

**Evaluation of Serum Interleukin-6 Levels in Diabetic Foot Ulcers.****Santosh Kumari Sharma<sup>1</sup>, Sunil Kumar Bairwa<sup>2</sup>, Devendra Ajmera<sup>3</sup>, Atul Kumar Sharma<sup>\*4</sup>**<sup>1</sup>Assistant Professor, Dept. of Biochemistry, GMC, Kota<sup>2</sup>Associate Professor, Dept. of Biochemistry, GMC, Kota<sup>3</sup>Assistant Professor, Dept. of Medicine, GMC, Kota<sup>\*4</sup>Associate Professor, Dept. of Surgery, GMC, Kota

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Conflict of interest: Nil

**Abstract:**

**Introduction:** Interleukin-6 (IL-6) is a cytokine, which has an important role in inflammation. Diabetic Foot Ulcers are one of the complications of Diabetes Mellitus (DM). DM is a chronic inflammatory disease and up to one-third of diabetic patients may suffer from Diabetic foot ulcers (DFU) during their life span. So this study aimed to evaluate the serum levels of IL-6 in diabetic patients with infective or non-infective foot lesions (IDFU/NIDFU).

**Methodology:** In this study total 100 patients were enrolled and divided into three groups containing 40, 30 and 30 in each group. All patients went through full history taking and clinical examination of diabetic foot ulcer. Serum IL-6 was estimated by ROCHE Cobas e411 machine.

**Results:** Serum IL-6 level in control group were found  $38.65 \pm 22.37$  pg/ml. In NIDFU patients Serum IL-6 level were found  $135.1 \pm 139.26$  pg/ml. In IDFU patients Serum IL-6 level was  $580.97 \pm 398.15$  pg/ml ( $p < .0001$ ).

**Conclusion:** IL-6 appears to be a reliable marker in Diabetic Foot Ulcers progression.

**Keywords:** Diabetes Mellitus, Diabetic Foot Ulcer, Interleukin-6.

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**Introduction**

Cytokines play a major role in immunity, inflammation, embryonic development, regeneration, angiogenesis, metabolism, obesity, aging and so on [1]. Among these diverse functions, their roles in inflammation have attracted attention in relation to disease development and treatment.

Inflammation is a complex process in which a variety of cells, cytokines, chemokines and growth factors are involved. Pro-inflammatory cytokines such as IL-1 $\beta$ , tumor necrosis factor alpha (TNF $\alpha$ ) and Interleukin-6 (IL-6) play crucial roles in inflammation. Among them, IL-6 is an important role player in autoimmune diseases, cancer, cytokine storm and chronic inflammatory diseases [2-10].

Diabetes Mellitus (DM) is a chronic metabolic disorder that has several complications that affect the quality of life [11,12]. It has become a global health problem in the last decades [13]. Diabetic Foot Ulcers (DFU) are one of the complications of DM. Up to one-third of diabetic patients may suffer from Diabetic foot ulcers during their life span [14,15]. The recurrence rate of DFUs is high [14] and prevalence is reported being more common in men than women [16].

As the literature shows the role of IL-6 in chronic inflammatory disease, we performed this study to evaluate the level of IL-6 in diabetic patients with foot lesions because the early recognition of infection is of paramount importance in the management of diabetic foot disease.

**Material and Methods**

This study was carried out in Department of Surgery and Department of Biochemistry, Govt. Medical College, Kota (Rajasthan) from April 2023 to September 2023.

This study was including 100 patients, dividing into three groups:

Group I including 40 diabetic control patients who have no diabetic foot ulcers (DFU).

Group II including 30 patients with non infected diabetic foot ulcers (NIDFU)

Group III including 30 patients with infected diabetic foot ulcers (IDFU).

IDFU diagnosis was based on IWGDF (The International Working Group on The Diabetic Foot) classification of foot infections.

### Patient Selection

#### Exclusion Criteria

Patients with the following criteria were excluded:

- Current inflammatory bowel disease,
- Pneumonia meningitis,
- Gestational diabetes,
- Thyroid and liver disorder patients.
- Who underwent surgery in the past 2–3 weeks.

#### Inclusion Criteria

- Patients who fit in the IWGDF criteria of diabetic foot ulcers.

#### Study Design

All patients went through full history taking and clinical examination of diabetic foot ulcer.

Diabetic complications (retinopathy, nephropathy and cardiovascular diseases) were documented for all groups.

A written informed Consent was taken from the all participants. Ethical approval was taken from institutional ethical committee, GMC, Kota.

#### Laboratory Work Up

Serum IL-6 level estimation was done on Roche Chemiluminescence analyzer.

Statistical analysis: data was estimated on excel sheet and 'p' Value < 0.05 was taken as significant.

#### Result and Discussion

IL-6 was discovered in 1986 [17] and functions as a mediator for notification of the occurrence of some emergent event in inflammation. It is generated in an infectious lesion and sends out a warning signal to the entire body. The signature of exogenous pathogens, known as pathogen-associated molecular patterns, is recognized in the infected lesion by pathogen-recognition receptors (PRRs) of immune cells such as monocytes and macrophages [18, 19].

In present study we evaluated the serum IL-6 levels in non-infected diabetic foot ulcers (NIDFU), infected diabetic foot ulcers (IDFU) and compared with diabetic control patients who have no diabetic foot ulcers (DFU). We found the age group ranging from 28-75 yrs, 40-75 yrs and 41-85 yrs in control, NIDFU and IDFU patients respectively shown in table no.1.

**Table 1: Distribution of Age, Sex and Duration of Diabetes**

Characteristics	Control	NIDFU	IDFU
Age (Yrs)			
Min.-Max.(Median)	28-75(50)	40-75(52.5)	41-85(62)
Mean±SD	47.875±12.70	56.03±9.890725	62.3± 14.05
Gender	40	30	30
M	19(47.5)	16(53.3)	20(66.6)
F	21(52.5)	14(46.6)	10(33.3)
Duration of Diabetes(Yrs)			
Min.-Max.	1-28	1-32	2-33
Median	14.55±8.34	12.36±7.004	13.13± 6.66

NIDFU - non infected diabetic foot ulcers, IDFU - infected diabetic foot ulcers

19 were male and 21 were female out of 40 in control group. 16 were male and 14 were female out of 30 in NIDFU group. 20 were male and 10 were female out of 30 in IDFU group. The duration of diabetes in respective three groups was 1-28 yrs, 1-

32 yrs and 2-33 yrs.

Serum IL-6 levels in control group was 38.65±22.37 pg/ml ranging from 4.9-102.7 pg/ml with median 31.7 shown in table no. 2.

**Table 2: Distribution of IL-6**

IL-6 (pg/ml)	Control	NIDFU	IDFU
Min.-Max	4.9-102.7	10.2-528.7	158.9-2002.8
Median	31.7	81.85	483.2
Mean±SD	38.65±22.37	135.1±139.26	580.97±398.15 (p < 0001)

In NIDFU patients Serum IL-6 level was 135.1±139.26 pg/ml ranging from 10.2-528.7pg/ml with median 81.85. In IDFU patients Serum IL-6 level was 580.97±398.15pg/ml ranging from 158.9-2002 pg/ml with median 483.2. Serum IL-6 levels of IDFU patients were determined to be significantly higher compared to NIDFU patients (p

< .0001) and diabetic control groups (p < .0001). Serum IL-6 levels of NIDFU patients were determined to be significantly higher compared to the diabetic control group (p < .0001).

In support of our study, Korkmaz p et al (2018) and Raheem G S (2017) also suggested that serum IL-6 may be useful parameters in the diagnosis of IDFU

[20, 21]. Gahlot G et al (2021) also suggested that Serum IL-6 levels seem to be promising inflammatory markers in the discrimination of IDFU. The efficiency of serum IL-6 levels for the discrimination of infected and non-infected ulcer in infections of ulcers associated with type 2 diabetes was also shown in this study [22].

### Conclusion

Serum IL-6 levels might have a role in the diagnosis of DFU. This study also makes an attempt to investigate the possible relationship between the stages of disease and IL-6 level. Further studies with large sample population are required for confirmation.

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