



Diabetic Foot Ulcer

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ABSTRACT

Diabetic foot ulcers are one of the most challenging complications of diabetes. Up to one third of patients with diabetes mellitus may develop a diabetic foot ulcer in their lifetime. India is second only to China in the global diabetes epidemic with 77 million people living with diabetes, including 1.1 million over the age of 65, estimated to reach 27.5 million by 2024. Diabetic foot problems are caused by a number of factors, such as neuropathy, peripheral vascular disease, trauma and infection. Patients at risk should be identified and preventive measures taken according to the risk category. Glycemic control, diagnosis and treatment of vascular disease, local wound care, diagnosis and treatment of infections should be addressed in conjunction with appropriate assessment and management of general health status. The clinical pharmacist plays an important role in preventing many of the complications and can improve the patient's quality of life, along with other healthcare professionals, by educating and advising the patient on foot care and diabetes documentation.

Keywords: Diabetic foot Ulcer, osteomyelitis, diabetes.

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INTRODUCTION

Diabetes mellitus is one of the most serious problems the world is currently facing, and avoiding its complications requires a healthy lifestyle and access to medical care. Diabetes complications rank among the top contemporary public health problems due to the incidence of both type 1 diabetes (T1D) and type 2 diabetes (T2D), both of which are on the rise. Diabetes consequences might include sudden, possibly catastrophic conditions such as acute hypoglycemia or ketoacidosis. Retinopathy, nephropathy, neuropathy, and cardiovascular disease are just a few examples of the multiple organ systems that might experience chronic, incapacitating consequences.¹

The majority of diabetics will encounter one or more of these issues. For instance, a recent study by the META-EYE study group estimated that 93 million people around the world have diabetic retinopathy. Three half of people who have had diabetes for 20 or more years have diabetic retinopathy.²

End-stage diabetic complications can lead to amputations, myocardial infarction, stroke, severe eyesight loss, end-stage renal disease requiring dialysis or transplant, and

end-stage renal disease.¹ One of the most severe and expensive effects of diabetes mellitus is foot complications.³ A strategy that combines preventive, patient and staff education, multidisciplinary foot ulcer treatment, and close monitoring can lower amputation rates by 49–85%. Since India is an agricultural nation, the majority of people are unaware of proper foot care. As a result, many nations and organisations, including the World Health Organization and the International Diabetes Federation, have established objectives to cut the rate of amputations by as much as 50%.³

Diabetic foot

Diabetes is becoming a worldwide epidemic, and with it comes a higher risk of complications. One of the most dreaded diabetes consequences is foot disease. The phrase "Diabetic Foot" refers to a variety of illnesses, such as diabetic neuropathy, peripheral vascular disease, Charcot's neuroarthropathy, foot ulceration, osteomyelitis, and the eventual result-limb amputation-which may be prevented.⁴ According to some reports, a person with diabetes has a 25%.⁵ lifetime risk of developing foot ulcers. According to estimates, more than a million people with diabetes need to have a limb amputated every year. This means that one major amputation is carried out every 30 seconds worldwide.

Amputation has severe social, psychological, and economical repercussions in addition to being associated with high rates of morbidity and mortality.^{6,7} It is crucial to develop measures to stop foot ulceration because it is the primary cause of limb amputations in diabetic patients.⁴ Patients with diabetic foot issues are more likely to also have nephropathy, retinopathy, ischemic heart disease,



and cerebrovascular disease than patients without diabetic foot issues. Therefore, a multidisciplinary strategy is more likely to be beneficial for these people in order to handle these difficult issues. Furthermore, there is evidence that suggests a multidisciplinary team approach can be used to decrease the incidence of significant amputation.⁸

Epidemiology

Males and people over 60 are more likely to develop diabetic foot problems.⁴ With 77 million diabetics, 1.1 million of whom are over 65, India is in second position after China in the global diabetes epidemic. By the year 2045, it is predicted that there will be 27.5 million diabetics in India. In India, the number of adults with diabetes is believed to be close to 57%, or 43.9 million, undiagnosed.⁹

Pathogenesis

Numerous conditions, including neuropathy, peripheral vascular disease, trauma, and infection, can result in diabetic foot issues.¹ Neuropathy is thought to be the most significant of these various causal variables, which interact to produce diabetic foot problems.¹⁰

Various degrees of diabetic neuropathy can impair sensory, motor, and autonomic functions. The subtle nature of neuropathy makes it possible for patients to be unaware of it, which emphasises the significance of routine examinations of the diabetic foot. Muscle atrophy, foot deformities, altered foot biomechanics, and redistribution of foot pressures are all effects of motor neuropathy and eventually make the foot more prone to ulceration. Due to sensory neuropathy, stimuli that would typically cause pain or discomfort make the foot "deaf and blind." As a result, the foot is more vulnerable to recurrent damage, which could go untreated until ulceration develops. Loss of perspiration due to autonomic neuropathy makes the skin dry and more prone to fissures and cracks. A further factor is the altered autonomic control of cutaneous blood flow.¹¹

Charcot neuroarthropathy is a non-infectious condition that affects a healthy, unresponsive foot. Bone and joint breakdown, fragmentation, and remodelling are its hallmarks. Although Charcot's neuroarthropathy was formerly thought to be a side effect of tabes dorsalis, it can arise from any kind of sensory neuropathy, with diabetes currently being the most common cause.¹ Around 16% of diabetic patients with a history of neuropathic ulceration have been documented to have Charcot foot. 30% of patients may have bilateral involvement, according to reports.¹² It is uncertain what exact mechanism causes Charcot neuroarthropathy. According to the neurotraumatic theory, loss of pain and proprioception, along with repeated mechanical trauma to the foot that is generally undetected by the patient while they continue to bear weight, leads to bone deterioration.¹³ According to the neurovascular theory, periarticular osteopenia and increased blood flow caused by an autonomically driven vascular response that activates osteoclasts also contribute to joint degradation.^{14,15} Microfractures are spread by repeated stress to the insensitive foot, and the persistent

weight-bearing delays the healing of these fractures. By causing intrinsic muscle imbalance, ligament strain, and spontaneous dislocations, motor neuropathy may be a factor. Eccentric loading of the foot and high plantar pressures as a result encourage the growth of microfractures and gradual bone degeneration. The danger of developing an ulcer is higher on this unresponsive malformed foot. 2-3 times greater risk of accelerated atherosclerosis is linked to diabetes. People who have peripheral vascular disease are more likely to have slow wound healing. This emphasises how crucial it is to recognise and take strong steps to manage the related vascular risk factors such hypertension, dyslipidaemia, and smoking.¹⁶ Poor glucose control also has a negative impact on wound healing because it impairs collagen cross-linking and matrix metalloproteinase activity.¹⁷ Additionally, poor glycaemic control inhibits polymorphonuclear leucocyte function, makes people more susceptible to onychomycosis, and increases the risk of toe-web tinea infections, all of which can cause damage to the skin.^{18,19}

The diabetic foot does not ulcerate on its own; instead, it usually develops as a result of trauma, which the patient may not even be aware of. This trauma may be brought on by wearing uncomfortable shoes, going barefoot, stepping on foreign objects, or being scalded by hot water.¹ It is reassuring to know that daily physical exercise is not a risk factor for developing new or recurring foot ulcers.²⁰ Due to concomitant peripheral vascular disease and immunosuppression in diabetic patients, the local and systemic indications of inflammation may frequently be diminished. Neuropathy may make the infected foot painless, which may cause people to put off getting medical help.¹¹

Assessment and Diagnosis

All diabetic patients must possess the following as part of their annual diabetic foot assessment, under National Institute of Clinical Excellence 12 recommendations:

- Neurological foot testing, which involves placing 10 g monofilament at four different locations on each foot and measuring one of the following: ankle reflexes, pinprick sensation, vibration perception threshold, or vibration using a 128 Hz tuning fork; protruding metatarsal heads/claw toes, hallux valgus, muscular atrophy, or Charcot deformity are examples of abnormal foot morphology.

- dermatological conditions such perspiration, erythema, and calluses.

- Vascular: pulses in the feet, the ankle brachial index, and Doppler waveforms (if applicable).

According to a prospective cross-sectional study conducted in Turkey, the Wagner classification system and the acute phase reactants (C-reactive protein, white cell count, and erythrocyte sedimentation rate) can be used to predict how long a patient will stay in the hospital.²¹ According to Tabur et al., a longer hospital stay was positively predicted by an



increase in acute phase reactants and greater Wagner grading.

System of classification for Wagner ulcers.

Grade 1: Diabetic superficial ulcer

Grade 2: Extension of ulcer involving ligament, tendon, joint capsule, or fascia without osteomyelitis or abscess

Grade 3: deep ulcer with osteomyelitis or an abscess

Grade 4 - severe foot gangrene

The National Institute for Clinical Excellence (NICE) has recommended risk categorization of the diabetic foot based on the aforementioned evaluations, as indicated in Table 1.

Table 1: Risk stratification of the diabetic foot ¹

Risk Stratification	Clinical Features	Suggested foot review
At low risk	Normal sensation, palpable pulses	Annual
At increased risk	Neuropathy or absent pulses	3-6 monthly
At high risk	Neuropathy or absent pulses in addition to deformity or skin changes or previous ulcer	1-3 monthly
Ulcerated foot	Foot Ulcer	Active multidisciplinary foot care team follow-up

Intense glycemic control can halt the onset and progression of diabetes microvascular problems (retinopathy, nephropathy, and neuropathy). This conclusion has been demonstrated in type 1 diabetes, however the type 2 evidence at this time is insufficient.²²⁻²⁴

However, aside from glycemic management, no one therapeutic intervention or strategy can alter the development of microvascular complications.²⁵⁻²⁸

Management

1. Considerations for managing diabetic foot ulcer

Lower limb amputations (LEA) without trauma are most commonly caused by diabetic foot ulcers worldwide^{29,30}. Once a diabetic foot ulcer develops, immediate implementation of management techniques is required. A multidisciplinary team approach is essential for the therapy of these patients, according to many studies^{29,31,32}. The multidisciplinary team needs to concentrate on four key areas: glycemic control, vascular disease diagnosis and treatment, wound assessment and local care, and infection detection and treatment³².

Diabetic foot ulcer prevention strategies Preventative actions ^{25,33}

- 1 Don't smoke
- 2 Steer clear of walking barefoot, in sockless shoes, or in slippers with thin soles.
- 3 Steer clear of hot sand and ground
- 4 Examine both feet and the inside of the shoes every day.
- 5 Wash the feet every day.
- 6 Check the water's temperature before taking a bath.
- 7 Avoid chemicals and lubricate dry skin
- 8 Trim your toenails neatly.
- 9 Avoid removing calluses
10. Put on snug shoes (customize if feet have deformity)
- 11 Regularly replace your socks

It is essential to inform individuals about the value of getting early medical consultation and proper foot care. A multidisciplinary strategy should be used to manage diabetes and the issues that come with it. The best possible glycaemic management is crucial.¹

It is crucial to get treatment as soon as possible for diabetic foot ulcers to heal. The underlying cause of diabetic foot ulcers, such as ischaemia, neuropathy, or a mix of both, determines how best to treat them.¹

2. Treating ischaemic ulcers

Since diabetes is a vascular illness, it is crucial to take precautions to lower the overall risk of atherosclerosis. Quitting smoking, aggressively treating hypertension and diabetic dyslipidemia, and regularly using anti-platelet drugs are essential in lowering this cardiovascular risk.³³⁻³⁶ Revascularization may be required in some patients in order to achieve prompt and reliable recovery. Patients with supra-inguinal (aorto-iliac) illness might be candidates for angioplasty (with or without stents), which has a low risk and can produce good long-term effects.³⁷

If there is no endovascular alternative available for the patient, open bypass surgery may be explored.³⁷ Infra-inguinal illness is more challenging to cure³⁸ For these individuals, femoro-distal bypass using autogenous tissue, like the long saphenous vein, is still the standard of care.^{37,39} Grafts made from prosthetic materials can be employed if such tissue is not accessible.⁴⁰ The majority of vascular surgeons and interventionalists concur that traditional transluminal angioplasty is unlikely to be effective in treating the multilevel, distant, and calcified arterial disease encountered in diabetics.⁴¹

The BASIL research, which was conducted more recently, demonstrated for the first time that percutaneous angioplasty may be regarded as a viable treatment option for some patients with severe limb ischaemia.⁴² Given the significant difference in early morbidity found in this trial,



angioplasty may be preferred as the initial treatment when technically possible. A post-hoc study, however, revealed that patients who underwent surgery in BASIL may have a late-survival advantage (beyond 2 years). These findings highlight the importance of collaboration between surgeons and interventionalists. In addition, the high overall mortality (37%) found in BASIL raises the possibility that the ischemic limb is simply the tip of a larger problem, underscoring the significance of a multidisciplinary team approach to managing the overall risk. Last but not least, the authors of BASIL correctly note that in certain cases, primary amputation may be the best option, and that by early identification of these patients, it may be possible to prevent the incorrect use of these expensive and sometimes risky treatments.

3. Treating infected ulcers

On the basis of the clinical outcome and the findings from the wound culture and sensitivity, the antibiotic regimen is then changed.^{43,44}

Cleaning the incision, removing any necrotic matter, and using a blunt, sterile device to probe for any foreign objects or exposed bone are all part of general treatment.⁴⁵

Oral antibiotic regimens with ciprofloxacin, cephalexin, clindamycin, and amoxicillin-clavulanic acid are frequently prescribed.⁴⁵, based on Table 1. Assessment of the diabetic foot's risk stratification of risks clinical traits Foot review advice minimal danger normal feeling, discernible pulses Annual at higher risk neuropathic pain or no pulse 3 to 6 monthly Highest risk Along with deformities, skin abnormalities, or a history of ulcer, there may also be neuropathy or absent pulses. 1 to 3 monthly 1 foot with ulcers.

When treating ulcers that are just mildly infected, topical antibiotics are frequently beneficial; however, parenteral antibiotics may be necessary if the infection is severe. Amoxicillin-clavulanic acid, imipenem-cilastin, ampicillin-sulbactam, piperacillin-tazobactam, and broad-spectrum cephalosporins like cefuroxime are among the regularly utilised intravenous regimens.⁴⁶ The inclusion of metronidazole to this regimen may be necessary if an anaerobic infection is suspected. The ideal time frame for receiving antibiotics is still mostly unknown. While more severe soft tissue infections may require up to 2-3 weeks of therapy, minor infections often respond to a 7–10 day course of antibiotics.⁴⁵ Remember that the goal of antibiotic therapy is to treat the infection rather than the wound, which typically takes significantly longer to heal. In addition to raising the possibility of antibiotic-related side effects, prolonged antibiotic use has the potential to create antibiotic-resistant types of bacteria. As a last treatment challenge, addressing underlying osteomyelitis is crucial. If osteomyelitis is present, it is necessary to treat the patient for a minimum of 4-6 weeks with antibiotics that can penetrate deeply into the bone, such as fluoroquinolones, clindamycin, or fusidic acid.⁴⁶ The most effective treatment

for osteomyelitis is still surgical excision, particularly for those patients who do not react to antibiotics.⁴⁷

4. Use of custom footwear

In addition to fitting foot abnormalities, prescription shoes for high-risk patients may help by lowering high plantar pressures and friction.⁴⁸ Patients with low risk can wear well-fitting, premium over-the-counter walking shoes without any problems.¹

5. Prophylactic foot surgery

Reconstructive foot surgery for diabetic feet has shown a sharp increase in attention over the past ten years. Elective surgery (to relieve discomfort), preventative surgery (to lower risk of ulceration), curative surgery (to treat an open wound), and emergency surgery are the four categories into which non-vascular foot surgery in diabetes can be divided (to control limb and life threatening infection).⁴⁹ In this group of individuals, toe extensor tenotomies may lessen toe deformity and avoid recurring ulcerations.⁵⁰ In patients with prominent metatarsal heads, metatarsal osteotomy may lower the likelihood of recurrent ulcers.⁵¹ To generate a more plantigrade (anatomical) foot, patients with a mid-foot prominence may benefit from having the prominence surgically removed.⁵² However, there is currently no RCT data contrasting medical therapy with surgery.¹

Clinical Pharmacist Roles in the management of diabetic foot ulcer care⁵³

- Develop, assess, and record drug treatment procedures for diabetic foot ulcers.
- Develop treatment guidelines for diabetic foot ulcers in conjunction with other healthcare specialists.
- Provide education to all medical personnel involved in pharmaceutical treatment.
- Take part in health checks for diabetes and diabetic foot ulcers (HbA1c, FBS, PPBS, etc.)
- Holding health promotion and education programmes for quitting smoking, managing obesity, practising self-care for diabetic foot ulcers, developing preventative strategies, holding awareness events for the condition, etc.
- Provide community pharmacists with training and collaboration so they can better manage and prevent diabetic foot ulcers.
- Recommendations for management from community pharmacies and counselling services.
- Research in the field of pharmacotherapeutics pharmacoepidemiology; pharmacy practice; health economics in diabetes and Diabetic Foot Ulcer.
- To assess and record research findings in order to enhance all facets of pharmaceutical treatment.



- Contribute to the development of antibiotic policy and its rules.
- To create auditing protocols and professional standards.

CONCLUSION

The incidence of diabetes mellitus has been rising over the past ten years, and it is now a major public health concern on a global scale. It causes a variety of systemic problems that, if untreated or improperly managed, exacerbate morbidity and hasten death.

Disease of the foot is among one of the most feared complications of diabetes and comprises of varied pathologies such as, neuropathy, vasculopathy, neuroarthropathy, foot ulceration, infection and the potentially preventable endpoint, amputation. As the majority of amputations are preceded by foot ulceration, it is crucial to identify those at an increased risk. Once identified, specific interventions can be directed to reduce this risk. The clinical pharmacist can also play an important role in prevention of many of its complications and can improve patient quality of life, along the side of other health care professionals.

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