# Diagnostic Value of Serum Procalcitonin Level for Detecting Infected Diabetic Foot Ulcers

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## Abstract

**Introduction:** Differentiating infectious and non-infectious diabetic foot ulcers and determining its severity based on clinical finding is challenging for most physicians. In this study we tried to investigate diagnostic value of procalcitonin level for diabetic foot ulcers and compare it with other customary inflammatory biomarkers. **Material and methods:** fifty-seven diabetic patients with foot ulcers, who were intended in endocrinology clinic of Imam Khomeini hospital were selected and classified based on infectious foot ulcer (N=37) versus non-infectious ulcer (N=20). Serum levels of procalcitonin and White blood cell (WBC) count were measured concomitant with recording demographic data. The results were analyzed. **Results:** the mean age of the patients was 68.5 ± 4.9 years; the diabetes disease duration was 11.6 ± 0.46 years. The serum procalcitonin level and WBC count in diabetics with infectious ulcer were higher (p<0.05). The sensitivity and specificity of procalcitonin in diagnosis of infectious diabetic foot ulcer were measured 23.3% and 100% respectively. There was no statistically meaningful intergroup difference according to CRP level. **Conclusions:** This study showed procalcitonin has high specificity for diagnosis of infectious diabetic foot ulcers, so it could be used in the setting of suspicious infected diabetic foot ulcer but due to its low sensitivity, it is not useful screening test.

**Keywords:** Diabetic foot ulcer; Procalcitonin; Infection

## Introduction

Diabetic foot ulcers with prevalence of 15% in diabetic patients, is one of the most important and relatively prevalent causes of admission in these patients. [1] Forty to 80% of diabetic foot ulcers progress to infected ulcers. [2] involvement of surrounding soft tissue and underlying bone, causes worst outcomes –means amputation- that is 10-30 times more prevalent in diabetics compared normal population. [3,4] Amputation related mortality (13% during first year and reaches 80% after 5 years) is the most fearing complication in diabetic patients, [1] so early diagnosis and prompt treatment is of high priority.

Differentiating infectious diabetic foot ulcers (IDFUs) and non-infectious diabetic foot ulcers (NIDFUs) and determining its grading just base on clinical signs is challenging for most physicians. Judgment just base on ulcer appearance to determine infectious ones causes unnecessary antibiotic administration, emerging drug resistance and even delay in tissue repair. On the other hand, some infectious ulcers lack any signs of erythema, pain, tenderness or warmth. [5-7] Applying biochemical markers of CRP, ESR or WBC count could be misleading due to their low sensitivity and specificity. [5,6]

Procalcitonin- precursor of calcitonin hormone- is one of biomarkers which rose up during bacterial infections and many studies prove its benefits for diagnosing sepsis and bacterial infections. [8,9] In this study we tried to evaluate serum procalcitonin level in patients with diabetic foot ulcer, compare it with other customary biomarkers and to investigate its diagnostic value in IDFUs.

## Subjects and Methods

Fifty-seven diabetic patients with foot ulcer-who were intended to the endocrinology clinic of Imam Khomeini hospital recruited to study. Exclusion criteria includes: antibiotic consumption during last month and presence of active liver disease sings. Then patients were classified according to IDSA-IWGDF [Table 1] to IDFUs (N=37) and NIDFUs (N=20) groups. Blood samples of all patients sent immediately to laboratory and kept at -4 centigrade degree and procalcitonin level measured at the same day. Serum procalcitonin, glucose, HbA1C, WBC and CRP levels were measured and concomitantly demographic data of age, sex, diabetes duration, ulcer location and depth were recorded. Eventually results were analyzed by SPSS-16. All patients were signed consent letter in order to participate in the study.

## Results

Of 57 participants, 36 were male (63.2%) and other 21 ones

**Table 1: IWGDF/IDSA classification for diabetic foot ulcers.**

| Clinical classification of infection, with definitions | IWGDF/IDSA classification |
|---|---|
| No systemic or local symptoms or signs of infection | 1 (Uninfected) |
| - At least 2 of the following items are present: • Local swelling or indurations, • Erythema > 0.5 cm* around the wound, • Local tenderness or pain, • Local warmth, • Purulent discharge<br>Other causes of an inflammatory response of the skin should be excluded (e.g., trauma, gout, acute Charcot neuro-osteoarthropathy, fracture, thrombosis, venous stasis)<br>- Infection involving only the skin or subcutaneous tissue (without involvement of deeper tissues and without systemic manifestations as described below).<br>- Any erythema present extends < 2 cm* around the wound<br>- No systemic signs or symptoms of infection | 2 (Mild infection) |
| - Infection involving structures deeper than skin and subcutaneous tissues (e.g., bone, joint, tendon, muscle) or erythema extending >2 cm* from the wound margin.<br>- No systemic signs or symptoms of infection | 3 (Moderate infection) |
| - Any foot infection with the systemic inflammatory response syndrome (SIRS), as manifested by ≥2 of the following:• Temperature >38˚ or <36˚ Celsius, • Heart rate >90 beats/minute, • Respiratory rate >20 breaths/minute or PaCO2 < 4.3 kPa (32 mmHg), • White blood cell count >12,000 or <4,000/mm3, or >10% immature (band) forms | 4 (Severe infection) |

**Table 2: Patient's demographic data.**

| Variables | | Patients with Infectious diabetic foot ulcer (N=37) | Patients with Non-Infectious diabetic foot ulcer (N=20) | p-value |
|---|---|---|---|---|
| Age (years) | | 68.2 ± 4.4 | 67.3 ± 5.6 | >0.05 |
| Gender (number) | Male | 24(69.4%) | 12(60%) | >0.05 |
| | Female | 13(35.1%) | 8(40%) | |
| Diabetes disease duration | | 11.9 ± 0.5 | 1.9 ± 10.9 | >0.05 |
| HbA1C (%) | | 9.02 ± 1.02 | 8.8 ± 1.02 | >0.05 |
| Smokers | | 10(27%) | 8(40%) | >0.05 |
| History of foot ulcer | | 20(54.1%) | 9(45%) | >0.05 |
| Retinopathy | | 12(32.4%) | 5(25%) | >0.05 |
| nephropathy | | 11(29.7%) | 4(20%) | >0.05 |

Results are shown as mean ± standard deviation and reveal that there were no intergroup statistically significant differences considering demographic data.

**Table 3: Comparing inflammatory biomarker in study groups.**

| Variables | | Patients with Infectious diabetic foot ulcer (N=37) | Patients with Non-Infectious diabetic foot ulcer (N=20) | P- value |
|---|---|---|---|---|
| WBC (/ml) | | 10807 ± 2898 | 8187 ± 3116 | <0.05* |
| CRP (mg/l) | | 6.2 ± 2.0 | 5.8 ± 4.01 | >0.05 |
| SIRS positive | | 7(18.9%) | 0(0%) | <0.05* |
| Procalcitonin (number) | ≥ 0.5 ng/ml | 7(18.9%) | 0(0%) | <0.05* |
| | L | 30(81.1%) | 20(100%) | |

Results are shown as mean ± standard deviation. All inflammatory markers were statistically higher in patients with infectious diabetic ulcer, except CRP.

were female (8.36%). The average age was 56.8 ± 9.4 (56 to 78) years. 6.31% were smokers, 3.26% had nephropathy and 8.29% had retinopathy [Table 2]. In our study group the most prevalent site of ulcers were thumb and metatarsus (4.47% and 7.33%).

Inflammatory biomarkers assessments revealed higher WBC count in IDFUs compare with NIDFUs (p<0.05), this result was also true for systemic inflammatory response syndrome (SIRS) signs as none of NIDFUs had SIRS signs. There was no intergroup statistically significant difference according to CRP level [Table 3].

Although average disease duration, smoker patients, previous foot ulcers, retinopathy and nephropathy were higher in IDFUs group, but these associations were not significant [Table 2].

As procalcitonin test kit, measure its level semi-quantitatively, level lower and higher than 0.5 ng/ml were considered negative and positive respectively. Positive results were found just in patients with infected ulcer and procalcitonin were negative in

all patients having noninfectious ulcers. There were considerable association with procalcitonin concentration and infectious diabetic ulcers [Table 3] in this study procalcitonin sensitivity and specificity in diagnosis of infectious diabetic ulcer measured 23.3% and 100% respectively and positive predictive value 0f 100% and negative predictive value of 40%.

## Discussion

This study revealed benefits of using WBC count, serum procalcitonin and also SIRS criteria for diagnosis of infectious diabetic foot ulcer but not CRP.

Uzun et al. at 2007, studied 27 diabetic patients with infectious foot ulcers, 22 patients without infectious ulcer and control group consists of diabetics without foot ulcers and showed that if we consider higher procalcitonin level cut-off, the test sensitivity reduces but specificity increases. [10]

In 2008 "Jeandrot" and coworkers studied 70 diabetic patients had infectious foot ulcers and 23 noninfectious foot ulcers

compared with diabetic patients without ulcers. CRP introduces as the best diagnostic test and combination of CRP and procalcitonin had the highest diagnostic vale. [5]

While our study did not show statistically significant difference intergroup CRP level (p >0.05) similar to Uzun et al. study, [10] many other studies emphasize higher CRP level in infectious diabetic foot ulcers. It may because of measuring serum CRP levels in diabetic patients with infectious foot ulcers compared control group of diabetic patients without foot ulcer while in "Uzun" and our studies compared with non-infectious diabetic foot ulcers.

The important point which less frequently noticed is choosing appropriate inflammatory biomarkers in diabetic patients for following up after initiating treatment. Disappearance of inflammatory biomarkers is one of the earliest signs of ulcer recovery. Some studies had shown that customary markers such as WBC count, [11,12] ESR [13-15] and CRP [16] could not be used as an appropriate marker for confirming transforming infectious to no-infectious ulcers. As mentioned, procalcitonin level has 100% specificity, so it could be used as a marker for ulcer follow up.

In this study prevalence of SIRS positive patients in infected foot ulcer was 9.18% and no one in non-infected foot ulcer group (p<0.05). This emphasizes importance of meticulous physical examination of SIRS positive diabetic patients and searching for infected foot ulcers as a source of systemic infection.

This study showed procalcitonin has high specificity for diagnosis of infectious diabetic foot ulcers.

## Conclusion

According to this and similar studies, [5,10,17,18] that consider 100% specificity of procalcitonin for IDFUs, it could be used in conditions which differentiating infected and non- infected ulcers are difficult, but due to its low sensitivity could not be used as a screening test.

## Conflict of Interest

All authors disclose that there was no conflict of interest.

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