CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://zenodo.org/records/10624497

https://www.iajps.com/volumes/volume11-january-2024/27-issue-01-january-24/

Available online at: http://www.iajps.com Review Article

# AN OVERVIEW OF CURRENT TREATMENT FOR DIABETIC FOOT ULCERS

**J.S Venkatesh[1], Vinuth Chikkamath[2], Naresha A G[3], Nikitha Prakash[4], Nishana P N[5], Sherin P Thomas[6]**

[1] Professor SCS college of Pharmacy, Harapanahalli

[2]Assistant professor SCS college of Pharmacy, Harapanahalli

[3,4,5,6] Pharm D Interns SCS College of Pharmacy, Harapanahalli

Department of Pharmacy practice, SCS College of Pharmacy, Harapanahalli, Karnataka, India

**Abstract:**

*Severe complications from diabetes mellitus include diabetic foot ulcers, which have a major socioeconomic impact and raise patient morbidity. The current study focuses on the current management of this serious and preventable health disease while summarizing the many classification systems, the pathophysiology and causes of diabetic foot ulcers, and current practices.*

***Keywords****: Diabetes mellitus, Diabetic foot ulcer, Diabetic foot ulcer management, classification*

**Corresponding author:**

**Nikitha Prakash,**

*Pharm D Interns,*

*S C S College of Pharmacy,*

*Harapanahalli, Karnataka, India*

QR code

*Please cite this article in press Nikitha Prakash et al.,* ***An Overview Of Current Treatment For Diabetic Foot Ulcers****, Indo Am. J. P. Sci, 2024; 11 (01).*

## INTRODUCTION:

Diabetes is a chronic illness that needs to be treated carefully. It is also known as a "global epidemic." Globally, 415 million individuals, or 1 in 11 people, suffer with diabetes. With 69 million patients with diabetes, India has the second-largest diabetic population in the world. A foot ulcer will occur in about 15% of diabetics at some point in their lifespan.[1,6] The aging of the population, the significant rise in the prevalence of obesity, and the decline in physical activity have all been linked to an increase in the incidence of Type-2 Diabetes Mellitus.[2] (DM 2) over the past few decades[2].Early onset of diabetes and longer lifespans among diabetic patients have increased the risk of developing complication that are duration dependent.[3] The best method for measuring the level of chronic glycemia is the glycosylated hemoglobin assay (HbA1c Level), which is dependent on both duration and level.[3,5] Diabetic foot ulcers lead to amputations and increase morbidity and high therapeutic management costs. Preventing diabetic foot ulcers can reduce the frequency of lower limb amputations.[7,8]

## ETIO-PATHOGENESIS OF DIABETIC FOOT ULCERS

Risk factors linked to the development of diabetic foot ulcers includes gender, duration of diabetes, advanced age, high BMI, and comorbidities like retinopathy, peripheral vascular disease, diabetic peripheral neuropathy, glycosylated hemoglobin level (HbA1c), foot deformity, elevated plantar pressure, infections, and improper foot care practices.[9-11] Ischemic, neuropathic, or mixed neuro-ischemic abnormalities are the most common causes of diabetic foot ulcers. 10% of diabetic foot ulcers are just ischemic, and 90% are brought on by neuropathy, either by itself or in conjunction with ischemia.[12-14] Diabetic patients most frequently suffer foot difficulties as a result of peripheral sensorimotor and autonomic neuropathy. This condition increases the chance of developing ulcers by causing excessive foot pressure, deformities, and unstable gait.Plantar pressure is raised by foot abnormalities and unstable gait, which can lead to foot ulcers.[13-16]

## DIABETIC FOOT LESIONS CLASSIFICATION

Currently, a number of classification schemes that aim to take into account the various aspects of an ulcer—such as its location, depth, neuropathy, infection, and ischemia—are used to assess the severity of diabetic foot such as the PEDIS System, the University of Texas System, the Wagner System, and a hybrid system.[17,18]

Classification system that are commonly used are:

### *Wagner-Meggitt Classification*

Most extensively and frequently used. This system classifies foot lesions into five grades, ranging from grade 0 to grade 5. High-risk feet without an active lesion are classified as grade 0, and complete foot gangrene is classified as grade 5.

The issue of infection is only addressed in grade 3. The disadvantage of this system is that it makes no mention of ischemia or neuropathy (Table:1).

**Table 1: Wagner-Meggitt classification**

| GRADE | LESION |
|---|---|
| 0 | No open lesion |
| 1 | Superficial ulcer |
| 2 | Deep ulcer to tendon or joint capsule |
| 3 | Deep ulcers with abscess, osteomyelitis, or joint sepsis. |
| 4 | Local gangrene-fore foot or heel |
| 5 | Gangrene of entire foot |

### *Depth-Ischemic classification*

It is a Wagner-Meggit system modification.This classification system aims to increase the accuracy and rationality of the classification, highlight the differences between grades 2 and 3, facilitate the distinction between wound and vascularity of the foot, and enhance the relationship between therapy and grade. (Table: 2).

**Table 2: Depth-ischemic classification**

| Grade | Lesion |
|---|---|
| 0 | No open lesion: may have deformity or cellulitis A ischemic B infected |
| 1 | Superficial ulcer A ischemic B infected |
| 2 | Deep ulcer to tendon or joint capsule A ischemic B infected |
| 3 | Deep ulcer with abscess, Osteomyelitis, or joint sepsis A ischemic B infected |
| 4 | Local gangrene-fore foot or heel A ischemic B Infected |
| 5 | Gangrene of entire foot A ischemic B Infected |

***University of Texas classification***

Lesion depth and ischemia are included in the University of Texas San Antonio System (Table 3). It is essentially a better version of the Wagner System that has been modified. Each Wagner System grade in this system is further separated into phases based on the existence of either an infection, ischemia, or a combination of both.

**Table 3. University of texas classification system.**

| Stages | Grade 0 | Grade 1 | Grade 2 | Grade 3 |
|---|---|---|---|---|
| A | Pre-or post-ulcerative lesions Completely epithelialized | Superficial wound not involving tendon capsule or bone | Wound penetrating to tendon or capsule | Wound penetrating to bone or joint |
| B | With infection | With infection | With infection | With infection |
| C | With ischemia | With ischemia | With ischemia | With ischemia |
| D | With infection and ischemia | With infection and ischemia | With infection and ischemia | With infection and ischemia |

**MANAGEMENT OF DIABETIC FOOT ULCERS**

The best practices for managing diabetic foot ulcers include wound debridement, glucose control, patient and carer education,treatment of any infection, off-loading of the ulcer, revascularization techniques where necessary, and reconstructive surgery as required. Additional techniques or adjunct therapies, such as negative pressure wound therapy (NPWT/VAC), the use of advanced wound care products, and hyperbaric oxygen therapy, may be helpful.

**PREVENTION/ EDUCATION**

Between 49 and 85 percent of diabetic foot issues are avoidable. This can be accomplished by combining appropriate foot care given by an inter-professional diabetes care team with suitable diabetes education. The diagnosis and management of individuals with chronic wounds require a collaborative approach and comprehensive care. An ideal strategy for attaining wound resolution is the integration of the work of an inter-professional care team, which consists of

physicians, nurses, and allied health professionals, with the patient, family, and carers. [1, 19, 20]

Patients with diabetes need to check their feet on a frequent basis, or they can have a family member or carer do it for them.A crucial component in the prevention of diabetic foot ulcers is daily inspection. All cuts, bruises, infections, and sores need to be treated carefully and promptly. Skincare routines that involve gentle cleansing with soapy water and topical moisturizer application help to maintain healthy skin that is more resilient to damage and breakdown. In the event of foot deformities or specific support requirements, custom shoes should be taken into consideration. Otherwise, properly fitting shoes with sufficient support should be prescribed (athletic or sports shoes and thick, cushioned socks). Topical antibiotics should be used to treat minor wounds after they have been gently cleaned.A doctor should also check for any minor wounds that take a long time to heal. Additionally, by encouraging patients to pursue preventive measures and doing frequent follow-up foot exams, doctors can assist patients in adopting and maintaining appropriate foot care habits. [1, 12, 13, 19, 20]

**BLOOD SUGAR CONTROL**

It is preferable for people with diabetic foot ulcers to have long-term glucose control. Self-monitoring blood glucose is the standard of care in the management of diabetes, and it permits the patient to check their blood sugar at any time.

The frequency of blood glucose monitoring should be customized and adjusted to meet the objectives of diabetes care.By integrating glucose readings with dietary history, medication adjustments, and other factors, the patient and the diabetes care team can enhance the treatment plan and activity history, which typically entails the use of drugs that decrease blood sugar (insulin preparations and noninsulin therapies).Glycated hemoglobin (HbA1c) measurement is the accepted method for evaluating long-term glycemic management. The goal for glycemic management, as shown by the HbA1c, needs to be customised, and the patient's goals for therapy should be established after taking a variety of social, medical, and lifestyle factors into account.

The objective is to attain a HbA1c as close to normal as possible while avoiding severe hypoglycemia. The goal values for HbA1c, peak postprandial capillary plasma glucose, and pre-prandial capillary plasma glucose, respectively, should be <7%, 4.4–7.2 mmol/L (80–130 mg/dL), and <10.0 mmol/L (<180 mg/dL) for the majority of patients.[21]

**DEBRIDEMENT/ WOUND BED PREPARATION**

Since chronic wounds cannot heal in the presence of dead tissue, debris, or significant colonization, demineralization of necrotic tissue is a crucial part of wound care. In closed wound areas or tissues that are weakened, bacterial colonization increases. Necrotic tissue debridement has several uses, including clearing away callus and necrotic tissue, lowering pressure, assessing the wound bed, assessing tracking, and tunnelling, and lowering the amount of germs present. Additionally, it promotes healing and drainage.

By encouraging the formation of granulation tissue, it facilitates healing and can be accomplished medically, through enzymatic means, physiologically, mechanically, or by autolysis. [22–27]

Surgical debridement, sometimes referred to as the "sharp method," is a quick and efficient way to remove dead tissue and hyperkeratosis. It is carried out with scalpels. It's one of the gold standards for managing wound healing; good granulation tissue needs to be protected.[22] Numerous enzymatic agents, such as papain, collagen produced from krill, collagenase from crabs, a combination of streptokinase and streptodornase, and dextran's, can be used to accomplish enzymatic debridement. Necrotic tissue is eliminated without endangering healthy tissue. For ischemic ulcers, enzymatic debridement is recommended despite its high cost because surgical debridement is quite unpleasant in these situations.[23]

Recently, sterile maggots have been used for biological debridement. Only necrotic tissues, germs, and surface debris are broken down by maggots; healthy tissue is left unharmed. According to recent research, this technique can also effectively remove drug-resistant bacteria from wound surfaces, such as MRSA. [24] A non-selective physical technique known as mechanical debridement is used to remove necrotic tissue. It can involve pulsed lavage, hydrotherapy, high-pressure irrigation, and wet-to-dry dressings. In an acute care context, one of the most often prescribed—and overused—methods of debridement is wet-to-dry. Whirlpool hydrotherapy has the potential to eliminate debris, germs, wound exudates, and surface skin.

Although there might be a case for using this method in the early phases of a wound, it is harmful to granulation tissue that is friable.[25, 27]

Using dressings that produce a moist wound environment, autolytic debridement allows host defence systems (macrophages, neutrophils) to remove damaged tissue using the body's own enzymes. The use of appropriate dressings, such as hydrogels, films, and hydrocolloids, improves autolysis. Because autolysis is so selective, it doesn't harm the skin around it.[26, 27]

**ROLE OF ANTIBIOTICS/ BACTERIAL MANAGEMENT**

Compared to wounds of other etiologies, diabetic foot ulcers have a higher morbidity and death rate associated with infection. Therefore, early and aggressive treatment is more recommended in the presence of even minor symptoms of infection (save for immunocompromised individuals).

It should be noted that the ideal length of antibiotic treatment is not well defined and will vary depending on the infection's severity and treatment response.

**Table 5: General principles of bacterial management**.

| **General principles of bacterial management. (data adapted from)[27,28]** |
|---|
| When an infection first manifests, it's critical to determine its severity, obtain the necessary cultures, and decide whether surgery is necessary. |
| After the necrotic material has been initially cleaned and debrided, the best specimens for culture should be obtained. |
| Empirical broad-spectrum antibiotic therapy is necessary for patients with serious infections while waiting for culture results. A more targeted and narrow-spectrum antibiotic can be used to treat patients with mild infections (and many with moderate infections). |
| Due to immunological abnormalities in diabetic patients, even bacteria thought to be skin commensals can cause serious tissue damage and, when isolated from properly collected tissue specimens, should be considered pathogens. |
| Particularly when isolated from an ulcer swab, gram-negative bacteria are frequently colonising organisms that don't need to be treated specifically unless the patient is at risk of contracting such organisms. |
| If there is a fever and systemic toxicity, blood cultures should be sent. |
| The wound should be routinely examined for early indications of infection or infection spreading even after receiving the proper treatment. |
| The role of clinical microbiologists and infectious disease specialists is critical; when choosing an antibiotic, laboratory data should be considered with the patient's clinical presentation and medical history. |
| For certain bone infections, necrotic tissue, and deep abscesses, prompt surgical intervention is essential. |

**PRESSURE OFFLOADING**

In patients with peripheral neuropathy, it's critical to equitably disperse stress by offloading at-risk foot areas. Plantar ulcer healing depends critically on the ulcer area being offloaded, since insufficient offloading can lead to tissue damage and ulceration.

According to reports, improper offloading of the foot (in high-pressure areas) even after the ulcer closes increases the chance of recurrence. This is why ulcer off-loading is becoming more and more important. The permanent total contact cast (TCC) is considered the industry standard.

This cast for the lower leg and foot is well-molded, has little padding, and is composed of fast-setting fiberglass or plaster. It evenly distributes pressure across the foot's whole plantar surface. Absolute contraindications to using a non-removable TCC include osteomyelitis, severe foot ischemia, deep abscess, and poor skin quality. For these individuals, detachable medical equipment such as wheelchairs,

walkers, Scotch-cast boots, healing sandals, crutches, and walkers should be utilized. [29, 30]

**NEGATIVE-PRESSURE WOUND THERAPY (NPWT) / VAC**

A robust open-celled foam surface dressing wrapped with an adhesive drape to maintain a closed environment is attached to a specific pump (vacuum-assisted closure) that uses constant or intermittent sub-atmospheric pressure. After that, a canister is attached to the pump to collect exudates and wound discharge. NPWT maximises blood flow, reduces tissue oedema, and cleans the wound area of pathogens, proinflammatory cytokines, and exudates. Following debridement, it should be carried out continuously until the ulcer's surface begins to produce healthy granulation tissue. At present, NPWT is recommended for individuals with intricate diabetic foot wounds; yet, it is contraindicated in patients with an active bleeding ulcer. [31]

**HYPERBARIC OXYGEN THERAPY**

It entails the sporadic delivery of 100% oxygen at a p ressure higher than atmospheric pressure.The proced ure is carried out in a chamber where the patient breat hes 100% oxygen on and off for 1-
2 hours while the air pressure is raised to 2-
3 atmospheres.Thirty to forty sessions can make up a whole course.Patients who are ischemia may benefit, and amputations may not be necessary.[32, 33]

**OTHER NEWER/ ADVANCE THERAPIES**

Bioengineered skin substitutes, growth factors (PDG F beta, PRP), extracellular matrix proteins, and matrix metalloprote inases modulators (MMP) are some of the more recen t treatments that have been found to help individuals with diabetic foot ulcers recover more quickly overall .

For the management of diabetic foot ulcers that are n ot infected, bioengineered skin substitutes have promi se as a therapeutic adjunct therapy to normal wound c are.

Although some research has demonstrated promising outcomes with novel treatments, randomised trials ar e unquestionably required to determine their usefulne ss in the management of diabetic ulcers. [35, 34]

**RECONSTRUCTIVE SURGERY**

Whenever an ulcer has not lessened by more than 10% following two months of conservative treatment, it should be treated, especially if it exposes bone or tendons. Under consideration for surgical reconstruction. The available donor tissue and the needs of the defects will determine the spectrum of surgical choices, which include skin grafts and local, regional, or free flaps.

Commonly employed flaps for treating foot ulcers include distally-based sural neurocutaneous flaps, fillet flaps, medial plantar artery flaps, local muscle flaps, and V-Y plantar flaps. Foot issues and ulcer prevention can be reduced by procedures to address tendon imbalance, especially Achilles or gastro-soleus tightness correction. Flexor tendonotomies are a treatment option for metatarsal head ulcers in claw-toe patients. Table 5.[36–39]

## CONCLUSION:

Foot ulcerations are more likely to occur in patients with diabetes mellitus. Success is mostly dependent on the team's management style and patient education. Management of diabetic foot ulcers is still a significant therapeutic issue, meaning that current approaches and therapies must be reviewed immediately to meet objectives and lessen the burden of care in an economical and effective manner.

*Funding: No funding sources*
*Conflict of interest: None declared*
*Ethical approval: Not required*

## REFERENCES:

1. Bakker K, Riley PH. The year of the diabetic foot.Diabetes Voice. 2005;50(1):11-4.
2. Harris MI, Flegal KM, Cowie CC, Eberhardt MS, Goldstein DE, Little RR, Wiedmeyer HM, Byrd-Holt DD. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in US adults: the Third National Health and Nutrition Examination Survey, 1988–1994. Diabetes care. 1998;21(4):518-24.
3. Complications in newly diagnosed type II diabetic patients and their association with different clinical and biochemical risk factors. Diabetes Res 1990;13:1 -11.
4. Diabetes Control and Complications Trial Research Group. The relationship of glycemic exposure (HbA1c) to the risk of development and progression of retinopathy in the Diabetes Control and Complications Trial. Diabetes. 1995;44(8):968-83.
5. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, Hadden D, Turner RC, Holman RR. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. Bmj. 2000;321(7258):405-12.

6. Nathan DM, Mc Kitrick C, Larkin M et al. Glycemic control in diabetes mellitus: have changes in therapy made a difference? Am J Med 1996; 100: 157-63.
7. Mayfield JA, Reiber GE, Sanders LJ, Janisse D, Pogach LM. Preventive foot care in people with diabetes. Diabetes Care. 2001;24:S56.
8. International Diabetes Federation. The Global Burden. IDF Diabetes Atlas.2012:5.
9. Frykberg RG, Zgonis T, Armstrong DG, Driver VR,Giurini JM, Kravitz SR, Landsman AS, Lavery LA,Moore JC, Schuberth JM, Wukich DK. Diabetic foot disorders: a clinical practice guideline (2006 revision). J foot and ankle surg. 2006;45(5):S1-66.
10. Bortoletto MS, de Andrade SM, Matsuo T, Haddad MD, González AD, Silva AM. Risk factors for foot ulcers—a cross sectional survey from a primary care setting in Brazil. Primary care diabetes.2014;8(1):71-6.
11. Waaijman R, de Haart M, Arts ML, Wever D, Verlouw AJ, Nollet F, Bus SA. Risk factors for plantar foot ulcer recurrence in neuropathic diabetic patients. Diabetes care. 2014;37(6):1697-705.
12. Monteiro-Soares M, Boyko EJ, Ribeiro J, Ribeiro I,Dinis-Ribeiro M. Predictive factors for diabetic foot ulceration:a systematic review. Diabetes/metabolism research and reviews. 2012 Oct 1;28(7):574-600.
13. Alavi A, Sibbald RG, Mayer D, Goodman L, Botros M, Armstrong DG, Woo K, Boeni T, Ayello EA,Kirsner RS. Diabetic foot ulcers: part II. Management. J Americ Acad Dermatol. 2014;70(1):21-e1.
14. Boulton AJ, Vileikyte L, Ragnarson-Tennvall G, Apelqvist J. The global burden of diabetic foot disease. The Lancet. 2005;366(9498):1719-24.
15. Formosa C, Gatt A, Chockalingam N. Diabetic foot complications in Malta: prevalence of risk factors.The Foot. 2012;22(4):294-7.
16. Sawacha Z, Gabriella G, Cristoferi G, Guiotto A,Avogaro A, Cobelli C. Diabetic gait and posture abnormalities: a biomechanical investigation through three dimensional gait analysis. Clinical biomechanics. 2009;24(9):722-8.
17. Jones EW, Peacock I, McLain S, Fletcher E, Edwards R, Finch RG, Jeffcoate WJ. A Clinico-pathological Study of Diabetic Foot Ulcers. Diabetic medicine. 1987;4(5):475-9.
18. Lavery LA, Armstrong DG, Harkless LB. Classification of diabetic foot wounds. J Foot and Ankle Surg. 1996;35(6):528-31.
19. Spraul M. Education—Can It Prevent Diabetic Foot Ulcers and Amputations?. The Foot in Diabetes,Third Edition. 2000:111-20.
20. Sibbald RG. Cost–effective faster wound healing of critically colonized wounds with a sustained release silver foam dressing, based upon the symposium"Bacteria, sustained release of silver and improved healing", An official satellite symposium of the WUWHS 2004. Published at www.worldwidewounds. Com:2005.
21. Kasper D, Fauci A, Hauser S, Longo D, Jameson J,Loscalzo J. Harrison's principles of internal medicine, 19e. USA2015. 2015.
22. Lebrun E, Tomic-Canic M, Kirsner RS. The role of surgical debridement in healing of diabetic foot ulcers. Wound repair and regeneration. 2010;18(5):433-8.
23. Smith RG. Enzymatic debriding agents: an evaluation of the medical literature. Ostomy/wound management. 2008;54(8):16-34.
24. Margolin L, Gialanella P. Assessment of the antimicrobial properties of maggots. Int wound J. 2010;7(3):202-4.
25. American Diabetes Association. Consensus Development Conference on Diabetic Foot Wound Care: 7-8 April 1999, Boston, Massachusetts. American Diabetes Association. Diabetes care. 1999;22(8):1354-60.
26. Hilton JR, Williams DT, Beuker B, Miller DR, Harding KG. Wound dressings in diabetic foot disease. Clinical Infectious Diseases. 2004;39(Supplement_2):S100-3.
27. Schultz GS, Sibbald RG, Falanga V, Ayello EA, Dowsett C, Harding K, Romanelli M, Stacey MC, Teot L, Vanscheidt W. Wound bed preparation: a systematic approach to wound management. Wound repair and regeneration. 2003;11(s1).
28. European Wound Management Association (EWMA). Position document: Wound bed preparation in practice. London: MEP Ltd, 2004. Available at http://woundsinternational.com Accessed March 2013.
29. Cavanagh PR, Bus SA. Off-loading the diabetic foot for ulcer prevention and healing. J vascular surg.2010;52(3):37S-43S.
30. Frykberg RG, Lavery LA, Pham H, Harvey C, Harkless L, Veves A. Role of neuropathy and high foot pressures in diabetic foot ulceration. Diabetes care. 1998;21(10):1714-9.
31. Xie X, McGregor M, Dendukuri N. The clinical effectiveness of negative pressure wound therapy: a systematic review. J wound care. 2010;19(11).
32. Broussard CL. Hyperbaric oxygenation and wound healing. J vascular Nurs. 2004;22(2):42-8.

33. Roeckl-Wiedmann I, Bennett M, Kranke P. Systematic review of hyperbaric oxygen in the management of chronic wounds. Brit J Surg. 2005;92(1):24-32.
34. Edmonds M, Bates M, Doxford M, Gough A, Foster A. New treatments in ulcer healing and wound infection. Diabetes/metabolism research and reviews. 2000;16(S1).
35. Ehrenreich M, Ruszczak Z. Update on tissueengineered biological dressings. Tissue Eng.2006; 12:2407–24.
36. Brem H, Sheehan P, Rosenberg HJ, Schneider JS,Boulton AJ. Evidence-based protocol for diabetic foot ulcers. Plastic and reconstructive surgery.2006;117(7S):193S-209S.
37. Attinger CE, Ducic I, Cooper P, Zelen CM. The role of intrinsic muscle flaps of the foot for bone coverage in foot and ankle defects in diabetic and nondiabetic patients. Plastic and reconstructive surgery. 2002;110(4):1047-54.
38. Pallua N, Di Benedetto G, Berger A. Forefoot reconstruction by reversed island flaps in diabetic patients. Plast Reconstr Surg 2000;106:823-7.
39. Laborde JM. Treatment of diabetic foot ulcers with tendon lengthening. American family physician.2009 Dec;80(12):1351.