visit the Diabetic and Endocrine Center of Al-Sadder Medical City in Najaf as inpatients and outpatients make up the research groups and controls. 50 patients involve men (n=25)and wemen (n=25)of both sexes, ages 31 to 71, with type 2 diabetes mellitus were included in the present study, To act as controls, a cohort of 50 healthy personsinvolve men (n=25) and wemen (n=25) were matched by sex and age was chosen from the same population.

Both patients and controls had around 3 milliliters of venous blood drawn. To separate the serum for the ELISA assessment of TNF-α levels, Platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), the blood samples were centrifuged for 10 minutes at 3000 rpm. An unopened kit can be stored at 2-8 $^{o}$C for 6 months.

### Statistical analysis

The findings of the epidemiological investigation were computed using percentages and numbers. The data were analyzed for normality, and they were normal. Since ANOVA was used to analyze them. Pearson correlation was used to investigate the correlation between variables. The T-test was employed to evaluate the mean value and standard error (SE) for each value. A P-value of $<0.05$ was believe as statistically respectable.

## RESULTS AND DISCUSSION

### *Results*

The basic symptoms including gender, age, were contrasted between the infected and non-infection groups indicating comparability (Table1). The mean gender was 50.38 ± 5.12. In infection group compared with 56.77 ± 8.02 of control, according to mean of age was 46.28 ±6.83 Compard with mean of control was 58.56 ± 8.45 there no notable variations were detected between the two study groups gender and age at (P>0.05).TNF-a amounts, PDGF and VEGF in serum were much greater in the team that was infected compared with the member free from infection with differences that are markedly noteworthy (P<0.05)).The results displayed the serum concentrations of TNF-α, was (49.85 ± 7.06) in infection group at p<0.05 , while mean of TNF-α was (28.68 ± 6.44) in the non-infection group. By result show there were markedly increased by patients with Diabetic Ulcers compared with the non-infection group (p<0.05). Serum levels of PDGF and VEGFin patients were (60.81 ± 6.82)and (9.81 ± 3.68) respectively showed higher in patients Overflowing in the set that was not ill with statistically important (P<0.05).

**Table 1.** The two patient groups baseline characteristics are compared.

| Characteristics | Infection group (n=50) mean±SD | Non-Infection group (n=50) mean±SD | P- value |
|---|---|---|---|
| Gender (Male/Female) | 50.38 ± 5.12 | 56.77 ± 8.02 | 0.336 |
| Age (31-71) | 46.28 ±6.83 | 58.56 ± 8.45 | 0.356 |

Notes: Mean ± SD are considered as mean ± standard deviation. A *P*-value <0.05 is significant.

**Table 2.** Comparison of serum levels of TNF-a, PDGFand VEGFbetween the patients and control.

| Indicator | Diabetic foot mean±SD | Control mean±SD | P-value |
|---|---|---|---|
| **TNF-a (ng/L)** | **49.85 ± 7.06** | **28.68 ± 6.44** | **0.037** |
| **PDGF (ng/L)** | **60.81 ± 6.82** | **49.38 ± 4.12** | **0.011** |
| **VEGF (ng/L)** | **9.81 ± 3.68** | **3.83 ± 1.81** | **0.021** |

Notes: Mean ± SD are considered as mean ± standard deviation. A *P*-value <0.05 is significant.

### *Discussion*

The current stady mainly conducts inquiries the association among inflammatory cytokines TNF-a, growth factors in patients with diabetic foot.These affect in determining

infection severity, aiming to provide valuble medical direction that support early therapeutic interference, so enhancing fate of the individual along improving overall level of living quality.The study showed that patients age and gendar there were no affact on severity of diabetic foot, this result disagree with another study [12], demonstratedthat people with DFU between the ages of 50 and 59 exhibited a higher risk of amputation compared with extra age categories. This inceased risk in those age groups may be attributed to the substantial economic and lifestyle pressures commonly experienced during the pre-retirement period, which can limit opportunities for adequate diabetes self-management education. Additionally, individuals within this age group may show inconsistent adherence to antidiabetic medicines due to occupational and family responsibilities, thereby increasing the probability of severe complications, such as amputation[13].The study results displayed a higher concentration of TNF-α in those with diabetes and foot ulcers. Itshows that foot ulcers provoke TNF more than diabete.TNF-α plays a beneficial role in the technique of wound recovery and shows its mechanism by reducing the formation of granulation tissue, but reducing the expression and concentration of this factor plays an essential role in the production of collagen. This factorcontrols the actions certain

keratinocytes, Vascular tissue cells and astrocytes. Furthemore, It plays an significant role in the production of metalloproteinases [14]. Thus, TNF increases in the response to the inflammation and exhibits its responses.TNF-a plays a pivotal role in the regulating Th17 alerting routeby its interactionBetween cells in tissues and dendrites stimulating IL -17 and IL-23 production to supportequilibrium of organs. Nevertheless, Overproduction of TNF-a cause lead to abnormal tissue harm and contribute to altering the immune system's equilibrium[15]. The serum concentration of PDGF was significantly higher in patients compared with uninfected subjects, this result agreement with another study that shows that PDGF concentration increases in response to metabolic disorders of diabetes and also damages patients with foot ulcers[16], PDGF was initially identified as a platelet-derived constituent released into the serum in conjunction with the blood coagulation process. The results also showed a increase in the concentration of VEGF in diabetic ulcer patientscompared with healthy subjects This result can be explained as follows vascular endothelial growth factor is one of the desired genes that intervenes in the wound healing process and acts as an endothelial cell mitogen and chemotactic [17]. The mechanism of this factor is not only by stimulating angiogenesis but also by increasing the permeability of the vessel and facilitating wound healing. VEGF is a cytokine that is responsible for inducing angiogenesis, cell migration, proliferation, and synthesis of extracellular fluid proteins [18]. In diabetic patients, due to impaired insulin secretion, The cells are unable to operate the

glucose inside the vessels in such a way that the inside of the cells is free of glucose and glucosemia, while the amount of glucose in the blood vessels and capillaries is high. Over time, high glucose can cause damage in the capillaries and nerves in such a way that improper blood supply and nerve damage in the lower limbs make them prone to diabetic ulcers [19].

## CONCLUSION

**Fundamental Finding :** Pro-inflammatory and inflammatory mediators are significantly elevated in patients with diabetes, particularly in those with diabetic foot ulcers, indicating a strong association between inflammatory response intensity and disease severity. **Implication :** These mediators can serve both as biomarkers for disease progression and as potential therapeutic targets, offering strategic value for improving clinical management and treatment outcomes of diabetic foot ulcers. **Limitation :** The conclusion does not incorporate a broader range of immunological markers, limiting the comprehensiveness of the inflammatory profile assessment. **Future Research :** Further investigations should include additional immunological markers such as IL-1 and IL-6 and explore preventive strategies emphasizing hygiene practices among individuals with diabetic foot ulcers.

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***Hind AL-Hammami (Corresponding Author)**
Faculty of Medical Sciences, Jabir Ibn Hayyan University for Medical and Pharmaceutical Sciences, Najaf, Iraq
Email: hind.f.al.hammami@jmu.edu.iq

**Anfal Abdulhussain Jawad**
Faculty of Medicine, Jabir Ibn Hayyan University for Medical and Pharmaceutical Sciences, Najaf, Iraq
Email: anfal.a.jawad@jmu.edu.iq

**Dhuha Abdullah Kadhim**
Faculty of Medicine, Jabir Ibn Hayyan University for Medical and Pharmaceutical Sciences, Najaf, Iraq
Email: dhuha.a.kadhum@jmu.edu.iq