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Immunological profile of diabetic foot ulcers: Update review

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Abstract

The most frequent consequence of diabetes mellitus, diabetic foot ulcers frequently do not heal and necessitate lower limb amputation. According to estimates, DFU accounts for 50% to 70% of all lower limb amputations, and 50% of patients with DFU have peripheral artery disease (PAD), which is occasionally brought on by atherosclerosis. Deformity of foot, peripheral artery disease (PAD), loss protective sensation (LOPS), and a history of foot ulcers. Global prevalence for DFUs varies by region. One of the frequent complications of diabetes in poor nations, such as Iraq, is diabetic foot; approximately two-thirds of the patients with diabetes have Diabetic Foot disorder (DFD) in Iraq and this health issue had significant negative social and economic effects. The Saudi Arabia and Bahrain have the highest prevalence rates of DFU; the reported yearly incidence of diabetic foot ulcers ranges from "2.1% to 7.4%". There are three types of diabetic foot ulcers: neuropathic, neuroischemic, and ischemic. An infected DFU often contains three to five different types of bacteria, including gram-positive aerobes, such as "Staphylococcus sp.", gram-positive anaerobes, gram negative aerobes, gram negative anaerobes, and fungi (Candida spp.). Numerous studies have demonstrated that effective management of DFU can significantly decrease, postpone, or even completely avoid consequences like infection, gangrene, amputation, and death.

Keywords: DFU, DFD, DM, Aerobic bacteria, Anaerobic bacteria

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Introduction

"Diabetes mellitus" is a collection of metabolic illnesses marked by an abnormal rise in blood glucose due to impaired insulin production, insulin action, or both [1]. The most frequent complication of diabetes mellitus, diabetic foot ulcers sometimes fail to heal and result in lower limb amputation. Indeed, if the right care is not given, DFU can result in infection, gangrene, amputation, and even death [2].

DFU is thought to be the cause of 50% to 70% of all lower limb amputations [3]. It is crucial to highlight that not all diabetic individuals are at risk of developing diabetes foot ulcers (DFU), as there are several factors that contribute to them. It is estimated that approximately 26 million people globally experience diabetes foot ulcers every year [4].

Peripheral artery disease (PAD), which is a risk factor for lower limb amputations and is occasionally brought on by atherosclerosis, affects 50% of people with diabetes foot ulcers. The injury-triggered complicated biological systems that make up the wound-healing process include four essential steps: Hemostasis, inflammation, proliferation, and tissue remodeling were four factors that affected the healing of diabetic foot ulcers, along with the ulcer's location, the duration of the patient's diabetes, the age of the ulcer, the existence of heart failure, and peripheral arterial disease [5].

Epidemiology of Diabetic Foot

Global prevalence of DFUs varies by region. In Iraq, the prevalence of diabetes mellitus in our country was 9.3% in 2015 according to statistics published on International Diabetes Federation [6]. One of the frequent complications of diabetes in impoverished nations, such as our "own country". Approximately two-thirds of the patients with diabetes have Diabetic Foot disorder (DFD) in Iraq and This health issue had significant negative social and economic effects. In study by [7] in Babylon, Iraq, illustrated that incidence rate was increasing and more prominent among urban-dwelling, low-educated women. As well as, in study by [8] in Basrah, Iraq showed that DFD were strongly associated with long duration of diabetes and the female gender. According to a study by [9], the prevalence rates of DFU were lowest in Iraq and highest in Saudi Arabia and Bahrain.

The lifetime risk of getting a diabetic foot ulcer has been estimated to be as high as25%, and the reported annual incidence of diabetic foot ulceration ranges from 2.1% to 7.4% [10]. It has been estimated that up to 15% of persons with T2DM have DFUs [11]. Globally, the incidence is estimated to be 6.3% (95%) with a reported 13.0% prevalence in North America. 5.5% is cited as the prevalence in Asia; in Europe it is 5.1 %, in Africa it is 7.2 % and in the Oceania region it is 3.0 %. Additionally, individuals with DM for longer than ten years are more prone to acquire a DFU [12]. Amputation is the diabetic foot ulcer's final outcome in 15% to 27% of cases if it is not treated promptly and effectively [13]. Additionally, amputation typically has negative social, psychological, and financial effects in addition to high morbidity and mortality [14].

Classification of diabetes foot ulcers:

There are three types of diabetic foot ulcers: neuropathic, neuroischemic, and ischemic [15]. In order to describe the severity of an ulcer, doctors also use the Wagner Grades. The Wagner Grades are designed to help professionals better monitor and care for diabetic foot

ulcers. This grading scale uses numbers from 0 to 5, as shown in the table, to categorize diabetic foot ulcers [1-2].

Table 1.

Classification of diabetic foot ulcers suggested via Wagner (Wagner *et al*., 1983) [16].

Grade-0	No ulcer in a high-risk foot.
Grade - I	Superficial ulcer involving the full skin thickness but not underlying tissues.
Grade - II	Full-thickness ulcers, penetrating through fat to tendon, or joint capsule without causing a deep abscess or osteomyelitis.
Grade - III	Deep ulcer with abscess formation, often with osteomyelitis.
Grade - IV	Localized gangrene.
Grade - V	Extensive gangrene that involves the entire foot

Microbial etiology of diabetic foot ulcer

Aerobes and anaerobic microorganism usually cause diabetic foot wounds to get infected, and this infection subsequently results in the production of microthrombi, which causes ischemia, necrosis, and progressive gangrene before being amputated [17]. Patients with diabetic foot have reduced microvascular circulation, which restricts phagocyte availability and encourages the development of infection. Several of studies illustrated at present a wide variety of microorganisms discovered from infections in diabetic feet, demonstrating the long-lasting, exposed, and anatomical position of these infections.

Both mono- and polymicrobial DFIs are possible, with polymicrobial DFIs being more prevalent in chronic illnesses that have already received antibiotic treatment. Human skin is home to a wide variety of pathogenic and non-pathogenic microorganisms. An infected DFU often contains three to five different types of bacteria, including the following: gram-positive anaerobes (Enterococcus species, Propionibacterium species, Streptococcus species, Peptostreptococcus species, Peptococcus species), gram-negative aerobes (Pseudomonas aeruginosa, Acinetobacter species), gram-negative anaerobes (Proteus mirabilis, Escherichia coli, Bacteroides species), and (Candida spp.).

In low-income countries, there is a higher prevalence of gram-negative pathogens, the most common of which is Pseudomonas aeruginos. Streptococcus and gram-positive cocci, in particular Staphylococci, are frequently isolated [18,19, 20].

Some investigations have revealed that the presence of anaerobic microbes is related to deeper DFIs. Diabetes patients are more prone to foot infections due to neuropathy, vascular dysfunction, and lowered neutrophil activity. A foot infection develops mostly as a result of peripheral neuropathy, which affects between 30 and 50 percent of diabetic individuals [21]. In addition, bacteria typically create biofilms that thwart immune clearance and encourage the development of antimicrobial resistance; in one research, 78.2% of chronic wounds exhibited biofilm creation. To guide the development of innovative therapies and inform antimicrobial therapy, a deeper comprehension of the microbiology of DFIs is crucial [22, 23].

Ethical Approval

The study was approved by the Ethical Committee. It was conducted in accordance with the ethical standards of the Helsinki Declaration of 1975, as revised in 2008.

Conflicts of Interest

The authors declare that they have no competing interests.

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Study registration

Not required.

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