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A Review on Decoding Diabetic Foot Ulcers

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Abstract

A diabetic foot ulcer is an open sore or wound that can develop on the foot of someone with diabetes. It's a common complication of diabetes that can occur due to a number of reasons, including neuropathy. High blood sugar levels can damage nerves in the feet, causing numbness, tingling, or burning. This can make it difficult to feel injuries, such as scrapes, cuts, or punctures, which can lead to ulcers. Diabetic foot ulcer is a major consequence of diabetes, increasing morbidity and having a large socio-economic impact. It can develop in up to 25% of diabetic people throughout the course of their lives, and more than half of those patients become infected. The abstract reviews the current understanding of the pathophysiology, risk factors, and management strategies for diabetic foot ulcers. We discuss the role of pressure offloading, and advanced wound care techniques in improving outcomes. Additionally, emerging treatments, including herbs and other ongoing techniques, are explored. Treatment for diabetic foot ulcers focuses on healing the wound as quickly as possible to reduce the risk of infection. Treatments include, debridement, removing dead or infected tissue with a whirlpool bath, syringe and catheter, wet to dry dressings, or enzymes. This review evaluates diabetic foot ulcers in all areas. Our discussion will cover both traditional and innovative therapies for managing diabetic feet.

Keywords: Diabetes; Foot Ulcer; Therapy; Management; Morbidity

Abbreviations

IWGDF: The International Working Group on the Diabetic Foot; DFUs: Diabetic Foot Ulcers.

Introduction

Diabetes mellitus, often known as diabetes, is a metabolic disorder characterized by elevated blood glucose levels (hyperglycemia). Pancreatic β-cells secrete insulin, which transfers sugar from the blood into the body's cells, where it is stored or utilized for energy. Diabetic foot is defined by the International Working Group on the Diabetic Foot (IWGDF) as an infection, ulceration, or degeneration of the foot's tissues in the lower extremity of a person with (a history of) diabetes mellitus that is linked to neuropathy and/or peripheral artery disease [1].

One of the most dangerous side effects of diabetes is diabetic foot ulcers (DFUs), which lower quality of life and raise financial burden for the patients who have them. Put another way, DFU therapy is frequently difficult, and patients struggle financially as a result of the high expense of care. As a result, it is critical that both diabetic patients and medical professionals understand the fundamental ideas guiding the prevention of DFUs. Methods of instruction should be

carefully planned to guarantee that patients with diabetes understand and foot care is offered in accordance with the intended aim [2].

Pathophysiology

The three main components of DFU are peripheral artery disease, concurrent secondary bacterial infection, and neuropathy. Intrinsic muscle atrophy and functional anatomical alterations in the foot may result from peripheral neuropathy. Diabetic foot ulcers (DFUs) are a common and serious complication of diabetes, particularly in patients with poorly controlled blood glucose levels. The pathophysiology of DFUs involves a complex interplay of several factors.

Neuropathy

Diabetes often leads to peripheral neuropathy, which impairs sensation in the feet. This loss of sensation means that patients may not feel pressure, trauma, or injuries to their feet, which can lead to the development of ulcers. Neuropathy can also affect the autonomic nerves, leading to changes in sweat and oil gland function, which can result in dry, cracked skin.

Peripheral Vascular Disease

Diabetes increases the risk of atherosclerosis, which can reduce blood flow to the extremities. Poor circulation impairs the body's ability to heal wounds and can contribute to the formation of ulcers. The reduced blood supply also affects the delivery of essential nutrients and oxygen needed for tissue repair.

Infection

Once a foot ulcer forms, it can become infected due to the presence of bacteria. Diabetes impairs the immune response, making it more difficult for the body to fight off infections. Infections can further complicate the healing process and increase the risk of severe outcomes, such as cellulitis or osteomyelitis (Figure 1).

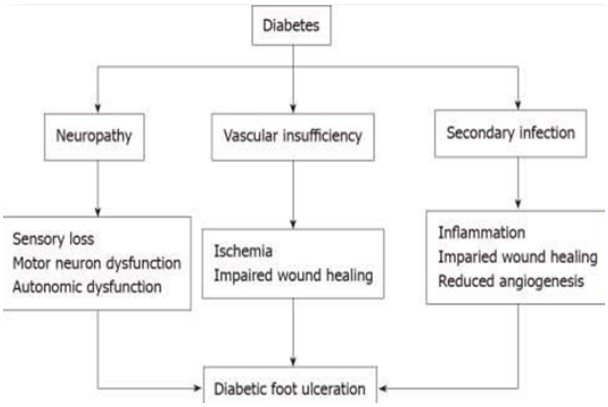

Figure 1: Pathophysiology of diabetic foot ulcers.

Diabetic Foot Ulcer Classification

When managing patients with DFUs, healthcare providers might employ classification systems as effective tools. Determining and classifying the DFU according to severity facilitates provider-to-provider communication and enables more precise outcome analysis across treatment modalities (Table 1).

Classification			
DFU Classification System Name	**Author**	**Year of Establishment**	**Comments**
PEDIS	Lipsky, et al. / International Working Group on the Diabetic Foot	2012	Developed by the IDSA, user-friendly (clear definitions, few categories) for diabetic footmanagement.
SINBAD	Ince, et al.	2008	Includes site, ischemia, neuropathy, bacterial infection and depth
University of Texas Wound Classification System	Laverym et al.	1996	validated and typically indicative of the result, as wounds with higher grades and stages have a lower propensity to heal without revascularization or amputation.
Wagner Classification System	Wagner	1981	More recent categorizations demonstrate that not all DFUs and illnesses are sufficiently addressed by the Wagner method.
WIFI	Millsm, et al.	2014	combines several current classification methods into a single, simple scheme, such as the IDSA classification for diabetic foot infections.

Table 1: Selected DFU`s classification framework use.

Hence, diabetic foot ulcers (DFU`s) occur through various factors including neuropathy, poor- glycemic control, infections, trauma/mechanical injury. Among them diabetic neuropathy is the most common factor in patients with diabetic foot ulcers (Figure 2).

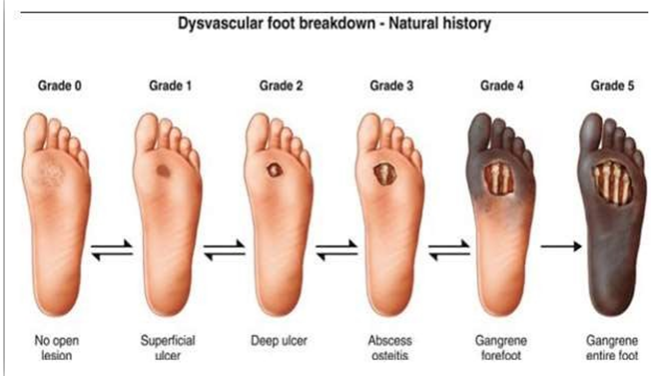

Figure 2: Stages of diabetic foot ulcers.

Causes of Diabetic Foot Ulcer

Ulcers in people with diabetes are most commonly caused by poor circulation, high blood sugar (hyperglycemia), nerve damage and irritated or wounded feet. Poor blood circulation is a form of vascular disease in which blood doesn't flow to your feet efficiently. Poor circulation can also make it more difficult for ulcers to heal. High glucose levels can slow the healing process of an infected foot ulcer, so blood sugar management is critical. People with type 2 diabetes and other ailments often have a harder time fighting off infections from ulcers. Nerve damage is a long-term effect and can lead to a loss of feeling in your feet. Damaged nerves can feel tingly and painful. Nerve damage reduces sensitivity to foot pain and results in painless wounds that can cause ulcers. Ulcers can be identified by drainage from the affected area and sometimes a noticeable lump that isn't always painful.

Early Signs & Symptoms

The early stages of diabetic foot problems often go unnoticed since they are not specific sign to diabetic foot. Learning how to identify these changes can help you prevent serious complications. The common symptoms are [3].

- Numbness (loss of sensation) or the ability to feel heat or cold in your feet.
- Pain or cramps in your legs, calves, thighs, or buttocks, especially during physical activity.
- Burning, tingling, or pain in your feet.
- Dry, cracked skin on your feet.
- Loss of hair on your feet, toes, and lower legs.
- Athlete's foot (tinea pedis) or other fungal infections between your toes.
- Thickened, yellow toenails.
- A sore, blister, ulcer, infected corn, or ingrown toenail.
- Edema (swelling)
- Redness or warmth on your feet.
- Changes in the shape of your feet, possibly leading to a "rocker bottom," which is a sign of a rare form of diabetic foot called Charcot foot neuropathy, in which the bones in your feet and toes shift or break [4].

Diabetes pain that spreads to leg

While leg pain is not a common symptom of diabetes, it can occur as a result of peripheral neuropathy due to uncontrolled diabetes. Having neuropathy that involves your legs typically leads to the following symptoms [2] (Figure 3).

- Pain that starts in your toes and gradually spreads toward your knees
- Pain when you walk
- Changes in the way you walk
- Loss of balance causing more falls
- Progressing signs of the ulcers in the foot.

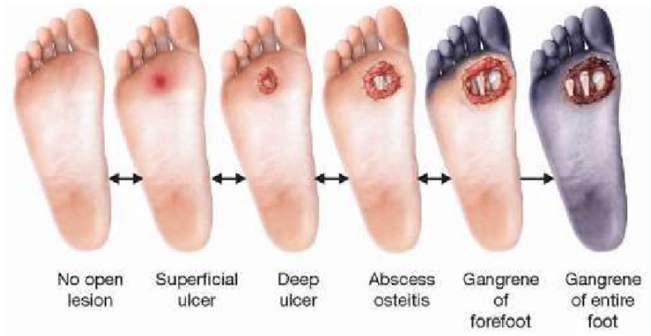

Figure 3: Progressing signs of ulcers in foot.

Risk Factors of Diabetic Foot Ulcers

- All people with diabetes are at risk for foot ulcers, which can have multiple causes. Some factors can increase the risk of foot ulcers, including
- Poorly fitted or poor-quality shoes
- Poor hygiene (not washing regularly or thoroughly or not drying the feet well after washing)
- Improper trimming of toenails
- Alcohol consumption
- Eye disease from diabetes
- Heart disease
- Kidney disease
- Obesity
- Tobacco use (inhibits blood circulation) (Table 2)

General / systemic contributions	Local issues
Uncontrolled hyperglycaemia	Peripheral neuropathy
Duration of diabetes > 10yrs	Structural foot deformity
Peripheral vascular disease	Trauma/ ill fitted shoes
Blindness or visual loss	Callus
Chronic renal disease	History of prior ulcer/ amputation
Older age	Prolonged elevated pressures
High body mass index	Limited joint mobility

Table 2: Risk factors and their local effects.

Assessment & Diagnosis of Diabetic Foot Ulcers

A thorough assessment is crucial for accurate diagnosis. This includes evaluating the severity of the ulcer, checking for infection and assessing the blood flow. Tools like the monofilament test can aid in identifying neuropathy. A monofilament test is done to test for nerve damage, which may be caused by conditions such as diabetes. The monofilament is a small strand of nylon attached to a plastic base. The provider uses this monofilament to check for the loss of feeling on the foot (Figure 4).

Figure 4: Monofilament test.

Treatment & Prevention Of Diabetic Foot Ulcers

While there is no cure for diabetic foot ulcer, treatment can slow its progression and manage complications before they become serious. Initially, DFUs were treated with prolonged bed rest, although it was observed that the wound would reemerge once the patient returned to activity [5].

With early diagnosis, the doctors may be able to treat the diabetic foot with one of the following nonsurgical treatments:

Wound dressings: Specialized wound dressings and topical creams can protect a diabetic foot ulcer from infection and promote healing.

Antibiotics: These drugs are given orally or intravenously (through an IV within a vein) therapy to treat an infection and prevent it from spreading. The choice of antibiotic therapy mainly depends on microbiological findings and antibiotic resistance. Therefore, obtaining deep tissue cultures during debridement is recommended before antibiotic therapy [6].

Off-loading: Devices like special casts, shoes, or braces can be used to remove pressure from a diabetic foot ulcer, a process known as off-loading, and promote healing. Methods can include bed rest, wheelchair use, crutch walking, and removable cast walkers. Among these, non-removable knee-high offloading devices such as total contact casts or prefabricated knee-high orthoses are considered first-line recommendations [7].

Debridement: This involves the removal of contamination (foreign matter) and necrotic (dead or dying) tissue from a diabetic foot ulcer to promote healing and infection. Debridement can be achieved either surgically or with non-surgical methods that involve the use of special dressings and gels. Consequently, the IWGDF guidelines recommend sharp debridement as the best standard of care that is preferred over autolytic, bio-surgical, hydro-surgical, chemical, or laser debridement [8].

Relieve limb ischemia (restricted blood flow): Nonsurgical interventions such as balloon angioplasty and stenting may be appropriate if your diabetic foot ulcer is linked to vascular disease such as peripheral artery disease.

Hyperbaric oxygen therapy: In this, the patients inhale 100% oxygen at greater than 1 atmosphere of pressure, which has been recognized to promote local tissue oxygenation, improve tissue hypoxia, and reduce wound infection through an antibacterial effect [9].

Herbs Used for Treatment of Diabetic Ulcers

There are several ways to treat diabetic wounds, but one option that has attracted attention internationally in the recent two decades is the use of medicinal plants.

The medicinal plants that are most commonly used for the treatment of diabetic foot ulcers are;

Neem: Neem also known as Azardirachta indica is an Indian

native plant. The phytochemical constituents present in neem are steroids, triterpenoids, reducing sugars, alkaloids, tannins and flavonoids. It has strong anti-inflammatory and anti-pyretic properties [10,11]. The topical application of the neem significantly helps in healing of diabetic foot ulcer (Figure 5).

Figure 5: Herbs used in treatment of diabetic foot ulcers.

Aloevera: Aloevera also known as Aloe barbadensis is native of North Africa and Spain. The phytoconstituents present are anthraquinone and glycosides [12]. It has been depicted that aloe reduces inflammation, diabetes and microbiological infections. A survey reported that application of Aloe vera gel has reduced the ulcer surface with no adverse effects.

Kiwi: Kiwi also known as Actinidia deliciosa is native of China. The active constituent present is actinidin. In terms of wound healing and contraction kiwi fruit was more successful to heal wounds faster with ulcer debridement, angiogenesis and disinfection compared to sulfadiazine cream [13].

Sesame: Sesame is also known as Sesamum radiatum (S. radiatum) is native to Africa [14]. The phytochemical constituents present are tannins, alkaloids and saponosides [15]. Nimbadi kalka is an ayurvedic preparation in which sesame is a major constituent helps in wound healing by reducing the size of wound in diabetic foot ulcers (Table 3).

S.no	Herb	Common name	Part used	Phyto - constituents	Inference
1	Azadirachta indica	Neem	Leaves	Alkaloids, tannins, flavonoids. triterpenoids, steroids.	reduction in wound size
2	Aloe barbadensis	Aloe vera	Gel	Anthraquinone glycosides	reduction in the wound size
3	Actinidia deliciosa	Kiwi	Fruit	Actinidin	effective in reduction of wound size
4	Sesamum radiatum	Sesame	Leaves	Alkaloids, tannins, saponosides	reduces wound size and exudates (decreased)

Table 3: Herbal drugs used to treat diabetic foot ulcers.

Novel/ Advanced Therapies

Newer therapies include use of Bio-engineered Skin Substitutes, Growth Factors (PDGF-beta, PRP), Extracellular Matrix Proteins, and Matrix Metalloproteinases Modulators (MMP) which can also contribute to the overall healing process of the Diabetic foot ulcers wounds in affected patients. Bio-engineered skin substitutes may be a promising therapeutic adjunct therapy to the standard wound care for the management of non-infected diabetic foot ulcers. Some studies have shown encouraging results with new therapies, but certainly, randomized trials are necessary in order to establish their role in the treatment of diabetic ulcers [16,17].

Future Prospective

With diabetes and DFU rates rising rapidly in the APAC region, education and raising awareness are of key importance.
Education is required in the following ways:
For clinicians to increase their confidence and competence in managing DFUs and providing the best options for patients to improve outcomes

- For patients to increase awareness of DFU prevention and to facilitate effective self- care.
- For carers/relatives of patients to ensure that patients receive appropriate care, even when access to a clinical setting is not possible, or to know when to contact a clinician if 'red flags' arise, or further care is required.
- Developments in telemedicine may help many patients to receive the care they need, particularly if they are in rural areas where access to clinicians or a clinical setting is not easily available.
- Advances in technology are aiding in the identification of DFUs and potential infection and thus facilitating early intervention, which may help to improve outcomes.
- It is vital to keep the patient at the Centre of care in all clinical settings, and to tailor treatment to the patient's individual health, needs and preferences.
- The ultimate aim is to optimize DFU prevention and management to improve outcomes and patient's quality of life as much as possible, given this serious and growing issue.

Conclusion

DFUs are one of the serious complications of diabetes. Many risk factors lead to the occurrence of the disease, and the amputation rate is high. Once diabetes is diagnosed, we should perform more work on the management of diabetes, including screening for high-risk factors for DFUs, such as neuropathy and arteriopathy. With the development of artificial intelligence, intelligent detection instruments and evaluation tools (such as intelligent insoles) can be applied to the prevention and treatment of DFUs. The management of DFUs requires multidisciplinary cooperation, mainly including endocrinologists, vascular surgeons, orthopedic doctors, wound specialists, shoe technicians, rehabilitation physicians, psychological consultants, and specialized nurses. The correct evaluation and comprehensive management of DFUs by multidisciplinary teams are essential to protect the function and quality of life of patients. Optimizing diabetes management is still the most important step to prevent diabetes-related complications.

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Conflict of Interest

None

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