Research Journal of Pharmaceutical, Biological and Chemical Sciences

Letter to the Editor

Role of Biochemical Markers in detection and assessment of severity of Diabetic foot

Parinita Kataraki[1], and Usha Adiga[2]*.

[1]Professor & Head, Dept of Biochemistry, Srinivas Institute of Medical Sciences, Mangalore, Karnataka, India.
[2]Professor, Dept of Biochemistry, K S Hegde Medical Academy, Mangalore, Karnataka, India.

*Corresponding author

INTRODUCTION

Diabetes is a complex, chronic illness requiring continuous medical care with multi-factorial risk-reduction strategies beyond glycemic control. Ongoing patient self-management education and support are critical to preventing acute complications and reducing the risk of long-term complications(1). Diabetes is a global health concern with a prevalence of 5-11% in different countries. Diabetic foot ulcer (DFU) is one of the major complications of diabetes which affects 10%-25% of patients (2). The loss of a limb or foot is one of the most feared complications of diabetes and yet foot problems remain the commonest reason for diabetic patients to be hospitalized. Diabetic foot ulcers are common and estimated to affect 15% of all diabetic individuals during their lifetime (3). In developed countries, one in every six people with diabetes will have an ulcer during their lifetime. The risk is even higher in developing countries (4) . It is estimated that approximately 45,000 lower limbs are amputated every year in India and the vast majority of these are probably preventable (5).

Despite considerable advances made over the last 25years, diabetic foot ulcers (DFUs) continue to present a very considerable health care burden done that is widely unappreciated. The cost to health care services is also enormous. The estimated global cost of diabetes in 2015 was $1.3 trillion (6), and it has been reported that up to one-third of diabetes expenditure is on lower-limb–related problems in the U.S. Iversen et al (7) have also shown that the occurrence of a DFU was an independent predictor of mortality even at 10 years (8).

Diabetic foot and procalcitonin

Diabetic foot ulcers are frequently infected. Such ulcers take longer to heal and are more likely to lead to amputation compared to non-infected ulcers. Therefore, determining the presence of infection occupies an important place in diabetic foot management. Since DFI can progress rapidly and cause extremity loss it must be identifi ed at an early stage and treated without delay(9). Diagnosis of diabetic foot ulcer infection continues to rely on symptoms, principally pain, and signs, including erythema, warmth, oedema and discharge. However, pain may be absent due to concomitant neuropathy and signs may be attenuated by vasculopathy [10]. Failure to treat mild infection with antibiotics risks progression to severe infection and amputation. Conversely, unnecessary over-prescription of antibiotics exposes the person to the risk of adverse effects, increases the risk of subsequent infection with resistant organisms, and contributes to increasing antimicrobial resistance in society, one of the highest current public health priorities [11].

In recent studies procalcitonin (PCT), a 116-amino acid peptide, has been proposed as a useful marker of bacterial infection. Procalcitonin (PCT) is the protein precursor of calcitonin, synthesized and released by C-cells in the thyroid gland. It is suggested that PCT production after inflammation is performed by the liver and peripheral blood mononuclear cells and is modulated by lipopolysaccharides and sepsis related cytokines (9 , 12).

Inflammatory markers and diabetic foot

Calprotectin is a marker of neutrophilic inflammation and therefore may be useful as a marker of infection. It is currently largely used as a marker of inflammatory bowel disease through testing faecal samples, is available as a dipstick test, and is resistant to protease degradation (13). This makes it a candidate to directly assess wound exudate, whose relatively high protease levels prevent the use of several other candidate inflammatory biomarkers (14).

Interleukin-6 (IL-6) is one of the pro-inflammatory cytokines that can be detected in serum in the early stages of infection. It plays a critical role, especially in the induction of CRP and fibrinogen synthesis in the liver during the course of bacterial infection. Therefore, it was suggested that this cytokine could increase earlier than CRP during bacterial infection and that it could enable an earlier diagnosis (15, 16).

Nematollah Jonaidi Jafari et al suggested that procalcitonin can be a diagnostic marker in combination with other markers like ESR and CRP to distinguish infected from non-infected foot ulcers, when clinical manifestations are un specific. Additional research is needed before the routine usage of PCT to better define the role of PCT in IDFU (20).

Suzan Tabur et al showed that serum calprotectin levels were increased in diabetic peripheral neuropathy. It may have a role in the pathogenesis of the disease. But there are no studies showing the role of serum calprotectin in detecting the role in infected diabetic foot ulcer and its severity (21).

Ammal A.W et al showed that IL-6 levels were significantly higher in the serum of the patients with diabetic foot ulcers as compared with diabetic subjects with no foot ulcers. The study also revealed that the excessive presence of IL-6 might play a role in diabetic foot ulcer pathogenesis and development (22).

There is a limited number of studies evaluating the role of serum IL-6 and serum calprotectin levels in diabetic ulcers

Future Perspectives

There are very few studies about the biochemical markers predicting the infection and the severity of the diabetic foot ulcer which has been the economic burden and one of the leading cause for mortality and morbidity amongst the diabetics. Not being able to diagnose the infections at the early stage without a set of indicators for early detection, lead to amputations of the limb which handicaps the patient physically and also mentally.

Considering this, the present review deals with the role of markers which can help in the early detection of diabetic foot ulcer.Further research needs to be done to explain the role of calprotectin, interleukin-6, and procalcitonin in detection and assessment of diabetic foot infection and its severity.

Significance of proposed study

The role of the markers in early detection of the infection in a diabetic foot ulcer and its severity, if established can help in treating the patients in the early stage and can lessen the burden of unnecessary antibiotics and prevent the amputations of limbs in these patients and hence reduce the morbidity and psychosocial burden in the community.

The mode of treatment can be designed if these markers help in assessing the severity of the infection in the diabetic foot ulcer and take appropriate measures towards the betterment of the patient and patient care.

REFERENCES

[1]   Diabetes Care Volume 42, Supplement 1, January 2019
[2]   Hamid Owaysee Osqueea, Abolfazl Pourhassana, Parisa Sadeghiana, Hadi Pourjafarb and Fereshteh Ansari; Procalcitonin as a Biomarker for Diabetic Foot Ulcer; Immun. Endoc. & Metab. Agents in Med Chem 2017;17: 135-139
[3]   Medicine Update 2005; Vijay Viswanathan, Sharad pendsey, Arun Bal; diabetic Foot in india
[4]   Tesfamichael G. Mariam, Abebaw Alemayehu, Eleni Tesfaye, Worku Mequannt, Kiber Temesgen, Fisseha Yetwale et al. Prevalence of Diabetic Foot Ulcer and Associated Factors among Adult Diabetic Patients Who Attend the Diabetic Follow-Up Clinic at the University of Gondar Referral Hospital, North West Ethiopia, 2016: Institutional-Based Cross-Sectional Study; Journal of Diabetes Research Volume 2017; 1-8.
[5]   Vibha SP, Muralidhar MK, Kirthinath B, Asha Kamath et al. Community based study to assess the prevalence of diabetic foot syndrome and associated risk factors among people with diabetes mellitus; BMC Endocrine Disorders 2018; 18:43
[6]   Bommer C, Heesemann E, Sagalova V, et al. The global economicburdenof diabetes inadults aged 20-79 years: a cost-of-illness study. Lancet Diabetes Endocrinol 2017;5:423–430
[7]   Iversen MM, Tell GS, Riise T, et al. History of foot ulcer increases mortality among individuals with diabetes: ten-year follow-up of the NordTrøndelag Health Study, Norway. Diabetes Care 2009;32:2193–2199
[8]   William J. Jeffcoate, Loretta Vileikyte, Edward J. Boyko, David G. Armstrong, and Andrew J.M. Boulton; Current Challenges and Opportunities in the Prevention and Management of Diabetic Foot Ulcers; Diabetes Care 2018;41: 645 – 652

[9]   Gunalp Uzun, Emrullah Solmazgul, Hayrettin Curuksulu, Vedat Turhan, Nurittin Ardic, Cihan Top et al; Procalcitonin as a Diagnostic Aid in Diabetic Foot Infections; Tohoku J Exp Med 2007; 213: 305 – 312.

[10]   Balci C, Sungurtekin H, Gurses E, Sungurtekin U , Kaptanoglu B.   Usefulness of procalcitonin for diagnosis of sepsis in the intensive care unit. Crit Care 2003; 7: 85-90

[11]   Castelli GP, Pognani C, Meisner M, Stuani A, Bellomi D , Sgarbi L. Procalcitonin and C-reactive protein during systemic infl ammatory response syndrome, sepsis and organ dysfunction. Crit Care 2004;8: R234-R242.

[12]   Pınar Korkmaz , Havva Koçak, Kevser Onbaş Polat Biçici, Ahmet Özmen, Cemile Uyar, and Duru Mıstanoğlu Özatağ; The Role of Serum Procalcitonin, Interleukin-6, and Fibrinogen Levels in Differential Diagnosis of Diabetic Foot Ulcer Infection; Journal of Diabetes Research Volume 2018, 1 – 7.

[13]   Chen CC, Huang JL, Chang CJ, Kong MS. Fecal calprotectin as a correlative marker in clinical severity of infectious diarrhea and usefulness in evaluating bacterial or viral pathogens in children. J Pediatr Gastroenterol Nutr 2012; 55: 541–547.

[14]   Ingram JR, Cawley S, Coulman E, Gregory C, Thomas-Jones E, Pickles T, Cannings-John R, Francis NA, Harding K, Hood K , Piguet V. Levels of wound calprotectin and other inflammatory biomarkers aid in deciding which patients with a diabetic foot ulcer need antibiotic therapy (INDUCE study); DIABETIC Medicine

[15]   Buck C, Bundschu J, Gallati H, Bartmann P, Pohlandt F.Interleukin-6: a sensitive parameter for the early diagnosis of neonatal bacterial infection. Pediatrics 1994; 93(1): 54–58.

[16]   Silveira RC,Procianoy RS. Evaluationofinterleukin-6, tumour necrosis factor-α and interleukin-1β for early diagnosis of neonatal sepsis. Acta Paediatrica 1999;88(6):647– 650.

[17]   Nematollah JJ, Mahdi SF, Morteza Izadi, Mohammad S, Safaee F, Amin S.Can Procalcitonin Be an Accurate Diagnostic Marker for the Classification of Diabetic Foot Ulcers? Int J Endocrinol Metab 2014 ; 12(1): e13376.

[18]   Suzan Tabur et al. Is calprotectin a novel biomarker of neuroinflammation in diabetic peripheral neuropathy? Diabetology & Metabolic Syndrome 2015;7: 36.

[19]   Ammal AW, Sallam MD and Ayman MH, Sharawy EL. Role of Interleukin-6 (IL-6) and Indicators of Inflammation in the Pathogenesis of Diabetic Foot Ulcers; Australian Journal of Basic and Applied Sciences2012; 6(6): 430-435.