ABSTRACT

Diabetic foot problems are common throughout the world, resulting in major medical, social and economic consequences for the patients, their families and society. Foot ulcers affect 15% of diabetic patients during their lifetime. Foot ulcers are more likely to be of neuropathic origin and therefore eminently preventable. Infected diabetic foot ulcers are a major cause of hospitalization in diabetic patients and most non-traumatic amputations are associated with diabetic foot infections. The most commonly used classification systems are the Wagner-Ulcer Classification system and the University of Texas Wound Classification. The management of diabetic foot ulcer (DFU) should be optimized by using a multidisciplinary team, due to a holistic approach to wound management is required. Based on studies, blood sugar control, wound debridement, advanced dressings and offloading modalities should always be a part of DFU management. Treatment of chronic wounds should be essentially directed against the main etiologic factors responsible for the wound. Amputations are usually the treatment of last resort but occasionally can be considered early to allow for faster mobilization and rehabilitation. This article will focus the causes, pathogenesis and recommended management pathways of diabetic foot ulcers.

KEYWORDS: Diabetes mellitus, Amputation, Neuropathic, Debridement, Etiology.

INTRODUCTION

Diabetes mellitus (DM) is one of the main problems in health systems and a global public health threat that has increased dramatically over the past two decades.\(^{[1]}\) In India approximately 61.2 million people are diabetic and it is expected to increase to 101.2 million
by 2030. In addition, people with T2DM are often accompanied by complications, such as cardiovascular diseases, diabetic neuropathy, nephropathy, and retinopathy.

Foot ulcers are the most common medical complications of patients with diabetes, with an estimated prevalence of 12-15% among all individuals with diabetes. The term “Diabetic foot ulcer” is used to define a clinical condition, but simply put it is merely a wound on the foot of a patient who is diabetic. Diabetic foot ulcers are responsible for more hospitalizations than any other complication of diabetes. Ulcerations can have potential devastating complications as they cause up to 90% of lower extremity amputations in patients with diabetes.

Infection in foot wounds should be defined clinically by the presence of inflammation or purulence, and then classified by severity. This approach helps clinicians make decisions about which patients to hospitalize or to send for imaging procedures or for whom to recommend surgical interventions. Many organisms, alone or in combinations, can cause DFI, but gram-positive cocci (GPC), especially staphylococci, are the most common.

Diabetic foot complications are the most common cause of non-traumatic lower extremity amputations in the industrialized world. They are complex infections and the prognosis is influenced by many factors, depending on the ulcer (location, extension, whether chronic or not, previous amputation, ischemia grade), and the patient (age, renal impairment, time of onset of diabetes, associated co-morbidity). All these must be taken into account when establishing its treatment.

**EPIDEMIOLOGY**

Globally, diabetic foot infections are the most common skeletal and soft-tissue infections in patients with diabetes. The incidence of diabetic foot infections is similar to that of diabetes in various ethnic groups and most frequently affect elderly patients. There are no significant differences between the sexes. Mortality is not common, except in unusual circumstances.

Even today, seven out of top ten countries with the largest number of diabetes patients are low or Middle - income countries, including India, China, Russia, Brazil, Pakistan, Indonesia, and Bangladesh among which the prevalence rates are 12.1% and 9.7% in India and China, respectively. The annual incidence of foot ulceration is estimated to be approximately 1% - 4% and its prevalence ranges from 4% to 10%, whereas, the lifetime risk for the development of a diabetic foot ulcer in patients with diabetes ranges from 15% to as high as 25%.
Although the costs derived from DF ulcers and other infections are not accurately known, in the U.S. it is estimated that an ulcer episode costs from $4,500 to $28,000 at two years after diagnosis, with a mean of $5,500 per patient per year. Although mean hospital stay of an amputation has decreased, it remains a costly procedure, ranging from $20,000 to $40,000 depending on the level of amputation, hospital stay, or patient co-morbidities. More up-to-date and similarly high values are available for Europe.\textsuperscript{[8]}

A National Rural Diabetes Survey was done between 1989 and 1991 in different parts of the Indian’s rural populations which showed diabetic prevalence as 2.8 per cent. The prevalence of 6.1 percent in individuals aged above 40 years was unexpectedly high at that time for rural area with low socio-economic status and decreased health awareness.\textsuperscript{[11]}

**ETIOLOGY OF DIABETIC FOOT ULCER**

In most patients, peripheral neuropathy and peripheral arterial disease (PAD) (or both) play a central role and DFUs are therefore commonly classified as (Table 1).

a) Neuropathic

b) Ischaemic

c) Neuroischaemic (Figures 1-3)\textsuperscript{[12]}

<table>
<thead>
<tr>
<th>Feature</th>
<th>Neuropathic</th>
<th>Ischaemic</th>
<th>Neuroischaemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensation</td>
<td>Reduced or absent sensation to touch, vibration, pain, and pressure</td>
<td>Sensation may be present but decreased if there is associated neuropathy</td>
<td>Degree of sensory loss</td>
</tr>
<tr>
<td>Foot temperature</td>
<td>Warm</td>
<td>Cold or decreased temperature</td>
<td>Cool</td>
</tr>
<tr>
<td>Ulcer location</td>
<td>On the plantar aspects (forefoot 80%) of the foot/toes</td>
<td>Distal/tips of the toes, heel, or margins of the foot</td>
<td>Margins of the foot and toes</td>
</tr>
<tr>
<td>Foot pulses</td>
<td>Present and often bounding, Dilated, prominent veins</td>
<td>Absent or markedly reduced</td>
<td>Cool with absent pulses</td>
</tr>
<tr>
<td>Callus present</td>
<td>Commonly seen on the weight-bearing areas and is generally thick</td>
<td>Not usually. If present, distal eschar or necrosis</td>
<td>Minimal callus Prone to necrosis</td>
</tr>
<tr>
<td>Other</td>
<td>Dry skin and fissuring</td>
<td>Delayed healing</td>
<td>High risk of Infection</td>
</tr>
</tbody>
</table>
SITES OF AND CAUSES OF DIABETIC FOOT ULCERS

The site of ulcer, etiology and treatment methodology varies according to the population of different region. Several reported that several factors were contributing to the outcome of DFU, which is irrespective of similar type of care treatment. Diabetic foot ulcers usually develop in areas of the foot that are exposed to either friction and sustained pressure, and/or areas of the foot that are exposed to repetitive trauma e.g. rubbing of toes on the stitching of a shoe. The most common foot ulcer sites are.

• The heel
• On the underside of the toes
• The tips of any prominent toes (usually the 1st or 2nd toe)
• The tips of deformed toes (e.g. tips of hammer toes).

PATHOGENESIS OF DIABETIC FOOT ULCER

DFU is characterized by a classical triad of neuropathy, ischemia, and infection. Due to the impaired metabolic mechanisms in DM, there is an increased risk of infection and poor wound healing due to a series of mechanisms which include decreased cell and growth factor response, diminished peripheral blood flow and decreased local angiogenesis. Thus, the feet are predisposed to peripheral vascular disease, damage of peripheral nerves, deformities, ulcerations and gangrene (Figure 5).

a) Neuropathy

Peripheral neuropathy in diabetes is one of the major causes of foot ulcers. Studies reported that metabolic abnormalities due to hyperglycemia cause neuropathy. There are various other factors accounting for origination of neuropathy, like pre-diabetes neuropathy, abnormalities in fatty acid metabolism, activation of protein kinase-C pathway, formation of advanced glycated end products, myoinositol, polyol pathway, production of nerve growth factor and production of antibodies to neural tissues. The four prime mechanisms causing hyperglycemic nerve damage are elevated levels of intracellular advanced glycated end
products, activation of protein kinase C, increased hexosamine pathway flux and polyol pathway.[15]

Peripheral neuropathy may predispose the foot to ulceration through its effects on the sensory, motor and autonomic nerves.

✓ The loss of protective sensation experienced by patients with sensory neuropathy renders them vulnerable to physical, chemical and thermal trauma.
✓ Motor neuropathy can cause foot deformities (such as hammer toes and claw foot), which may result in abnormal pressures over bony prominences.
✓ Autonomic neuropathy is typically associated with dry skin, which can result in fissures, cracking and callus. Another feature is bounding pulses, which is often misinterpreted as indicating a good circulation.

Loss of protective sensation is a major component of nearly all DFUs. It is associated with a seven–fold increase in risk of ulceration.[12]

b) Peripheral vascular disease

Peripheral vascular disease (PVD) is an atherosclerotic occlusive disease of lower extremity. Diabetes is an important risk factor for PVD. PVD is an important prejudiced cause towards development of foot ulcers in about 50% of cases. Patients with diabetes have a higher incidence of atherosclerosis, thickening of basement membranes of capillaries, hardening of arteriolar walls and endothelial proliferation. Atherosclerotic blockage of large and medium-sized arteries, such as femoropopliteal and aortoiliac vessels leads to acute or chronic ischemia.[15] Atherogenesis is the developmental process of atheromatous plaques. It is characterized by a remodeling of arteries leading to subendothelial accumulation of fatty substances called plaques.[11] In combination with digital artery disease, ulcers can develop and instantaneously progress to gangrene due to inadequate blood flow. Decreased arterial perfusion causes abate in peripheral pulses and patient comes to a risk of ulceration, infection with impaired healing rates and finally leading to chronic state involving gangrene and amputation.[15] It is important to remember that even in the absence of a poor arterial supply, microangiopathy (small vessel dysfunction) contributes to poor ulcer healing in neuroischaemic DFUs.[12] DM is associated with a near 3-fold increased risk of accelerated atherosclerosis, which is histologically identical to that seen in the non-diabetic population. This underlines the importance of identifying and aggressively managing associated vascular
risk factors, such as obesity, cigarette smoking, dyslipidemia, hypertension, and sedentary behavior.\textsuperscript{[16]}

c) Neuroarthropathy
Charcot neuroarthropathy (CN) is a chronic painless progressive degenerative arthropathy resulting from the disturbance in sensory innervations of the affected joint. The impairment of the autonomic nervous system due to DM causes an increase in local blood supply and the resting blood flow is much higher than in the normal patient. The sudden increase in blood flow causes calcium to dissolve, leading to osteoclastic activity of the bone and thus damaging the bone. Another theory is that the repetitive minor trauma to the insensate joints leads to fracture and disintegration.\textsuperscript{[14]} In peripheral blood monocytes isolated from Charcot patients, the osteoclast formation was significant increased compared to diabetic patients and healthy controls. The osteoclastic resorption increased after addition of receptor activator of NF-κB ligand (RANKL). So in the acute stage of CN, the osteoclast activity is increased probably by increased expression of receptor activator of NF-κB ligand (RANKL) via release of proinflammatory cytokines as TNF-alfa. Central role in this process of local inflammation is trauma. Trauma will induce pro-inflammatory cytokines like TNF-alfa and RANKL will be expressed. Due to loss in pain perception by the distal neuropathy, the TNF-alfa release will persist and the RANKL pathway is persistently stimulated (Figure 4).\textsuperscript{[17]}
d) Infection

Once the protective layer of skin is broken, the deep tissues are exposed to bacterial colonization.

Staphylococcus aureus and β-hemolytic streptococci are the first microorganisms to colonize and acutely infect breaks in the skin. Chronic wounds develop more complex polymicrobial microbiology, including aerobic Gram-negative rods and anaerobes. Anaerobes are rarely the sole pathogen, but they often participate in a mixed infection with aerobes, especially in cases of deep tissue infection. These mixed infections provide an optimal opportunity for microbial synergy, which increases the net pathogenic effect and hence the severity of infection.
Accordingly, the composition of the polymicrobial wound flora is likely to be more important than the presence of specific pathogens.\cite{16}

e) Other risk factors
Recent studies have indicated multiple risk factors associated with the development of DFU. These risk factors are as follows: gender (male), duration of diabetes longer than 10 years, advanced age of patients, high Body Mass Index, and other co-morbidities such as retinopathy, glycated hemoglobin level (HbA1C), foot deformity, high plantar pressure and inappropriate foot self-care habits.\cite{1}

![Figure 5: Diabetic foot ulcer (DFU) pathophysiology. DFU results from a complex interaction of a number of risk factors.\cite{16}](image)

**CLASSIFICATION OF DIABETIC FOOT**
There is no one universally accepted classification system. Most systems employ a matrix of grades based upon depth and size of wound.\cite{8} There are three main diabetic foot classification system are discussed that are commonly used in clinical diagnosis of diabetic foot.\cite{11}
These were
a) Wagner-Meggitt Classification
b) Depth-Ischemic classification
c) University of Texas classification

**Wagner Meggitt Classification**

One of the oldest well-known classifications was proposed by Wagner and Meggitt in the 1970s. This classification is most commonly known as the “Wagner Classification” in the United States and its uses six grades in classifying diabetic foot lesions.\(^7\) This system is basically anatomical with gradations of superficial ulcer, deep ulcer, abscess osteitis, gangrene of the fore foot, and gangrene of the entire foot. Only grade 3 addresses the problem of infection. In this system foot lesions are divided into different grades starting from grade 0 to grade 5. Grade 0 includes high risk foot but no active lesion and grade 5 includes gangrene of entire foot. But this system does not mention about ischemia or neuropathy and that is the drawback of this system (Table 2).\(^{11}\)

**Table 2: Wagner-Meggitt Classification System.**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade0</td>
<td>No open Lesion</td>
</tr>
<tr>
<td>Grade1</td>
<td>Superficial ulcer</td>
</tr>
<tr>
<td>Grade2</td>
<td>Deep ulcer to tendon or joint capsule</td>
</tr>
<tr>
<td>Grade3</td>
<td>Deep ulcer with abscess, osteomyelitis, or joint sepsis</td>
</tr>
<tr>
<td>Grade4</td>
<td>Local gangrene- fore foot or heel</td>
</tr>
<tr>
<td>Grade5</td>
<td>Gangrene of entire foot</td>
</tr>
</tbody>
</table>

**Texas Classification**

A more recently proposed and popularized DFU classification is the University of Texas Health Science Center San Antonio (UT) classification system. This system incorporates a matrix structure of four grades of wound depth with subgroups to denote the presence of infection, ischemia or both. Wounds with frank purulence and/or two or more local signs of inflammation such as warmth, erythema, lymphangitis, lymphadenopathy, edema, pain and loss of function may be classified as ‘infected.’ Lower extremity vascular insufficiency is made by a combination of one or more clinical signs or symptoms of claudication, rest-pain, absent pulses, dependent rubor, atrophic integument, absence of pedal hair or pallor on elevation coupled with one of more non-invasive values such as a transcutaneous oxygen (TCPO\(_2\)) <40 mmHg, ankle brachial index (ABI) <0.8 or absolute toe systolic pressure <45 mmHg (Table 3).\(^{19}\)
Table 3: Texas Classification.

<table>
<thead>
<tr>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preulcerative or postulcerative lesions completely</td>
<td>Superficial wound not involving tendon, capsule or</td>
<td>Wound penetrating tendon or capsule</td>
<td>Wound penetrating to bone or joint</td>
</tr>
<tr>
<td>epithelialized</td>
<td>bone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td>Infection</td>
<td>Infection</td>
<td>Infection</td>
</tr>
<tr>
<td>Stage 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischaemia</td>
<td>Ischaemia</td>
<td>Ischaemia</td>
<td>Ischaemia</td>
</tr>
<tr>
<td>Stage 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection and Ischaemia</td>
<td>Infection and Ischaemia</td>
<td>Infection and Ischaemia</td>
<td>Infection and Ischaemia</td>
</tr>
<tr>
<td>Stage 4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Depth-Ischemic Classification

This classification is a modification of Wagner–Meggit system. The purpose of this classification system is to make the classification more accurate, balanced and easier to distinguish between wound and vascularity of foot, to elucidate the difference among the grades 2 and 3, and to advance the correlation of treatment to the grade (Table 4).[15]

Table 4: Depth-Ischemic Classification.

<table>
<thead>
<tr>
<th>Depth Grade</th>
<th>Definition</th>
<th>Ischemia Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>At risk, foot with previous ulcer that may cause new ulcer</td>
<td>A</td>
<td>No ischemia</td>
</tr>
<tr>
<td>1</td>
<td>Superficial non-infected ulcer</td>
<td>B</td>
<td>Ischemia no gangrene</td>
</tr>
<tr>
<td>2</td>
<td>Deep ulcer with tendon or joint exposed (+/− infection)</td>
<td>C</td>
<td>Partial forefoot gangrene</td>
</tr>
<tr>
<td>3</td>
<td>Extensive ulcer with bone exposed or deep abscess</td>
<td>D</td>
<td>Total foot gangrene</td>
</tr>
</tbody>
</table>

DIAGNOSIS OF DIABETIC FOOT ULCER

Patients with a DFU should be assessed by the team within one working day of presentation or sooner in the presence of severe infection. Patients with a DFU need to be assessed holistically to identify intrinsic and extrinsic factors. This should encompass a full patient history including medication, co-morbidities and diabetes status.[20] It should also take into consideration the history of the wound, previous DFUs or amputations and any symptoms suggestive of neuropathy or peripheral arterial disease.[12]

a) History and Physical examination

First, the physician enquire patient about their symptoms and will examine them. This examination should include the patient's vital signs (temperature, pulse, blood pressure, and respiratory rate), examination of the sensation in the feet and legs, an examination of the circulation in the feet and legs, a thorough examination of any problem areas.[9] A thorough
medical and foot history must be obtained from the patient. The history should address several specific diabetic foot issues (Table 5).\(^{[18]}\)

<table>
<thead>
<tr>
<th>Medical History</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Global History</strong></td>
</tr>
<tr>
<td>- Diabetes-duration</td>
</tr>
<tr>
<td>- Glycemic management/control</td>
</tr>
<tr>
<td>- Cardiovascular, renal and ophthalmic evaluations</td>
</tr>
<tr>
<td>- Other co-morbidities</td>
</tr>
<tr>
<td>- Treating physicians</td>
</tr>
<tr>
<td>- Nutritional status</td>
</tr>
<tr>
<td>- Alcohol, tobacco and drugs</td>
</tr>
<tr>
<td>- Current medications</td>
</tr>
<tr>
<td>- Allergies</td>
</tr>
<tr>
<td>- Previous hospitalizations/surgery</td>
</tr>
<tr>
<td>- Daily activities</td>
</tr>
<tr>
<td>- Footwear</td>
</tr>
<tr>
<td>- Chemical exposures</td>
</tr>
<tr>
<td>- Callus formation</td>
</tr>
<tr>
<td>- Previous foot infections, surgery</td>
</tr>
<tr>
<td>- Neuropathic symptoms</td>
</tr>
<tr>
<td>- Claudication or rest pain</td>
</tr>
</tbody>
</table>

**b) X-rays**

X-rays studies of the feet or legs were performed to assess for signs of damage to the bones or arthritis, damage from infection, foreign bodies in the soft tissues. Gas in the soft tissues, indicates gangrene - a very serious, potentially life-threatening or limb-threatening infection.\(^{[9]}\)

**c) Examination of ulcer**

A sterile stainless steel probe is used for assessing the ulcer to determine the depth and if there is sinus tracts present. The location, size, shape, depth, base and margins of the ulcer should be examined clinically. Presence of granulation tissue or slough should be looked for in the floor of the ulcer to determine subsequent management. Diagnosing a soft tissue infection in patient with diabetes is sometimes difficult, as the signs of inflammation of the overlying ulcer may be absent. The infection is mainly diagnosed based on presence of clinical signs and symptoms such as redness, warmth, tenderness, purulent secretions and fever. Palpation of the bone at the base of the ulcer with a sterile, blunt stainless steel probe has been suggested as positive predictor of underlying osteomyelitis.\(^{[14]}\)
d) Neurological testing
Peripheral neuropathy is the most common component cause in the pathway to diabetic foot ulceration. The clinical exam recommended, however, is designed to identify loss of protective sensation (LOPS) rather than early neuropathy. Five simple clinical tests (Table 6) each with evidence from well conducted prospective clinical cohort studies are considered useful in the diagnosis of LOPS in the diabetic foot. The task force agrees that any of the five tests listed could be used by clinicians to identify LOPS, although ideally two of these should be regularly performed during the screening exam-normally the 10-g monofilament and one other test. One or more abnormal tests would suggest LOPS, while at least two normal tests (and no abnormal test) would rule out LOPS. However, identification of the patient with LOPS can easily be carried out without Biothesiometer or other expensive equipment.[21]

Table 6: Simple bed side clinical tests.

<table>
<thead>
<tr>
<th>SI. NO</th>
<th>Clinical Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10-g monofilaments</td>
</tr>
<tr>
<td>2</td>
<td>Pinprick sensation</td>
</tr>
<tr>
<td>3</td>
<td>Ankle reflexes</td>
</tr>
<tr>
<td>4</td>
<td>Tuning fork test</td>
</tr>
<tr>
<td>5</td>
<td>Vibration perception threshold testing</td>
</tr>
</tbody>
</table>

e) Ultrasound
Doppler ultrasound to see the blood flow through the arteries and veins in the lower extremities. The test is not painful and involves the technician moving a non-invasive probe over the blood vessels of the lower extremities.[9]

f) Laboratory investigations
Clinical laboratory tests that may be needed in appropriate clinical situations include fasting or random blood glucose, glycohemoglobin (HbA1c), complete blood count (CBC) with or without differential, erythrocyte sedimentation rate (ESR), serum chemistries, C-reactive protein, alkaline phosphatase, wound and blood cultures and urinalysis. Caution must be exercised in the interpretation of laboratory tests in these patients, because several reports have documented the absence of leukocytosis in the presence of severe foot infections. A common sign of persistent infection is recalcitrant hyperglycemia despite usual anti hyperglycemic regimens.[18]
g) Angiogram
If the vascular surgeon determines that the patient has poor circulation in the lower extremities, an angiogram may be performed in preparation for surgery to improve circulation. With an angiogram, a catheter is inserted through the artery in the groin and dye is injected while x-rays are taken.\[9\]

DIABETIC FOOT INFECTIONS
Foot infections in persons with diabetes are an increasingly common problem and are associated with potentially serious sequelae. The continued rise in incidence of diabetes in developed, and to an even greater degree in many lesser-developed, countries, the increasing body weight of many diabetic patients and their greater longevity all contribute to the growth of this problem.\[6\] Foot infections are common in patients with diabetes and are associated with high morbidity and risk of lower extremity amputation. Diabetic foot infections are classified as mild, moderate, or severe. Gram-positive bacteria, such as Staphylococcus aureus and beta-hemolytic streptococci, are the most common pathogens in previously untreated mild and moderate infection. Severe, chronic, or previously treated infections are often polymicrobial.\[22\] All infections begin as a slight problem may progress to involve deep tissues, joints or bones especially if not managed. The infection complicates the pathological depiction of diabetic foot. Study on diabetic foot ulcers reported that the presence of infection increase the risk of a lower extremity amputation by 50% compared to ulcer patients without infection. Around 60% of infected foot ulcers are headed by loss of lower limb, and becomes one of the most awful outcomes in diabetic foot patients.\[15\]

ETIOLOGY OF DIABETIC FOOT INFECTIONS
The microorganisms involved in the etiology of DF infection vary depending on the type of infection and specific patient situations.\[8\]

<table>
<thead>
<tr>
<th>Etiology of diabetic foot infections.</th>
<th>Microorganisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulitis</td>
<td>Staphylococcus aureus</td>
</tr>
<tr>
<td>Erysipelas</td>
<td>Beta-hemolytic streptococci (A, B, C and G)</td>
</tr>
<tr>
<td>Ulcer untreated with antibiotics</td>
<td>Staphylococcus aureus</td>
</tr>
<tr>
<td></td>
<td>Beta-hemolytic streptococci (A, B, C and G)</td>
</tr>
<tr>
<td>Ulcer treated with antibiotics or</td>
<td>Staphylococcus aureus</td>
</tr>
<tr>
<td>long-term (generally polymicrobial)</td>
<td>Methicillin-resistant Staphylococcus aureus</td>
</tr>
<tr>
<td></td>
<td>Coagulase-negative staphylococci</td>
</tr>
<tr>
<td></td>
<td>Streptococcus spp.</td>
</tr>
<tr>
<td></td>
<td>Enterococcus spp.</td>
</tr>
</tbody>
</table>
PATHOPHYSIOLOGY OF DIABETIC FOOT INFECTIONS
Several factors predispose diabetic patients to developing a DFI, including neuropathy, vasculopathy and immunopathy. Peripheral neuropathy occurs early in the pathogenesis of diabetic foot complications and is considered the most prominent risk factor for diabetic foot ulcers. Patients with diabetes lose the protective sensations for temperature and pain, impairing awareness of trauma such as abrasions, blistering, or penetrating foreign body. Motor neuropathy can result in foot deformities (e.g., claw toe) that contribute to local pressure from footwear, making skin ulceration even more likely. Once the skin is broken (typically on the plantar surface), the underlying tissues are exposed to colonization by pathogenic organisms. The resulting wound infection may begin superficially, but with delay in treatment and impaired body defense mechanisms caused by neutrophil dysfunction and vascular insufficiency, it can spread to the contiguous subcutaneous tissues and to even deeper structures.

MICROBIOLOGY
Various aspects of wound microbiology are responsible for development of foot infection. These include microbial load, diversity of microbes, existence of infective organisms and synergistic association amongst microbial species. Infection is said to occur when microbial load is greater than 10^5 organisms per gram of tissue. The most common pathogens in acute, previously untreated, superficial infected foot wounds in patients with diabetes are aerobic gram-positive bacteria, particularly Staphylococcus aureus and beta-hemolytic streptococci (group A, B, and others). Infection in patients who have recently received antibiotics or who have deep limb-threatening infection or chronic wounds are usually caused by a mixture of aerobic gram-positive, aerobic gram-negative (e.g., Escherichia coli, Proteus species, Klebsiella species), and anaerobic organisms (e.g., Bacteroides species, Clostridium species, Peptococcus and Peptostreptococcus species). Anaerobic bacteria are usually part of mixed infections in patients with foot ischemia or gangrene. Methicillin-resistant...
Staphylococcus aureus (MRSA) is a more common pathogen in patients who have been previously hospitalized or who have recently received antibiotic therapy. MRSA infection can also occur in the absence of risk factors because of the increasing prevalence of MRSA in the community.[22]

**INFECTION CONTROL**

The selection of antibiotic therapy for diabetic foot infection involves decisions about choice of empiric and definitive antibiotic agent, route of administration, and duration of treatment. Initial empiric antibiotic therapy should be based on the severity of the infection, history of recent antibiotic treatment, previous infection with resistant organisms, recent culture results, current Gram stain findings, and patient factors (e.g., drug allergy).[22] Select specific antibiotic agents for treatment based on the likely or proven causative pathogens, their antibiotic susceptibilities, the clinical severity of the infection, and evidence of efficacy for DFI and costs. A course of antibiotic therapy of 1-2 weeks is usually adequate for most soft tissue diabetic foot infections.[23]

Antimicrobial preparations used in chronic wound care include topical antiseptics, topical antibacterials, and systemic antibiotics, all recently reviewed. Many preparations described in these reviews can effectively control bacterial growth; however, they can be toxic for host tissues. Currently, there is no conclusive evidence that one antibiotic or antiseptic is superior to any other achieving efficient elimination of infection and decreasing time to healing.[24] Mild to moderate infections with localized cellulitis can be treated on an outpatient basis with oral antibiotics such as cephalexin, amoxicillin with clavulanate potassium, moxifloxacin, or clindamycin. The antibiotics should be started after initial cultures are taken and changed as necessary.[25]

**PREVENTION OF DIABETIC FOOT ULCERS**

Prevention of diabetic foot ulcers begins with identifying patients at risk.[22] Primary prevention is the aim of diabetes management, but secondary prevention is the goal of effective foot ulcer care. The recurrence rates are high and ulcer healing must be accompanied by a well-coordinated program of secondary prevention.[5]

- Optimal glycaemic control which can dramatically reduce the recurrence of foot ulcers.
- Meticulous attention to foot care and proper management of foot injuries.
- Daily inspection of the feet.
• Gentle cleansing with a mild soap and water.[5]
• All patients with diabetes should have an annual foot examination that includes assessment for anatomic deformities, skin breaks, nail disorders, loss of protection sensation, diminished arterial supply and inappropriate footwear.
• Educating patients and caretakers about proper foot care and periodic self-foot examinations are effective interventions to prevent ulceration.[22]
• Wearing correct, well-fitting footwear that provides adequate support.
• Appropriate management of minor wounds and referral for any minor nonhealing wound.
• Avoid walking barefoot.[5]
• Skin is kept moisturized with the application of topical moisturizers after washing the feet gently with soap and water.
• Other co-morbidities like hypertension and hyperlipidaemia which predispose to vascular occlusion should be treated.[26]
• Other effective clinical interventions include optimizing glycemic control, smoking cessation, debridement of calluses, and certain types of prophylactic foot surgery.[22]

MANAGEMENT DIABETIC FOOT ULCERS
Standard care for DFU is ideally provided by a multidisciplinary team by ensuring glycemic control, adequate perfusion, local wound care and regular debridement, off-loading of the foot, control of infection by appropriate antibiotics and management of comorbidities. Educating patients helps in preventing ulcers and their recurrence.[26]

The essential components of management are.

a. Treating underlying disease processes
b. Ensuring adequate blood supply
c. Local wound care, including infection control
d. Pressure offloading.[12]

Debridement
Debridement consists of removal of all necrotic tissue, peri-wound callus and foreign bodies down to viable tissue. Proper debridement is necessary to decrease the risk of infection and reduce peri-wound pressure, which can impede normal wound contraction and healing. There are different kinds of debridement which includes surgical, enzymatic, autolytic, mechanical, and biological.[25]
Autolytic
Autolytic debridement uses the body’s own natural enzymes to break down and digest necrotic tissue. Autolytic debridement also involves the use of moisture in semi-occlusive or occlusive dressings to aid in the efficiency of liquefying devitalized tissue. Dressings for autolytic debridement include hydrocolloids, hydrogels and films. The hydrogels were significantly more effective than gauze dressings or standard care in healing diabetic foot ulcers.\cite{27}

Biological
Sterile maggots of the green bottle fly (Lucilia sericata) are placed directly into the affected area and held in place by a close net dressing. The larvae have a ferocious appetite for necrotic material while actively avoiding newly formed healthy tissue.\cite{28}

Mechanical
Although it is a simple and an inexpensive tool, it can remove both viable and also non-viable tissues leading to pain in sensate foot. The wet gauze dressing is applied to the wound bed and then kept to dry. The necrotic debris embedded in the gauze is mechanically stripped from the wound bed on gauze removal.\cite{10}

Enzymatic debridement
Enzymatic debridement speeds up the process and an ointment is applied to the wound, which contains special enzymes to accelerate the removal of the devitalised or dead tissue from the wound bed.\cite{5}

Dressing
Ideally, dressings should confer moisture balance, protease sequestration, growth factor stimulation, antimicrobial activity, oxygen permeability, and the capacity to promote autolytic debridement that facilitates the production of granulation tissues and the re-epithelialization process. Wound dressing can be categorized as passive, active, or interactive. Passive dressings are used as protective functions and for acute wounds because they absorb reasonable amounts of exudates and ensure good protection. Active and interactive dressings are capable of modifying the physiology of a wound by stimulating cellular activity and growth factors release. The main categories of dressings used for DFU are as follows: films, hydrogels, hydrocolloids, alginates, foams, and silver-impregnated.\cite{11}

New advanced dressings are being researched, for example Vulnamin© gel made of amino
acids and hyaluronic acid are used along with elastocompression has shown favourable results. Promogran© by Johnson and Johnson’s is a freeze dried matrix composed of collagen and oxidized regenerated cellulose. When in contact with wound exudates, it forms a biodegradable gel that physically binds and inactivates matrix metalloproteases that affects wound healing.\cite{14}

**Offloading**

Total contact cast (TCC), removable cast walkers, custom shoes, half-shoes, soft heel shoes, padded socks, and shoe inserts, wheelchairs, crutches etc. have been used for offloading the foot to prevent and treat the DFUs. The aim is to reduce the plantar pressure by redistributing it to a larger area, to avoid shear and friction, and to accommodate the deformities.\cite{26} Inadequate offloading leads to tissue damage and ulceration. The gold standard is the total contact cast (TCC). This is a well moulded, minimally padded foot and lower leg cast that distributes pressures evenly over the entire plantar surface of the foot. It ensures compliance because it is not easy for the patient to remove. Using a TCC in patients with a unilateral uncomplicated plantar ulcer can reduce healing time by around six weeks\cite{1}. Inappropriate application of TCCs may result in new ulcers, and TCCs are contraindicated in deep or draining wounds or for use with noncompliant, blind, morbidly obese, or severely vascularly compromised patients.\cite{25}

**Medical treatment**

Strict glycaemic control should be maintained with the use of diabetic diet, oral hypoglycaemic agents and insulin. Infections of the soft tissue and bone are the leading cause of hospital admissions in patients with DFUs. Antibiotics are preferably given intravenously for limb threatening infections. Gabapentin and pregabalin have been used for symptomatic relief for painful neuropathy in DM. Aldose reductase inhibitors are being studied and have shown to be effective in inhibiting progression of peripheral neuropathy. Autonomic dysfunction may require the use of beta-blockers. Medical management of symptoms of vascular insufficiency like intermittent claudication includes Cilostazol or Pentoxifylline besides exercise therapy.\cite{14}

**Adjuvant therapy**

Hyperbaric oxygen therapy (HBOT) has shown promise in the treatment of serious cases of non-healing DFU, which are resistant to other therapeutic methods. HBOT involves intermittent administration of 100% oxygen, usually in daily sessions. During each session,
patients breathed pure oxygen at 1.4-3.0 absolute atmospheres during 3 periods of 30 min (overall 90 min) intercalated by 5 min intervals in a hyperbaric chamber.\textsuperscript{[1]} Hyperbaric oxygen therapy (HBOT) has the advantage of reduction of tissue hypoxia, edema, increase angiogenesis and erythrocytes deformability, antimicrobial effects and increase fibroblastic activity. HBOT is approved as an adjunctive treatment to be used in chronic non-healing ulcers by the Undersea and Hyperbaric Medical Society.\textsuperscript{[10]} Low energy lasers have also been used as an adjunctive therapy for DFUs. They act by increasing microcirculation and improving healing of the ischemic DFU. Growth factors for example recombinant human platelet derived growth factor (rhPDGF), topical platelets and platelet rich plasma have also been used in treating DFUs and have shown favourable results.\textsuperscript{[14]}

**Surgical management**

**Revascularization surgery**

As diabetes is chronic and progressive, it makes sense to have conservative surgical approaches that include surgical revascularization. A successful surgical bypass of larger vessel disease may enable more conservative treatment of the diabetic foot.\textsuperscript{[28]} Revascularization by open surgery of occlusive disease of the distal arteries is carried out mainly by bypass with autologous material (preferably saphenous vein). In turn, endovascular surgery techniques mainly include percutaneous transluminal angioplasty (PTA), which may be combined with stenting, laser and plaque volume reduction techniques. The exponential increase of the use of these endovascular procedures, compared with open surgical revascularisation, is primarily due to the greater benefit with respect to the secondary risk of low percentages of morbidity and mortality associated with the percutaneous techniques. Mixed techniques (open + endovascular surgery) may be used.\textsuperscript{[8]}

**Wound closure**

Wound closure is attempted once the ulcer is clean with healthy granulation tissue. Primary closure is possible for small wounds; tissue loss can be covered with the help of skin graft, flap or commercially available skin substitutes. Split-thickness skin grafts are preferred over full thickness grafts DFUs with exposed tendon, ligament or bone require coverage with muscle flaps. Flaps can be either local (for smaller wounds) or freeflaps (for large area). Latissimus dorsi, gracilis or rectus abdominis are the commonly used free flaps. The limitations of standard flaps include donor site morbidity, difficulty in shaping the flaps and interference with footwear.\textsuperscript{[26]}
Amputation

Amputation may be indicated in the following circumstances.

- Ischaemic rest pain that cannot be managed by analgesia or revascularization
- A life-threatening foot infection that cannot be managed by other measures
- A non-healing ulcer that is accompanied by a higher burden of disease than would result from amputation. In some cases, for example, complications in a diabetic foot render it functionally useless and a well performed amputation is a better alternative for the patient.

Patients at high risk for ulceration (such as patients who have undergone an amputation for a DFU) should be reviewed 1–3 monthly by a foot protection team. At each review patients' feet should be inspected and the need for vascular assessment reviewed.\(^{(12)}\)

CONCLUSION

Diabetic foot complication is the most devastating complication of diabetes. This article is a clinical overview of diabetic foot ulcer and diabetic foot infection. Physician plays an important role in management of aetiological factors like vasculopathy, neuropathy and infection is essential to get good outcomes. The main components of management that can ensure successful and rapid healing of DFU includes wound debridement, advanced dressing, offloading, surgery, and advanced therapies, which are used clinically. Physician plays an important role in prescribing Guideline-based treatment for diabetic foot infections and the employment of multidisciplinary teams would help improve outcome and minimize amputations.

REFERENCE

4. Orthopedics one articles, 132-140.


