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# Diabetic Foot Ulcer: An Overview, Risk Factors, Pathophysiology, And Treatment

**Gudisa Bereda***

*Department of Pharmacy, Negelle Health Science College, Ethiopia*

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***Corresponding author:** Gudisa Bereda, Department of Pharmacy, Negelle Health Science College, Guji, Ethiopia

**Abstract**

Diabetic foot ulcer is one of the major health challenges that can decrease the quality of life, lengthen hospitalization and entails more cost to the patient. Diabetic foot disease outcome fifteen percent of the diabetic patients and person with diabetes are fifteen times more probably to undergo lower extremity amputation than their non-diabetic counterpart. Risk factors for ulceration are specific or systemic contributions such as uncontrolled hyperglycemia, duration of diabetes, peripheral vascular disease, blindness or visual loss, chronic renal disease, advanced age and local issues such as peripheral neuropathy, structural foot deformity, trauma and incorrectly suited shoes, callus, history of prior ulcer amputation, delayed elevated pressures, limited joint mobility. The initial goals of treatment for diabetic foot ulcer are to acquire wound closure as expeditiously as possible. Debridement includes remove of dead, injured, or exposed tissue, which improves the healing potential of the remaining healthy tissues. The principle of antibiotic management is depending on evidence provided by reports on bacteriological culture and sensitivity from distinctive centers worldwide. Use of anti-infective/antibiotics must be guided by proper cultures.

**Keywords:** Diabetic foot ulcer; Overview, Pathogenesis; Risk factors; Treatment

## Introduction

Diabetes mellitus is a severe, chronic metabolic disorders that described by elevated sugar level either when the pancreas does not secrete sufficient insulin, or when the body cannot effectively use insulin [1]. Infection is an often complication of diabetic foot ulcers (DFUs), with up to fifty eight percent of ulcers being exposed at primary presentation at a diabetic foot clinic, elevating to eight two percent in patients hospitalized for a DFU. These diabetic foot infections are correlated with poor clinical consequences for the patient and most expenses for both the patient and the health care system. Patients with DFIs have a fifty times accelerated risk of hospitalization and one hundred fifty times elevated risk of lower extremity amputation compared with patients with diabetes and no foot infection. Among patients with DFIs, five percent will undergo a major amputation and twenty thirty percent a minor amputation, with the availability of peripheral arterial disease (PAD) highly elevating amputation risk [2-5]. DFU notifies to a cover in the continuity of the skin epithelium enclosing its full thickness or beyond, distal to the ankle joints, in a people living with DM [6,7]. DFU is one of the major health challenges that can rupture the QOL, lengthen hospitalization and entails more cost to the patient. Diabetic foot disease outcome fifteen percent of the diabetic patients and person with diabetes are fifteen times further probably to undergo lower extremity amputation than their non-diabetic counterpart [8-10]. The challenge and features of diabetic foot are infection, ulceration, or gangrene. Neuropathy, poor circulation, and vulnerability to infection are the three major contributors to the development of diabetic foot; which when available, foot abnormalities or mild trauma can readily influence to ulceration and infection [11, 12].

Ulceration is the most common precursor of amputation and has been distinguished as a component in greater than 2/3 of lower-limb amputations. The availability or absence of infection and/or ischemia, footwear and pressure relief, and overall glycemic control lead the healing of ulcers. The depth of an ulcer is other significant factor that influences the consequence of DFUs [13]. Wounds on the feet, known as DFUs, are a major complication of diabetes. DFUs can become exposed, influencing to amputation of the foot or lower limb [14]. Limb amputation has a major impact on the individual, not solely in distorting body image, but also with respective to loss of productivity, elevating dependency, and costs of managing foot ulcers if patients necessitates inpatient care [15,16]. Lower limb amputation in diabetic patients is

correlated with important excess mortality. Foot ulceration is also believed to be correlated with enhanced deaths due to related cardiovascular disease. Furthermore, patients with foot ulceration frequently have developed diabetes complications [17-19]. 15% of those with diabetes will advance at least one DFU during their lifetime [20]. Foot challenges responsible for up to fifteen percent of healthcare resources in developed countries and 40% in developing countries. Among Ethiopian diabetic patients foot ulcer is a major health challenge. Foot ulcer correlated with sepsis sequences in twelve percent of death. Low follow-up and poor glycemic control are preponderance contributing factors. Understanding of the influential factors of foot ulcer in diabetics will enable great risk patients to be recognized early [21-25].

The main risk factors for DFUs involve sensory neuropathy, lower limb ischemia, and trauma [26]. Risk factors for ulceration are specific or systemic contributions such as uncontrolled hyperglycemia, duration of diabetes, peripheral vascular disease, blindness or visual loss, chronic renal disease, advanced age and local issues such as peripheral neuropathy, structural foot deformity, trauma and incorrectly suited shoes, callus, history of prior ulcer amputation, delayed elevated pressures, limited joint mobility [20,21,24]. The grades of the University of Texas (UT) system are as follows: grade zero (pre- or post-ulcerative site that has cured), grade one (superficial wound not involving tendon, capsule, or bone), grade two (wound penetrating to tendon or capsule), and grade three (wound penetrating bone or joint). Within each wound grade there are 4 stages: clean wounds (stage A), non-ischemic infected wounds (stage B), ischemic non-infected wounds (stage C), and ischemic infected wounds (stage D) [15]. DFUs can be medically categorized in several ways but all of them define the ulcer in terms of its depth and the availability of osteomyelitis or gangrene. As an example, the categorization according to Wagner's system is depending on the following grades: grade zero (no ulcer in a foot with a high-pitfall factor of complication); grade one (partial/full thickness ulcer); grade two (deep ulcer, penetrating down to ligaments and muscle, but no bone involvement); grade three (deep ulcer with cellulitis or abscess formation); grade four (localized gangrene); and grade five (extensive whole foot gangrene). The classification of diabetic foot ulcers is significant as it perhaps facilitate the choice of suitable dressing based on the wound type and on its phase [27-30] (Figure 1).

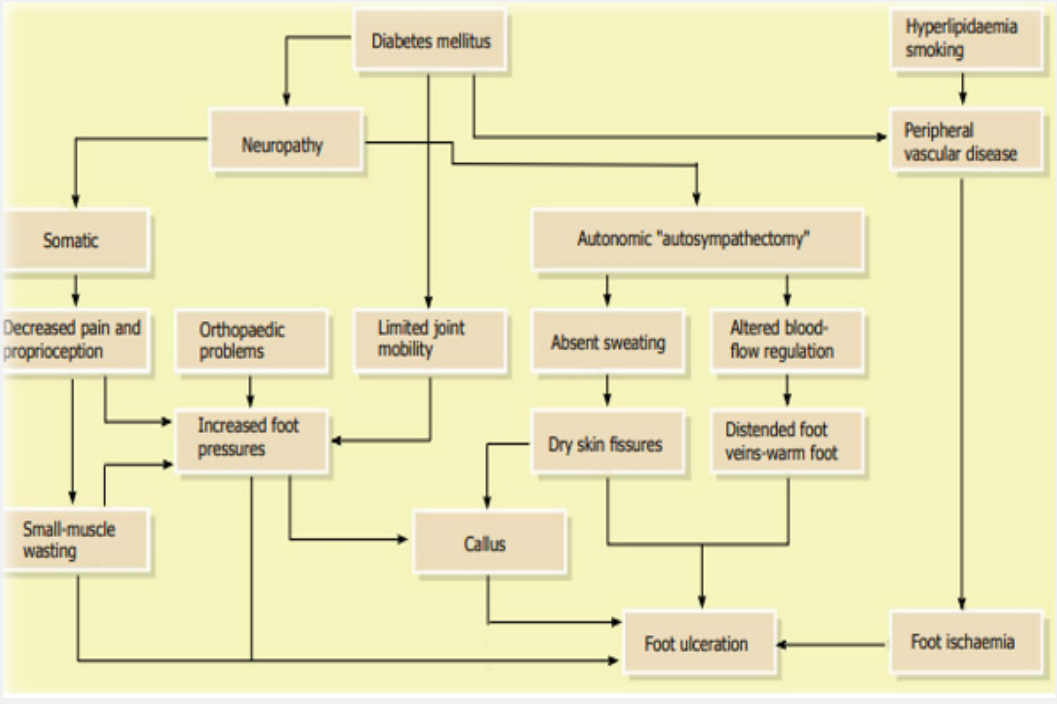


**Figure 1: Etiology of diabetic foot ulcer.**

## Pathophysiology

The most common contributing factors in creating DFU are neuropathy, peripheral artery disease (PAD), abnormality and minor trauma. Additionally contributing factors are necrosis, gangrene, infection, PAD, advancing age of the patient and other co-morbidities such as end ESRD, and heart failure. The DFU patients are ordinarily older males with a history of delayed DM combined with poor health situation. They ordinarily based on assistance of other to work their daily activities. The average


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age of these patients is sixty-five years and they are ordinarily presented with the disease for at least ten years. The majority of them has a history of uncontrolled diabetes additionally elevated degree of HbA1c, and in 1/3 of the cases other co morbidities are available. Neuropathy sequences in insensitivity and occasionally causes abnormalities in the foot. In these patients, even a minor trauma perhaps influences to a chronic ulcer. Additionally, the persistent walking on the influenced foot, which is insensitive to pressure sense, changes the healing procedure. In the availability of peripheral vascular disease (PVD), the wound becomes ischemic and a non-healing ulcer advance. In patients with neuro ischemic ulcer, unfortunately, the classic signs of infection such as pain, warmth and tenderness are masked. Decrease in pain and tenderness is owing to neuropathy and the warmth and redness declines indispensably because of ischemia. These alters perhaps confuse the physician and sequences in misdiagnosing for wound infection [31-33].

### Diagnostic criteria

In recent clinical practices, the evaluation of DFU comprises of several important works in early diagnosis, keeping track of advancement and number of lengthy actions received in the management and treatment of DFU for each case: 1) the medical history of the patient is evaluated; 2) a wound or diabetic foot specialist examines the DFU thoroughly; 3) additional tests like CT scans, MRI, X-Ray perhaps helpful to support advance a management plan. The patients with DFU specifically have a challenge of a swollen leg, although it can be itchy and painful based on each case. Ordinarily, the DFUs have aberrant structures and unusual outer boundaries. The visual appearance of DFU and its enveloping skin based upon the several stages i.e. redness, callus formation, blisters, and significant tissues types like granulation, slough, and bleeding, scaly skin. Thereby, the ulcer evaluation with the support of computer vision algorithms would be depending on the exact assessment of these visual signs as color descriptors and texture features [34].

## Treatment

The objectives of management are: (1) to create and maintain a plantigrade, stable foot; (2) to heal an ulcerated wound; (3) to heal fractures; (4) to suppress abnormalities. The initial goals of treatment for DFU are to acquire wound closure as expeditiously as possible [35]. Not all diabetic foots are preventable, but proper preventive measures can dramatically minimize their occurrences. Managing a DFI necessitates correct wound care and proper antibiotic therapy. Multiple factors involving assessment of the wound, its categorization, and the require for debridement involving sharp surgical, mechanical, chemical etc., have to be received onto consideration before proceeding with the correct selection of topical regimen [36]. The preventive measures and treatment of diabetic complications consists of the following: Lifestyle modification; BP control (the best indicator of glucose control over a period of time is HbA1C level. This test measures the average BS concentration over a ninety-d span of the average RBC in peripheral circulation. The higher the HbA1C level, the greater glycosylation of Hg in RBCs will happen. Surveys have reveal that BG levels > 11.1 mmol/L (equivalent to > 310mg/mL or an HbA1C level of > 12) is correlated with decreased neutrophil work, involving leukocyte chemotaxis [37]); lipid management; glycemic control; smoking cessation, BP control (ACE inhibitors or angiotensin receptor blockers were recommended for all patients with HTN, previous cardiovascular disease, and/or microalbuminuria, unless there was known renovascular disease. Beta-blockers were recommended for all patients with existing cardiovascular disease or in whom BP was still uncontrolled despite ACE inhibition.

### Education

Patients' training plays an indispensable function in suppression of DFU. The goal of training is to motivate the patient and create adequate skills in order to maximize the use of preventive methods. It is also crucial to make sure that the patient has understood all the instructions. Recently, a broad range and combinations of patient educational interventions have been evaluated for the prevention of DFU that different from brief education to intensive education involving observation and hands on teaching. Patients with DFU should be educated about risk factors and the necessity of foot care, involving require for self-inspection, monitoring foot temperature, proper daily foot hygiene, usage of correct footwear, and blood sugar control. Debridement: Debridement includes remove of dead, injured, or exposed tissue, which improves the healing potential of the remaining healthy tissues. Based on the wound tissue type, other debridement techniques are recommended: (1) Surgical debridement or sharp debridement-recommended for necrotic and exposed wounds. The terms surgical debridement and sharp debridement are frequently used intercalate, certain clinicians refer to surgical debridement as being settled in an operating room, whereas sharp debridement is settled in a clinic setting. Sharp surgical debridement is the most effective and quickest method of debridement; (2) Autolytic debridement-a selective procedure in which the necrotic tissue is liquefied. A wound filled in with an occlusive dressing permits concentration of tissue fluids containing macrophages, neutrophils, and enzymes, which remove bacteria and digest necrotic tissues. This is reached by a moist wound curing environment. Autolytic debridement is not advisable for the treatment of exposed pressure ulcers; (3) Mechanical debridement-includes remove of unhealthy tissue using a dressing, which is altered regularly by wound irrigation (pressure: 4-15psi), without injuring healthy/new tissues. Scrubbing the wound aids in remove of exudates and devitalized tissues, however this influences to bleeding as well as pain resulting from wound trauma. This technique is used in the treatment of surgical wounds and venous leg ulcers. The


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shortcomings of the method are that it is time consuming and high cost; (4) enzymatic debridement-a method of debriding devitalized tissue by topical enzymes such as collagenase, fibrinolysin, or papain. Recommended for sloughy, exposed, necrotic wounds where surgical debridement is contraindicated; and (5) Maggot debridement-a procedure in which maggots or fly larva that are accelerated in a sterile environment are used. The most frequently used fly is *Lucilia sericata*, which is used for human wound management when conventional managements fail. Maggots are placed on the wound pursued by wrapping with 2ndry dressing. The larvae feed on the necrotic (dead) tissue and bacteria available at the wound site and produce antimicrobial enzymes, which support in the wound healing procedure [38-40].

### Wound dressings for diabetic foot ulcer treatment

Natural skin is thought-out the perfect wound dressing and thereupon an ideal wound dressing should try to duplicate its properties. Historically, wound dressings were primary thought-out to play only a passive and protective function in the healing procedure. Although in current decades wound management has been revolutionized by the innovator that moist dressings can assist wounds heal quicker. In addition, a moist wound environment is also an indispensable factor to initiate the proliferation and migration of fibroblasts and keratinocytes as well as to accelerate collagen generation, influencing to decreased scar formation [41-43].

### Antibiotic selection

The principle of antibiotic management is depending on evidence provided by reports on bacteriological culture and sensitivity from other centers worldwide. Usage of anti-infective/antibiotics must be guided by proper cultures. Improper usage of antibiotics could influence to resistance and adverse drug reactions. Oral and parenteral antibiotics are prescribed for mild soft tissue infections and moderate to severe infections, respectively [44].

### Antibacterial agents

Used only or in combination for each class except dry necrotic wounds. Topical antibiotics have wide spectrum antibacterial coverage which lasts for twelve hour and are less toxic. Metronidazole gel has excellent anaerobic coverage and supports in maintaining a moist wound healing environment. By weight, gels are highly liquid, yet they behave like solids owing to a 3-dimensional cross-linked network within the liquid. It is the crosslinking within the fluid that bestows a gel its structure (hardness) and contributes to its adhesion [45]. Off-loading: Total contact casts and therapeutic shoes are appropriate alternatives for remove of pressure from the wound. The further effective offloading technique for the treatment of neuropathic DFU is total contact casts (TCC). TCC is minimally padded and molded carefully to the shape of the foot with a heel for walking.

### Surgery

Diabetic foot surgery plays a crucial function in the suppression and treatment of DFU and has been on elevate over the past two decades. Although surgical interventions for patients with DFU are not without peril, the selective correction of persistent foot ulcers can improve consequences. Vascular foot surgery such as bypass grafts from femoral to pedal arteries and peripheral angioplasty to ameliorate blood flow for an ischemic foot have been currently advanced [46-48].

### Advanced dressing

A major breakthrough for DFU treatment over the last decades was the observation of novel dressings. Ideally, dressings should confer moisture balance, protease sequestration, growth factors enliven, antimicrobial activity, $O_2$ permeability, and the capacity to accelerate autolytic debridement that facilitates the secretion of granulation tissues and the re-epithelialization procedure. Furthermore, it should have a delayed time of action, high efficiency, and improved sustained drug release in the case of medicated therapies [49].

## Conclusion

Diabetic foot disease outcome fifteen percent of the diabetic patients and person with diabetes are fifteen times further probably to undergo lower extremity amputation than their non-diabetic counterpart. Risk factors for ulceration are specific or systemic contributions such as uncontrolled hyperglycemia, duration of diabetes, peripheral vascular disease, blindness or visual loss, chronic renal disease, advanced age and local issues such as peripheral neuropathy, structural foot deformity, trauma and incorrectly suited shoes, callus, history of prior ulcer amputation, delayed elevated pressures, limited joint mobility. The preventive measures and treatment of diabetic complications consists of the following: Lifestyle modification; BP control (the best indicator of glucose control over a period of time is HbA1C level. This test measures the average BS concentration over a ninety-d span of the average RBC in peripheral circulation. Historically, wound dressings were primarily considered to play solely a passive and protective function in the healing procedure.

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## Data Sources

Sources searched include Google Scholar, Research Gate, PubMed, NCBI, NDSS, PMID, PMCID, Lancet, Scopus database, Scielo and Cochrane database. Search terms included: an overview, risk factors, pathophysiology and treatment of diabetic foot ulcer


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## Availability of Data and Materials

The datasets generated during the current study are available with correspondent author.

## Competing Interests

The author has no financial or proprietary interest in any of material discussed in this article.

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