



## A CROSS SECTIONAL STUDY TO EVALUATE THE SERUM LEVELS OF HbA1c, INTERLEUKIN-6 AND OXIDATIVE STRESS LEVELS AND THEIR CLINICAL CORRELATION IN DIABETES MELLITUS PATIENTS WITH AND WITHOUT DIABETIC FOOT ULCERS IN TERTIARY CARE HOSPITAL

Sangamesh B Tondare <sup>1</sup>, Shradha S Tondare <sup>2</sup>, Harish G Bagewadi <sup>3\*</sup>, Shivprasad S <sup>4</sup>,  
Renuka S Melkundi <sup>5</sup>, Rohini Kallur <sup>6</sup>, Shivalee A <sup>7</sup>

Assistant Professor<sup>1</sup>- Department of General Surgery, Gulbarga Institute of Medical Sciences, Kalaburagi.

Assistant Professor<sup>2</sup>- Department of Obstetrics and Gynecology, Gulbarga Institute of Medical Sciences, Kalaburagi.

Associate Professor<sup>3\*</sup> - Department of Pharmacology, Gulbarga Institute of Medical Sciences, Kalaburagi.

Associate Professor<sup>4</sup>- Department of Biochemistry, Gulbarga Institute of Medical Sciences, Kalaburagi.

Nodal Officer MRU, Professor & Head<sup>5</sup>- Department of ENT, Gulbarga Institute of Medical Sciences, Kalaburagi

Research Scientist-I<sup>6</sup>-Multi-Disciplinary Research Unit, Gulbarga Institute of Medical Sciences, Kalaburagi

Research Scientist-II<sup>7</sup>-Multi-Disciplinary Research Unit, Gulbarga Institute of Medical Sciences, Kalaburagi

**\*Corresponding Author: Harish G Bagewadi**

Associate Professor<sup>3\*</sup> - Department of Pharmacology, Gulbarga Institute of Medical Sciences, Kalaburagi.

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### Abstract:

**Background:** Type II diabetes mellitus (T2DM) is strongly associated with oxidative stress, which arises from an imbalance between excessive reactive oxygen species (ROS) generation and insufficient antioxidant defense. Diabetic foot ulcers (DFUs), affecting nearly 15% of individuals with diabetes, develop due to chronic hyperglycemia, impaired immune function, and secondary infections. Elevated inflammatory mediators such as interleukin-6 (IL-6) exacerbate oxidative stress, interfere with insulin signaling, and worsen complications including neuropathy,

nephropathy, and retinopathy. **Aims & Objectives:** To study the association of serum levels of HbA1c, IL-6, (8-OHdG) and their clinical correlation in diabetic foot ulcer patients.

**Methods:** A total of 80 participants were enrolled and divided into two equal groups: Group 1 (n=40) with T2DM without DFU, and Group 2 (n=40) with T2DM and DFU. Blood samples were analyzed for random blood sugar (RBS), glycated hemoglobin (HbA1c), lipid profile, 8-hydroxy-2-deoxyguanosine (8-OHdG) and IL-6 levels.

**Results:** In the present study, Patients with DFU had significantly higher serum concentrations of 8-OHdG ( $97.57 \pm 6.2$  ng/ml) and IL-6 ( $4.96 \pm 1.4$  pg/ml) compared with diabetic patients without DFU ( $48.11 \pm 2.67$  ng/ml and  $2.66 \pm 1.44$  pg/ml, respectively;  $p < 0.05$ ). Both markers showed a strong positive correlation with DFU severity, with correlation coefficient of (r) = 0.85 for 8-OHdG and (r) = 0.81 for IL-6. In addition, RBS and HbA1c levels were significantly higher in DFU patients and these glycemic markers also correlated with ulcer grades.

**Conclusion:** Poor glycemic control is closely linked with elevated oxidative stress and inflammation in DFU patients. Biomarkers such as 8-OHdG and IL-6 may serve as valuable tools for identifying high-risk individuals and tailoring interventions. Incorporating oxidative stress monitoring into personalized treatment strategies could improve outcomes and reduce the burden of diabetes-related complications.

**Keywords:** diabetic foot ulcer, oxidative stress, lipid profile, 8-OHdG, IL-6, ELISA, HbA1c

**Introduction-** Diabetic foot complications represent a major medical, social, and economic challenge worldwide. Type II Diabetes mellitus (T2DM) is associated with both micro vascular and macro vascular complications, including neuropathy, nephropathy, retinopathy, peripheral vascular disease, atherosclerosis, and recurrent infections [1]. Among these, DFUs are one of the most severe outcomes, arising from a combination of peripheral arterial disease, neuropathy, impaired immunity, and infection. These conditions impair blood flow, angiogenesis, and host defenses, ultimately leading to ulcer formation, gangrene, and in severe cases, amputation [2].

The clinical severity of DFU is commonly graded using Wagner's classification: Grade 0 (intact skin with deformity), Grade 1 (superficial ulcer), Grade 2 (deep ulcer involving full-thickness tissue), and Grade 3 (deep abscess or osteomyelitis), and Grade 4 (localized gangrene of the forefoot), and Grade 5 (extensive gangrene) [3]. Several studies indicate that improved glycemic control enhances wound healing and reduces the risk of amputation [4], although the exact relationship between HbA1c and ulcer healing remains incompletely understood. Chronic hyperglycemia promotes excessive ROS formation, resulting in oxidative stress and endothelial dysfunction [5]. While physiological levels of ROS are required for pathogen defense and wound repair persistent oxidative stress causes redox imbalance, DNA damage, and impaired healing [6]. A key indicator of oxidative DNA injury is 8-hydroxy-2-deoxyguanosine (8-OHdG), a modified guanine base formed under oxidative stress conditions [7]. Elevated 8-OHdG reflects cumulative DNA damage in both mitochondrial and nuclear DNA. Inflammatory mediators also contribute to DFU pathogenesis. Interleukin-6 (IL-6), a cytokine produced by immune and stromal cells, plays an important role in initiating wound healing by recruiting macrophages and stimulating fibroblast activity [8]. However, sustained IL-6 elevation contributes to chronic inflammation and worsens tissue damage.

Given this background, the present study was designed to evaluate the serum levels of HbA1c, 8-OHdG, and IL-6 in type II diabetes mellitus patients with and without DFU, and to analyze their correlation with ulcer severity.

**Methodology:** This was a hospital-based, single centre, cross-sectional study. The patients were recruited from the department of General Surgery. The research study was carried out from February 2025 to September 2025. The Ethical clearance was obtained from the Institutional Ethics

Committee (Approval No: GIMS/KLB/PHARMA/IEC/206/2023-24). A total of 80 individuals aged 30–65 years with a diagnosis of type 2 diabetes mellitus were included. They were divided into two groups: Group I: 40 patients with T2DM without foot ulcers. Group II: 40 patients with T2DM and diabetic foot ulcers. Inclusion criteria: Patients with type II diabetes mellitus patients aged 30–65 years, with and without diabetic foot ulcers.

Exclusion criteria: Patients with type 1 diabetes, thyroid disease, rheumatologic, hepatic, renal, cardiac, autoimmune disorders, malignancy, congenital vascular disorders, pregnancy.

Sample size calculations were done by the Epi Info a program version 7.1 developed by the Center for Disease Control and Prevention as explained in the previous study done by Sullivan KM et al [9]. Using a reported diabetic foot ulcers prevalence of 6% from Zhang P et al. [10], with 95% confidence, 5% margin of error, an odds ratio of 10, and 80% study power, the minimum sample was calculated to be 80 participants.

**Data collection-** All the study participants provided written informed consent prior to enrollment. The data was collected at Multi disciplinary research unit. The venous blood (5 ml) was collected from each participant. Samples were centrifuged at 3000 rpm for 10 minutes, and serum was separated and stored at 2–8 °C until analysis. Biochemical parameters assessed were: Random blood sugar, HbA1c, and lipid profile (HDL, LDL, triglycerides). The following Biomarkers were assessed: 8-hydroxy-2-deoxyguanosine (8-OHdG), measured using a commercial ELISA kit (Elabscience, Cat. No. E-EL-0028; sensitivity 0.94 ng/ml; detection range 1.56–100 ng/ml). Interleukin-6 (IL-6), measured using a human IL-6 ELISA kit (Elabscience, Cat. No. E-EL-H6156; sensitivity 0.94 pg/ml; detection range 1.56–100 pg/ml). The coefficient of variation for both assays was <10%.

**Statistical Analysis-** Data was entered into Microsoft Excel 2017 and analyzed using SPSS version 27. Continuous variables were expressed as Mean  $\pm$  standard deviation, while categorical variables were presented as counts and percentages. Comparisons between groups were made using Student's *t*-test. Correlations were assessed using Pearson's correlation coefficient. The *p*-value  $\leq 0.05$  was considered statistically significant.

## Results:

**Table 1. Demographic characteristics of the study population.**

| Parameters     | Descriptive characteristics | Diabetics(n=40)<br>Group I<br>Mean $\pm$ SD | Diabetic foot ulcers<br>(n=40)<br>Mean $\pm$ SD | p-value     |
|----------------|-----------------------------|---------------------------------------------|-------------------------------------------------|-------------|
| Age            | (years)                     | 55.32 $\pm$ 1.38                            | 58.20 $\pm$ 0.34                                | 0.723       |
| Gender         | Male                        | 25 (62.5%)                                  | 32 (80%)*                                       | $\leq 0.05$ |
|                | Female                      | 15 (37.5%)                                  | 8 (20%)*                                        | $\leq 0.05$ |
| BMI            | kg/m <sup>2</sup>           | 34.4 $\pm$ 1.72                             | 39.8 $\pm$ 4.36*                                | $\leq 0.05$ |
| Smoking status | Smoker                      | 22 (57.5%)                                  | 28 (70%)*                                       | $\leq 0.05$ |
|                | Non-smoker                  | 18 (32.5%)                                  | 12 (30%)                                        | 0.835       |

\**p*<0.05, versus Diabetic group, Data are presented as mean and standard deviation; Student's *t*-test was applied. *p*-value with\* indicates statistical significance (<0.05). BMI-Body mass index, (n) = number

Table 1. The mean age of the diabetic group was 55.32 $\pm$ 1.38 years, while DFU patients had a mean age of 58.20 $\pm$ 0.34 years. Male predominance was observed in both groups, with 80% of DFU patients being male. Smoking was more frequent among DFU patients (70%) compared to diabetics without ulcers (57.5%). Mean BMI was significantly higher in the DFU group (39.8 $\pm$ 4.36 vs. 34.4 $\pm$ 1.72 kg/m<sup>2</sup>, *p* < 0.05).

**Table-2. Showing the counts, percentage and grading of diabetic foot ulcers (DFU) according to Wagner's classification.**

| Different Grades of DFU | Descriptives -                          | Counts & Percentages- n (%) |
|-------------------------|-----------------------------------------|-----------------------------|
| Grade- I                | Superficial ulcer                       | 06 (15%)                    |
| Grade- II               | Deeper, full thickness extension        | 12 (30%)                    |
| Grade- III              | Deep abscess formation or Osteomyelitis | 15 (37.5%)                  |
| Grade- IV               | Partial gangrene of forefoot            | 07 (17.5%)                  |

Data are presented as numbers and percentages. Different grades of Wegener's classification of diabetic foot ulcers. n= number,

In table 2, among DFU patients, 15% (n=6) were classified as Grade I, 30% (n=12) as Grade II, 37.5% (n=15) as Grade III, and 17.5% (n=7) as Grade IV. No patients presented with Grade 0 or Grade V ulcers.

**Table 3. Comparison of serum HbA1c, S.TG, S.LDL, S.HDL levels in diabetes mellitus patients with and without diabetic foot ulcers.**

| Serum Biomarker | Diabetics Mean±SD (n=40) | Wegener's stage classification of DFU (Mean±SD) |                          |                            |                            |
|-----------------|--------------------------|-------------------------------------------------|--------------------------|----------------------------|----------------------------|
|                 |                          | I (n=6)                                         | II (n=12)                | III (n=15)                 | IV (n=7)                   |
| HbA1c (%)       | 8.1±1.12                 | 8.42±1.74                                       | 8.9 ±1.96*               | 9.2 ±1.90 <sup>*,†,‡</sup> | 9.8±1.68 <sup>*,†,‡</sup>  |
| S.TG (mg/dL)    | 173±1.3                  | 201±66.5*                                       | 242±3.5 <sup>*,†</sup>   | 285±2.1 <sup>*,†,‡</sup>   | 296±8.4 <sup>*,†,‡</sup>   |
| S.LDL (mg/dL)   | 135±2.01                 | 138±3.22                                        | 145±4.31 <sup>*,†</sup>  | 155±2.45 <sup>*,†,‡</sup>  | 185±3.38 <sup>*,†,‡</sup>  |
| S.HDL (mg/dL)   | 37.1±1.25                | 36.2±1.32                                       | 32.4±1.44 <sup>*,†</sup> | 30.2±1.38 <sup>*,†,‡</sup> | 24.5±1.28 <sup>*,†,‡</sup> |

Data are presented as Mean and Standard Deviation; Student's t-test was applied. (n) = number

\*p<0.05, versus Diabetic group, †p<0.01, versus DFU-I, ‡p<0.05, versus DFU-II

Table 3. Serum HbA1c and triglyceride levels were significantly higher in DFU patients compared to diabetics without ulcers. LDL levels also increased with higher DFU grades, whereas HDL levels decreased progressively with severity.

**Table 4. Comparison of serum HbA1c, IL-6 and oxidative stress levels in diabetes mellitus patients with and without diabetic foot ulcers.**

| Variables                                   | RBS (mg/dL)              | S.TG (mg/dL)             | S. HDL (mg/dL)         | S.LDL (mg/dL)            | S. 8-OHdG (ng/ml)        | S. IL-6 (pg/ml)          |
|---------------------------------------------|--------------------------|--------------------------|------------------------|--------------------------|--------------------------|--------------------------|
| <b>HbA1c ≤ 7</b><br>6.72±0.16<br>(n = 10)   | 210±11.6                 | 230±13.5                 | 35±4.3                 | 140±10.8                 | 47.37± 2.4               | 2.02±0.42                |
| <b>HbA1c ≥7-9</b><br>7.52±1.31<br>(n = 38)  | 259±22.4 <sup>#</sup>    | 237±10.3                 | 30±2.2 <sup>#</sup>    | 160±8.7 <sup>#</sup>     | 84.37±5.8 <sup>#</sup>   | 3.81±1.73 <sup>#</sup>   |
| <b>HbA1c &gt;9</b><br>9.58±2.36<br>(n = 32) | 290±18.2 <sup>#,††</sup> | 296±16.5 <sup>#,††</sup> | 26±1.3 <sup>#,††</sup> | 188±13.5 <sup>#,††</sup> | 97.3±7.3 <sup>#,††</sup> | 4.97±1.4 <sup>#,††</sup> |

Data are presented as Mean and Standard Deviation; Student's t-test was applied. (n) = number

#p<0.05 versus HbA1c  $\leq 7$  , ††p<0.05 versus HbA1c  $\leq 7-9$  , S. 8-OHdG- serum 8-hydroxydioxy-2-guanosine, S. IL-6- serum Interleukin-6. DFU- diabetic foot ulcer.

From table 4, it was observed that serum RBS, LDL, S.8-OHdG, S. IL-6 levels were high in diabetic patients with HbA1c  $\geq 7-9$  than diabetic patients with HbA1c  $\leq 7$  which was statistically significant (<0.05). The increased level of serum TG was not statistically significant.

From table 4, it was also observed that serum RBS, LDL, S.8-OHdG, S. IL-6 levels were high in diabetic patients with HbA1c >9 than diabetic patients with HbA1c  $\leq 7-9$  and HbA1c  $\leq 7$  which was statistically significant (<0.05).

**Table 5. Represents the Mean  $\pm$  SD values for serum 8-OHdG and IL-6 levels among diabetes mellitus patients with and without diabetic foot ulcers.**

| Serum Biomarker | Diabetics (n=40)<br>Mean $\pm$ SD | Wegener's stage classification of DFU (Mean $\pm$ SD) |                       |                      |                      |
|-----------------|-----------------------------------|-------------------------------------------------------|-----------------------|----------------------|----------------------|
|                 |                                   | I (n=6)                                               | II (n=12)             | III (n=15)           | IV (n=7)             |
| 8-OHdG (ng/ml)  | 48.11 $\pm$ 2.67                  | 52.57 $\pm$ 2.82                                      | 72.57 $\pm$ 3.57*,†,‡ | 85.57 $\pm$ 5.8*,†,‡ | 97.57 $\pm$ 6.2*,†,‡ |
| IL-6 (pg/ml)    | 2.66 $\pm$ 1.44                   | 2.82 $\pm$ 0.85                                       | 3.73 $\pm$ 1.62*,†,‡  | 4.22 $\pm$ 1.7*,†,‡  | 4.96 $\pm$ 1.4*,†,‡  |

Data are presented as Mean and Standard Deviation; Student's t-test was applied. (n) = number, \*p<0.05, versus Diabetic group , †p<0.01 versus DFU-I , ‡p<0.05 versus DFU-II, DFU- diabetic foot ulcer, S. 8-OHdG- serum 8-hydroxydioxy-2-guanosine, S. IL-6- serum Interleukin-6.

From table-5, It was observed that serum levels of 8-OHdG and IL-6 among DFU were high compared to diabetics. In addition, serum 8-OHdG and IL-6 levels were high among Grade IV and III compared to Grade II and I, which was statistically significant.

Increase in serum 8-OHdG, IL-6 levels was not statistically significant when DFU-I was compared with diabetic patients.

**Table 6. This presents the correlation between serum HbA1c and serum 8-OHdG, IL-6 levels in diabetes mellitus patients without diabetic foot ulcers**

| Parameters                          | Diabetics-<br>Correlation ( r )-value<br>- 8-OHdG<br>- IL-6 | p-<br>value    | DFU,<br>Correlation ( r )-value<br>- 8-OHdG<br>- IL-6 | p-<br>value    |
|-------------------------------------|-------------------------------------------------------------|----------------|-------------------------------------------------------|----------------|
| HbA1c $\leq 7$<br>6.72 $\pm$ 0.26   | 0.31<br>0.28                                                | <0.05<br>0.21  | 0.44<br>0.32                                          | <0.05<br>0.13  |
| HbA1c $\geq 7-9$<br>7.52 $\pm$ 1.41 | 0.51<br>0.46                                                | <0.05<br><0.05 | 0.62<br>0.68                                          | <0.05<br><0.05 |
| HbA1c > 9<br>9.58 $\pm$ 2.36        | 0.78<br>0.75                                                | <0.05<br><0.05 | 0.85<br>0.81                                          | <0.05<br><0.05 |

Data are presented as Mean and Standard Deviation; Pearson's correlation regression test was applied. (n)= number, (r) value: Pearson coefficient, DFU- diabetic foot ulcer, S. 8-OHdG- serum 8-hydroxydioxy-2-guanosine, S. IL-6- serum Interleukin-6

In table 6, In Diabetes group, it was observed that a positive correlation was found between serum level of HbA1c $\leq 7$  versus serum 8-OHdG levels which was statistically significant (p<0.05). There was weak positive correlation of HbA1c levels of  $\leq 7$ , (6.72 $\pm$ 0.26) with serum levels of IL-6 but, it was not statistically significant.

There was strong positive correlation found between serum levels of HbA1c $\leq 7-9$ , (7.52 $\pm$ 1.41) versus serum levels of 8-OHdG, IL-6 which was statistically significant (p<0.05).

There was strong positive correlation found between serum levels of HbA1c > 9, ( $9.58 \pm 2.36$ ) versus serum levels of 8-OHdG, IL-6 which was statistically significant ( $p < 0.05$ ).

In DFU, it was observed that a positive correlation was found between serum level of HbA1c  $\leq 7$  versus serum 8-OHdG levels which was statistically significant ( $p < 0.05$ ). There was weak positive correlation of HbA1c levels of  $\leq 7$ , ( $6.72 \pm 0.26$ ) with serum levels of IL-6 but, it was not statistically significant.

There was strong positive correlation was found between serum level of HbA1c  $\leq 7-9$ , ( $7.52 \pm 1.41$ ) versus serum levels of 8-OHdG, IL-6 which was statistically significant ( $p < 0.05$ ).

There was strong positive correlation was found between serum level HbA1c > 9, ( $9.58 \pm 2.36$ ) versus serum levels of 8-OHdG, IL-6 which was statistically significant ( $p < 0.05$ ).

**Discussion:** The present study evaluated HbA1c, 8-OHdG, and IL-6 levels in patients with type 2 diabetes, comparing those with and without diabetic foot ulcers. In our study, from table 1, we found that the diabetic patients were found to be more common in the 6th decade of life, with a mean age of ( $56.47 \pm 2.82$ ) years predominantly male and had higher rates of smoking. These demographic patterns are consistent with earlier studies by Yazdanpanah L et al [11], which also describe male predominance in DFU cases, possibly due to greater occupational stress on the feet and lower adherence to preventive care. In the current study, 70 % of the patients presented with a history of smoking. The previous study also concluded that smoking has a poor prognosis in patients with foot ulcers. Smoking affects the small blood vessels and slows down wound healing [11]. The mean HbA1c at presentation in our study was ( $8.9 \pm 1.96$ ) which is similar in a previous study by Fesseha BK et al [12]. Glycemic control played a central role in our findings. HbA1c levels were significantly higher among DFU patients than in those without ulcers. This aligns with previous research demonstrating that elevated HbA1c is associated with delayed wound healing and an increased likelihood of ulcer development. As HbA1c reflects long-term glucose regulation, poor control not only contributes to hyperglycemia but also amplifies the risk of chronic complications, including foot ulceration. Trauma has been established as one of the important causative factors for DFU [13]. In DFU, our study 70% of the patients had a preceding history of trauma.

In our study, from the table 2, according to Wagner's classification of diabetic foot ulcers, Majority of the patients were in 37.5% (n=15) as Grade III, followed by 30% (n=12) as Grade I, 17.5% (n=7) as Grade IV, 15% (n=6) as Grade I respectively. No patients presented with Grade 0 or Grade V ulcers.

From the table 3, we found there was strong positive correlation of HbA1c levels with different grades of DFU according to Wegener's classification. It was evident that the serum HbA1c, LDL, HDL levels were high in DFU-I patients compared to diabetics but it was not statistically significant. In addition, serum HbA1c, LDL levels were high among DFU Grade IV and III compared to Grade II and I, which was statistically significant. Our findings are in accordance with previous study done by Akyuz S et al. which showed that increase in diabetic foot ulcer grading, severity is associated with increased HbA1c levels, and HbA1c can be considered as an independent biomarker in assessing wound healing in patients with DFU [14]. Hyperglycemia reduces keratinocyte migration and proliferation and contributes to oxidative stress through the production of reactive oxygen [15]. However, previous studies done by Zubair et al [15] and Ozenc et al [16], established a contradictory correlation between HbA1c level and Wagner classification. The Zubair et al [15], study found a statistically significant, whereas the study by Ozenc et al [16] found a statistically insignificant correlation.

In our study, from table 4, we found that a high level of random blood sugar and HbA1c levels found in diabetics group and DFU groups, with the latter group having a greater increase as a consequence of poorly controlled glycaemia in these subjects. In this study, from table 5 it was evident that, the correlation coefficients obtained in this study revealed a strong association between these two parameters (RBS and HbA1c) and the level of (8-OHdG) in diabetic subjects with and

without foot ulcers. One of the characteristic features of chronic diabetes is lipid peroxidation resulting from excessive reactions of free radicals with polyunsaturated fatty acids (PUFAs) in cell membranes. This lipid peroxidation in turn leads to elevated production of free radicals [17].

As with other biomolecules, deoxyribonucleic acid (DNA) is also susceptible to damage induced by free radicals. In our study, from table 5, it was found that an elevated level of 8-OHdG in DFU group ( $97.57 \pm 6.2$ ) when compared to diabetic group ( $48.11 \pm 2.67$ ) which was statistically significant. This finding is in agreement with previous study done by Zitouni et al [18]. The elevated 8-OHdG levels observed in our study are consistent with sparse observations investigating oxidative stress in diabetes and its complications [19]. Similarly, other studies have demonstrated a correlation between high 8-OHdG levels and the severity of diabetes complications, including nephropathy, cardiovascular diseases and the risk of death in patients with type-2 diabetes [20]. In our study, from table 4, it was evident that there was increase in the level of (IL-6) in DFU patients with Mean  $\pm$  SD ( $4.76 \pm 2.67$ ) pg/ml when compared with the diabetic group ( $2.03 \pm 1.44$ ) pg/ml with a statistically significant difference of ( $p \leq 0.01$ ). The results of the current study found that there was high level of interleukin-6 levels in the serum of DFU and diabetic patients. This may be due to result of increase in the inflammatory process that leads to the response of the immune system and the activation of immune cells. Our findings in this study are consistent with other previous studies done by Korkmaz P, et al [21], where it is observed that diabetic foot disease is associated with high levels of interleukin-6. Our study findings with higher serum IL-6 levels in DFU patients is also in accordance with previous study done by Zubair M, et al [22]. From the literature, it was observed that (IL-6) reduces insulin sensitivity in the body and thus the concentration of (IL-6) independently predicts the future risks of developing type 2 diabetes and its complications [23]. A previous study by Karakas A et al [24], has shown that patients with diabetic foot ulcerations at various stages had higher levels of IL-6 levels of plasma compared to diabetic patients without foot ulcerations. In one of the previous study it was observed that in patients with diabetic foot ulcer they had higher plasma levels of IL-6 which could be linked to foot ulcers pathogenesis by micro vascular and inflammatory mechanisms [25]. Previous studies infer that serum oxidative stress biomarkers are recently recognized as potentially valuable tools in diagnostics and management of DF [26]. Namely, enhanced oxidative stress triggers the activation of the nuclear factor kappa B (NF- $\kappa$ B) pathway, which leads to increased production of pro-inflammatory mediators [27]. On the other hand, infiltration of leukocytes to the site of injury further contributes to ROS generation. As recently suggested, these biomarkers could add diagnostic and prognostic information in terms of concomitant infection and the risk of amputation and post-operative mortality [28]. Oxidative stress and inflammation affect the wound healing process, but whether these processes could differentiate between an infectious and non-infectious state is still insufficiently explored. Indeed, increased oxidative stress and inflammation are common features of both infectious and non-infectious diseases, such as cardio metabolic diseases, including diabetes mellitus [29].

However, the study's limitations include small sample size, inclusion of only type 2 diabetes mellitus patients. Additionally, minor infections in some participants could have influenced the inflammatory markers, although we made efforts to exclude those with overt illnesses. Our study strengths include- Our study finding add to the gap in the literature and explores the association of DNA damage, oxidative stress and inflammation mediators and their interplay in diabetes foot ulcers. Correlation analyses further emphasized the interplay between glycemic control, oxidative stress, and inflammation. HbA1c correlated positively with both 8-OHdG and IL-6, while 8-OHdG also correlated with IL-6. These results suggest that chronic hyperglycemia may drive a cycle of oxidative stress and inflammatory activation, ultimately contributing to impaired healing and progression of DFU.

**Conclusion:** This study demonstrates that poor glycemic control in type 2 diabetes is associated with higher levels of oxidative DNA damage (8-OHdG) and inflammatory activity (IL-6), both of

which were significantly elevated in patients with DFU compared to those without. These biomarkers showed strong correlations with HbA1c and with ulcer severity, indicating their potential role as predictors of disease progression. Future research should include larger, multicenter studies with extended follow-up to validate these findings. Randomized controlled trials are also needed to explore whether interventions such as antioxidant or anti-inflammatory therapies can reduce biomarker levels and improve wound healing outcomes. Comparative studies of 8-OHdG alongside other oxidative stress markers may further clarify its diagnostic and prognostic utility. Incorporating biomarkers such as 8-OHdG and IL-6 into clinical practice could provide a more comprehensive approach to risk assessment, guide personalized treatment strategies, and ultimately improve outcomes in patients at risk of DFU.

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