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Review article

Diabetic foot infections –A review

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ABSTRACT

Foot infections are among the most common bacterial infections encountered in patients with diabetes mellitus in clinical practice. These infections and their sequelae are also the most common cause of disability and the reason for most hospital admissions among diabetic patients. The objectives in the treatment of diabetic foot infections are to avoid major limb loss and to retain function. Diabetic foot infections are predominantly polymicrobial. A combination of gram-positive and gram-negative aerobes with anaerobes is likely to be found at the site of infection. Preventing the diabetic foot using the multidisciplinary team approach is a noble step in the right direction. Early recognition of lesions and prompt initiation of appropriate antimicrobial therapy as well as surgical debridement of necrotic tissue and bone are essential for controlling the infection and preventing additional morbidity.

1. Introduction

Diabetes mellitus is a disease known for chronic complications. Among them diabetic foot infection is one of the devastating complications. In addition to causing severe morbidities, they now account for the largest number of diabetes-related hospital bed–days and are the most common proximate, non-traumatic cause of amputations. Foot infections are among the most common bacterial infections encountered in patients with diabetes mellitus in clinical practice [1]. These infections and their sequelae are also the most common cause of disability and the reason for most hospital admissions among diabetic patients [2]. The objectives in the treatment of diabetic foot infections are to avoid major limb loss and to retain function.

A. Present status

- More than 50% of all non-traumatic lower limb amputations taking place every year are performed on diabetics [3].
- Diabetes is the leading cause of non traumatic lower extremity amputations [4].
- Today, more than 85% of lower extremity amputations in patients with diabetes are preceded by foot ulcers [5].

Among patients who have a lower extremity amputation, more than half will have a contralateral amputation within 5 years and half of those who undergo amputation will die within 3 years [4].

- Diabetes is a fairly common disease seen in India with a prevalence of almost 12% - 17% in the Indian urban population as per a study & with a prevalence of 2.5% in the rural population [6].
- TYPE II diabetes is the commonest form of diabetes constituting about 90% of the diabetic population in India [7].

B. Future Perspective

The World Health Organization has predicted that the major burden of diabetic patients will occur in the developing countries [7].

A 42% increase from 51 to 72 million in the developed countries and 170% increase from 84 to 228 million, in the developing countries, is predicted by 2025 [7].

The countries with the largest number of diabetic people are, and will be India, China and United States in 2025 [7]. In 2025, every 4th person will be a diabetic [8].

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2.Risk factors for diabetic foot infections

Race: Asian patients are less prone to foot ulcers than Caucasians due to hyper-mobility of subtalar joint and cultural differences in self care [9,10].

Age- Foot infection is more common with patients aged between 45 and 64 years. Elderly diabetics are also prone because these people have poor vision, live alone and have other concomitant medical problems [11].

Long duration of diabetes- Incidence of foot infection is directly proportional to duration of diabetes because of contribution by other risk factors such as peripheral neuropathy and peripheral vascular diseases, which develop with time. A six fold increase of foot ulceration is seen in patients with 20 years or more duration of diabetes [11].

Poor glycemic control- Severe hyperglycemia is associated with a higher incidence of diabetic foot ulceration and infection. In diabetes, leukocyte function is impaired leading to abnormalities of migration, phagocytosis and intracellular killing as discussed later in immunopathy section.

Peripheral neuropathy– It is the strongest initiating factor for diabetic foot and subsequent infection [12]. 40 % of type 2 and 28 % of type 1 diabetes patients have peripheral neuropathy. It is seen in 82% of patients with foot infection and 58% of patients with long standing disease [11].

Retinopathy- Poor vision interferes with patient's ability to detect foot lesion and leads to increased susceptibility to trauma [13]. It is associated with increased incidence of lower extremity amputation. Lower extremity amputation most commonly follows foot infection. Retinopathy reflects the severity of the microvascular disease.

Nephropathy- Non-vascular diabetic foot infection is mostly seen with diabetic nephropathy because as many as 40% of diabetic population have chronic renal failure [14]. Nephropathy is also present in diabetic patients having co-morbid illness like hypertension. Hypertension influences the prognosis of nephropathy in patients with diabetes.

Biomechanical factor- Non-enzymatic glycosylation of collagen results in stiffening of connective tissue surrounding the joint leading to limited joint mobility resulting in increased plantar pressure during normal gait. Atrophy of intrinsic musculature of foot leads to focal areas of high pressure, coupled with lack of sensation. This increases the risk of callus and ulcer formation over bony prominences [15].

Fungal infection of web space- Dermatophytic infections is most commonly found in the web space. This site provides a nidus for bacterial superinfection [16]. Super-infecting bacteria can readily enter through the web spaces, which are in close proximity to the digital vessels and other deep tissues.

Smoking- It is an indirect risk factor of diabetic foot infection as it predisposes to peripheral vascular diseases [17].

Obesity- There is an association between greater bodyweight and foot ulceration and infection. This can be related to the effect of body weight on plantar pressure [18].

History of previous foot ulceration and amputation- Alteration in foot dynamics due to foot ulceration, joint deformity or amputation cause abnormal distribution of plantar pressure and results in formation of new ulcer [19]. After previous foot ulceration, rate of amputation is 34% at 1 year and 70% at 5 years [20].

3.Socio-cultural factors that affect the development of diabetic foot infection

3.1.Bare foot walking

It leads to foot ulceration and subsequent infection due to the following practices:

Bare foot walking is a common practice in India particularly in rural areas because of poverty and the traditional practice of not wearing footwear even outside one's house,in temples, etc. Location of toilet in the garden and walking barefoot to toilet at night.

It is also a serious risk factor for thermal injuries due to absorption of heat especially in summer [21].

While traveling as a pillion rider on a motorbike –hot exhaust pipe often used as footrest results in thermal injury to the already insensitive skin.

Habit of sleeping on the floor inside house and on terrace (summer) –increases risk for rat bite [21].

3.2. Religion

Walking bare foot on fire is a form of worship to Hindu gods. Muslims due to their prayer posture develop ulcer on the foot particularly of lateral malleolus because of constant pressure on these points in the foot [21].

3.3.Improper foot care

Use of blade or a pair of scissors to cut nails often results in injury to the toes. Fissures in foot are a very common route of infection. Constant contact of foot with water during washing of clothes leads to fungal infection of nails. Tight or ill-fitting footwear could also lead to foot injury.

3.4.Customs

Certain practice like washing feet before entering the house, prayer room and before going to bed minimizes the risk of foot infection.

4. Pathophysiology of diabetic foot infection

A diabetic foot infection is defined as any inframalleolar infection in a diabetic. These include paronychia, cellulitis, myositis, abscesses, necrotizing fasciitis, septic arthritis, tendinitis, and osteomyelitis.The most common and classical lesion, however, is the infected diabetic "mal perforans" foot ulcer [22].

As a general rule, neuropathy predisposes the foot to infection and angiopathy influences the outcome. Neuropathy is responsible for the breakdown of the first line of defence.[16]

Neuropathy plays a central role contributing to half the foot ulcers. Nerve damage affects motor, sensory and autonomic fibres. Sensory neuropathy leads to loss of protective sensation from pain, pressure and heat.[23] Loss of pain sensation can indirectly damage the foot e.g. pressure from tightly fitting shoes, or walking across a hot surface. Motor weakness leads to muscle weakness,

atrophy of intrinsic muscle and paresis. Decreased action of intrinsic muscle of foot leads to neuropathic posture i.e. arch is raised, toes are clawed and pressure is concentrated on the meta-tarsal heads and heel due to unopposed pulling of the extensor and flexors.[24] Raised foot pressure while walking leads to skin thickening called a callus. Hemorrhages and necrosis commonly develop within callus leading to breakdown of skin and formation of ulcer. Autonomic neuropathy reduces sweat production, causing dry feet increasing the risk of cracks and fissures that serve as nidus for infection and ulceration. It also increases arterio-venous shunt with raised venous pressure.[25]

Ischemia contributes to one third of foot ulcer. Diabetes leads to peripheral vascular disease as a result of angiopathy-macrovascular and microvascular. Ischemia can be divided into 2 categories: accelerated atherosclerosis commonly involving femoral, popliteal and posterior tibial arteries, which severely decreases blood flow to the foot. Secondly there is decreased angiogenesis in diabetic wound, interfering with nutritive blood supply to the tissue bed. [23]

So the foot ulceration is caused by a combination of neuropathy, ischemia, foot deformity and trauma.

Foot infection- Because of certain anatomical peculiarities, foot infection can be limb threatening. Foot has several intercommunicating compartments, and the infection can spread from one to another. Lack of pain allows the patient to continue ambulation facilitating further spread. Secondly, foot has soft tissue like plantar aponeurosis, tendons, muscle sheath, and fascia, which cannot resist infection. [24]

4.1.Sequence of events in diabetic foot ulcer

Once the patient develops ulcer, infection supervenes. The various stages of foot infection are-

1. **Stage of cellulitis-** Following an injury or infection, swelling and edema develops in the foot.
2. **Stage of spreading cellulitis –** Cellulitis spreads upwards along the fascial planes.
3. **Stage of abscesses-** Secondary infection caused by mixed organisms includes anaerobes and non-clostridial gas forming organisms produces multiple abscesses.
4. **Stage of gangrene –** Tense edema and vascular compromise produce ischemia and gangrenous patches of skin and toes.
5. **Stage of osteomyelitis-** Infection spreads deeper to bone leading to osteomyelitis.[25]
6. **Stage of septicemia-** Untreated cases develop rapidly spreading cellulitis and gangrene producing septicemia and predisposing to ketoacidosis.[26]

5.Immunopathy

WHO has included diabetes in classification of immuno-deficiency diseases. Infection occurs with a greater frequency and severity in diabetics than in non-diabetics. Infection perpetuates a vicious cycle in which infection leads to uncontrolled hyperglycemia which in turn aggravates infection because sugar is good media for rapid and abundant growth of organisms and at the same time infection itself disturbs blood sugar levels and precipitates keto-acidosis.[27]

Etiology is multifactorial.

1.Hyperglycemia and immune disturbance :

There is an impaired function of neutrophils and macrophages including chemotaxis and adherence phagocytosis (increase in sialidase enzyme leads to decrease of cell membrane sialic acid and lactin receptor leading to failure of phagocytes to recognize target and initiate phagocytosis).[28]

The second reason is failure to kill intracellular microorganisms. After phagocytosis, macrophages and neutrophils produce toxic free radical, superoxide, H_2O_2 and release of lysosomal enzymes. This phenomenon is called Respiratory burst. Respiratory burst is important to kill phagocytosed microorganisms and is dependent on NADPH.[29] The generation of NADPH is reduced as maximum glucose entering the phagocytes is diverted to polyl pathway .

B cell function-There is alteration in immunoglobin production and complement function.

Cell mediated immunity-There is reduction in 'T' lymphocytes and CD4+ and CD8+ T ratio is altered.

2. Local factors like vascular disease, nerve damage, delayed wound healing, dehydration and increased blood sugar aggravate the process.

3. Antagonism of insulin action– Increase in secretion of counter regulatory hormones like glucagon, adrenaline, and growth hormone and cortisol which decrease insulin secretion and oppose its effect and produce gluco-neogenesis. Cytokines like interleukins and TNF α impair insulin action by inhibiting tyrosine kinase activity of insulin receptor.[30] Hence it is necessary to keep blood glucose level at near normal levels, as it has been found that leukocyte function is restored when the patient is euglycemic.

6. Microbiology

6.1.Colonization versus Infection

All open skin wounds are colonized with bacteria.[31] Such wounds provide a host environment conducive to bacterial invasion. Several key factors determine whether open skin wounds colonized with bacteria will become infected.These factors include the amount of bacteria per gram of tissue and the ability of the host to mount an effective immune response.[32] In general, bacterial growth greater than 100,000 (10^5) organisms per gram of tissue in a wound is necessary for infection to occur, except for beta-hemolytic streptococcus, a particularly virulent organism.[33] Normal skin flora, however, commonly contains micro colonies of 10^5 organisms per gram of tissue without problems . Infection is characterized by an invasion of bacteria into the tissue, whereas colonization usually is restricted to the wound surface. Prevention of progression from colonization to infection requires adequate medical management.

6.2.Microorganisms

Diabetic foot infections are predominantly polymicrobial. [34] A combination of gram-positive and gram-negative aerobes with anaerobes is likely to be found at the site of infection.[35]

1. Cellulitis of non-ulcerated skin are nearly always caused by Streptococci or Staph. aureus.

2. Acute infections in patients who have not received antimicrobials are often monomicrobial. Aerobic gram-positive cocci are the most common cause of infections in superficial ulcers.[36] Staph. aureus and the hemolytic streptococci (groups A, C, and G, but especially group B) are the most commonly isolated pathogens.

3. Infections associated with deep or penetrating ulcers and those characterized by marked tissue necrosis or gangrene are mixed infections-caused by gram positive cocci, gram negative bacilli like enterococci, various enterobacteriaceae, Pseudomonas aeruginosa ,obligate anaerobes, and sometimes, other non-fermentative gram-negative rods.

4. Clostridium perfringens is a virulent, gas-producing, anaerobic, gram-positive rod which is responsible for myonecrosis and gas gangrene.[37]

5. Necrotizing fasciitis is caused by beta hemolytic group A Streptococci, or Streptococcus pyogenes.

6. The impaired host defenses around necrotic soft tissue or bone may allow low-virulence colonizers, such as coagulase-negative Staphylococci and Corynebacterium species (diphtheroids), to assume a pathogenic role.[38]

7. Even bacteria regarded as normal skin flora commensals cause severe tissue damage for example Gram-negative Citrobacter, Serratia, Pseudomonas, Acinetobacter.[39]

8. Hospitalization, surgical procedures, and prolonged or broad-spectrum antibiotic therapy may predispose patients to colonization and infection with antibiotic-resistant organisms (e.g., MRSA or Vancomycin-resistant enterococci [VRE].[40] Vancomycin Vancomycin intermediate Staph. aureus has been isolated in several countries. The first 2 reported cases of vancomycin-resistant Staph. aureus involved a diabetic patient with a foot infection.[41]

9. Coliforms are commonly seen in neuro-ischemic ulcer and Staph. aureus is most commonly seen in neuropathic ulcers.[42]

7.Wound classification systems in diabetic foot

7.1. Diabetic foot can be classified depending on etiology as

1.Neuropathic foot
2.Neuro-ischemic foot
3.Purely ischemic foot

The major differences among them are as follows: [43]

	Non-ischemic neuropathic foot	Ischemic foot
Nature of foot	Warm, Numb, Dry	Cold, Sensitive
Pain	Painless	Painful
Foot pulses	Palpable	Absent
Site of ulcer	Plantarsurface	Sides of digits, Rest pain
Complications	Neuropathic ulcer, Neuropathic Charcot's joint Neuropathic edema	Ulceration/Necrosis Gangrene

Differentiating between these two entities is important as their complications and management strategies are different.

7.2. MEGGIT –WAGNER Classification (1979)

More specific for neuropathic foot and secondary infection.[25]

No mention of macro-vascular disease involvement.[44]

GRADES[45]

0 High risk foot, no ulceration, thick callus, prominent metatarsal head, claw toe.
1 Superficial ulceration, not clinically infected.
2 Deep ulceration, often with cellulitis, no abscesses or bone infection.
3 Deep ulceration, with bone involvement and abscess formation.
4 Localized gangrene of toe or forefoot.
5 Extensive gangrene of whole foot requiring major amputation.

7.3. Clinical classification of diabetic foot infections

This classification has been advocated to aid empirical antimicrobial selection.

Mild infection
Localized cellulitis
Superficial ulceration
Minimal purulence
No systemic signs or symptoms

Moderate infection
Cellulitis of foot or ankle
Deep or penetrating ulceration
Plantar abscess
Acute osteomyelitis
Systemic signs or symptoms

Severe infection
Proximal cellulitis, lymphangitis
Gangrene, necrotizing fasciitis
Clinical septicemia

8.Presentation of infection

Diabetic foot infections begin with a trivial injury resulting in a break in the integument with a contamination of wound with adjacent skin flora.[13] They do not always present with the classical signs of local infection.[46] The signs of inflammation and early infection often may be difficult to detect. Erythema and pain may be absent. The white blood count and body temperature should not be regarded as reliable indicators of infection in the diabetic foot as only 50 % cases of deep cellulitis manifest with fever and leukocytosis.[42]

The most common manifestation of infection is cellulitis. This is seen as bluish discoloration. As there is an inadequate supply of oxygen to the soft tissues, it leads to necrosis. Blue discoloration can occur in both the neuropathic and the neuroischemic foot, particularly in the toes.

Superficial foot infections may present as paronychia, infected ingrown toe-nails, infected shallow ulcers, and web space infections, commonly caused by bacteria, sepsis in combination with a dermatophyte. Among them, most of the patients present with ulcer.

Vascular insufficiency ulcers are found typically on the tips of the toes or on the margins of the foot. Neuropathic ulcers are commonly found in the sole where bony prominences are found, such as metatarsal heads. They have a central chronic ulcer surrounded by a halo of hyperkeratinization. They are seldom accompanied by systemic manifestations, toxicity, foot dysfunction, or hyperglycemia.

Deep foot infections may present as cellulitis, dorsal foot phlegmon, deep plantar space infection, and infected foot ulcer.[16] Generally the most common cause is foot ulceration because it provides an access for deep spaces of the foot. These foot infections commonly start superficially at the base of a toenail, the web space, or an ulcer. Subsequently, it spreads inwardly and to the rest of the foot. Another mode of deep foot infection is through direct penetration of the foot. Because of sensory neuropathy, the patient cannot feel puncture with a needle, nail, or wood splinter. The patient presents with swelling and erythema. This swelling may extend beyond the ankle. Systemic manifestations include fever, chills, malaise, lymphangitis, regional lymphadenitis and uncontrolled blood sugar.[42] Accumulation of purulent material in the central plantar space results in loss of skin creases and loss of longitudinal arch of the foot. When the infection spreads outside the central plantar space, destruction of the interosseous fascia permits the microorganisms to the foot and the infection to extend along the flexor tendons to the calf and lower leg regions.

Wet necrosis in the diabetic foot is usually owing to Infection. Early signs consist of a toe that is developing a blue or purple tinge, from previous pink colour . The tissue necrosis results from poor tissue perfusion that is caused by a combination of atherosclerotic narrowing of the arteries of the leg and a septic occlusive vasculitis

of the digital arteries. Gas gangrene caused by clostridia is a rapidly progressive and devastating infection characterized by crepitant cellulitis, myonecrosis, and systemic toxicity. It is an indication for amputation of limb.

If a sterile probe inserted into the ulcer reaches bone, this strongly suggests the diagnosis of osteomyelitis. Two clinical

findings have been shown to be predictive of the presence of osteomyelitis. First, the larger and deeper the skin ulceration, the more likely the underlying bone will be infected.[47] Deeper ulcers i.e.,>3 mm are more likely to overlie osteomyelitis than shallow ulcers. The second clinical finding of diagnostic help is the erythrocyte sedimentation rate (ESR).[48] An ESR of >70 mm/h is associated with almost a 12-fold increased likelihood of osteomyelitis.[49] Chronic osteomyelitis of a toe has a swollen, red, sausage-like appearance in the initial stages. In the initial stages, plain radiograph may be normal, and localized loss of bone density and cortical outline may not be apparent until at least 14 days later.

A noninfectious inflammatory condition, the Charcot foot, can mimic cellulitis. This soft tissue inflammation accompanying neuropathic joint of the foot can rapidly and progressively destroy the joint, and subsequently the bone.

9.Evaluation of diabetic foot infection

Diabetic foot ulcers are one of the most common causes of lower extremity amputation. This provides an opportunity to enhance amputation prevention. Systematic evaluation of wound characteristics is critical to plan treatment strategies. Poor wound outcomes have been associated with infection, peripheral vascular disease, and wound depth. These variables should be the focus of ulcer evaluation. These ulcers serve as entry points of pathogens leading to infection in diabetes. Due to peripheral neuropathy, these wounds are painless. Even in presence of severe infection, the patient has only minor subjective complaints like soaking of stockings and soiled foot wear. Locally there is reduced erythema (ischemia), limited abscess formation (immunopathy). Further there is reduced systemic reaction such as fever or leukocytosis.

A thorough foot examination to assess the extent of neuropathy and vascular disease should be done. Examination for sensory neuropathy is done by nylon monofilament. Generally patient should feel the filament when it is pressed to the point of buckling. It is reduced or absent in diabetic patients. Vascular status is assessed such as claudication pain, cold feet, diminished pulse, atrophic skin and thickened nails.

Adequate debridement is the first step for evaluation. It will remove all necrotic tissue and surrounding callus till a healthy bleeding edge is seen. Then the ulcer is probed with a sterile instrument to estimate the involvement of underlying structure like tendon, muscle, and joint capsule and lastly the bone.

Culture of the infected tissue should be properly performed to provide guidance to therapy.[16] Culture should be taken from deep ulcer or bone biopsy in case of osteomyelitis. Osteomyelitis is detected by probing the bone.

Plain radiograph will predict the soft tissue gas and foreign bodies as well as osteomyelitis or fractures. MRI has become the gold standard for evaluation of diabetic foot infection, as it is superior to other imaging techniques in the evaluation of bone marrow and soft tissue infection. It is also a very sensitive and specific test for osteomyelitis. Sensitivity is 99 % and specificity is 83%.[50]

Appropriate wound classification is based on involvement of underlying structures and presence or absence of infection or ischemia. Treatment plan based on wound classification is followed.

10.Treatment

10.1.Treatment Options

Local wound care.
Medical management – Antibiotic regimens.
Surgical management – Debridement.
Amputation
Revascularization
Other – Offloading
Emerging therapies- Dermagraft, Apligraf, Hyaff
Collagenase
Platelet derived growth factor.

10.2.Antimicrobials

Diabetic foot ulcers act as portals of entry for systemic infection (from cellulitis, infected foot ulcers, and osteomyelitis). These infections have deleterious effects on patients with diabetes, whose immunity is already compromised.[51]

Initial therapy is usually empirical and should be based on the severity of the infection, on available microbiological data, such as recent culture results, and later choosing the definitive regimen and duration of treatment. Factors that influence antimicrobial selection include the severity of the illness (local and systemic), the likely causative pathogens, and coexisting complications, such as underlying osteomyelitis. Host-specific factors (eg, glycemic control, history of drug allergy, concomitant renal disease) directly influence the need for hospital admission and can affect the choice of specific agents or their dosing interval. Finally, drug-specific factors, such as cost and side effects, can be important, especially in the outpatient setting.

Clinically uninfected ulcers should not be treated with antimicrobials because it will lead to antimicrobial resistance, incur financial cost, and unnecessary adverse drug effects .[52,53] Superficial bacterial infections are caused by aerobic gram positive cocci and are treated by antimicrobials alone. Mild to moderate cellulitis, including that associated with superficial ulceration, is effectively treated with Dicloxacillin , the oral first-generation cephalosporins (eg, cephalexin , cefadroxil), and clindamycin provide good defense against staphylococci and streptococci. Cefadroxil may be the preferred agent because of better bioavailability and a longer half-life that allows twice-daily dosing. Clindamycin is the drug of choice in patients with severe penicillin allergy. For severe cases of cellulitis in patients requiring hospitalization, an intravenous first-generation cephalosporin (eg, cefazolin) is preferred.

Deep infections require early surgical debridement of all devitalized tissue, followed by antibiotic treatment to address the polymicrobial nature of the infection. Parenteral antimicrobials should be used to treat serious infections . For deeply penetrating pedal ulcers, it is advisable to increase coverage against common enteric gram-negative bacilli and anaerobes. In the outpatient setting, amoxicillin and clavulanic acid provides adequate coverage for staphylococci, streptococci (including enterococci), and anaerobes (including Bacteroides fragilis). In patients allergic to penicillin, a fluoroquinolone plus clindamycin or metronidazole provides comparable coverage . For the hospitalized patient with a penetrating pedal ulcer, intravenous beta-lactam/ beta-lactamase inhibitor combinations provide optimal coverage . The combination drugs ampicillin and sulbactam ,ticarcillin and

clavulanic acid , and piperacillin and tazobactam all provide broad-spectrum coverage, which includes Staph. aureus (methicillin sodium-susceptible strains), streptococci, and most anaerobes. Ampicillin-sulbactam has the best activity against enterococci and may be the preferred agent in patients with fairly acute infection. The other third-generation cephalosporins should not be used as monotherapy for diabetic foot infections. Ceftriaxone and cefotaxime have moderate antistaphylococcal activity. Ceftazidime has relatively poor gram-positive activity, and all these drugs lack significant anaerobic coverage. In patients with a history of severe penicillin allergy (eg, anaphylaxis, angioedema), combination therapy can provide adequate empirical coverage. Clindamycin combined with aztreonam or a fluoroquinolone (eg, ciprofloxacin, Levofloxacin) is effective. For treatment of osteomyelitis oral fluoroquinolones like ciprofloxacin provide excellent bioavailability and achieve outstanding tissue penetration, including into bone . Oral clindamycin also has good bioavailability and bone penetration and maintains excellent activity against staphylococci, streptococci, and anaerobes. This pattern of antimicrobials changes due to increasing resistance among bacteria to antimicrobials used. This varies with different geographic locations.

Topical antimicrobials have potential advantages including high local concentration, lack of systemic toxicity, and increasing patient attention to the foot, including the need for more frequent dressing changes. Metronidazole and povidone iodine act synergistically. Metronidazole is a 5-Nitroimidazole antiprotozoal and antibacterial. The production of critical factors by one organism permits survival of other pathogen. Anaerobes depend on aerobes to lower local oxygen concentration. The resultant physical conditions are conducive for replication and invasion by anaerobes. Metronidazole has a concentration dependent killing effect on anaerobes. Povidone iodine (polyvinyl-pyrrolidone) is non-irritating, non-toxic, non-staining and exerts germicidal action by iodinating and oxidizing microbial protoplasm. It is bactericidal, fungicidal, virucidal, and trichomonacidal.

10.3.Metabolic Control

In severe infections, considerable metabolic decompensation occurs. Full resuscitation is urgently required with IV fluids and IV insulin by sliding scale, which is often necessary to achieve good blood glucose control while the patient is infected.

10.4.Surgical procedures

Debridement is the first and most important surgical procedure in treating a diabetic ulcer.[54] In some cases, amputation is the best or only option. Urgent amputation is usually required only when there is extensive necrosis or life-threatening infection.[22] Elective amputation may be considered for the

11.Debridement

The various types of debridement are as follows:

11.1.Surgical Debridement

Surgical debridement is the most rapid and efficient method of debridement.

It accomplishes four goals: removes local contaminant bacteria, stimulates healing; documents the absence of hyperkeratotic tissue and tumor, decreases local infection, and all sinus tracts are opened to allow drainage of pus in case of osteomyelitis.[8] Enzymatic debridement (addition of proteolytic enzymes like collagenase) leads to breakdown of any protein with cysteine residue.

11.2.Emerging Therapies

Biologic therapy or cell therapy presents an appropriate option in some cases based on the principle that accelerating healing time decreases the risk of wound infection. These biologic agents are applied topically.

Two commercially available grafts are fibroblasts in a vicryl mesh, called Dermagraft, and Apligraf, also known as human skin equivalent.[55,56] Fibroblasts synthesize collagen and secrete growth factors essential for wound healing and epithelialization. Becaplermin gel, is a platelet derived growth factor, is applied as a thin layer to the wound, and the wound is covered with a saline moistened gauze dressing.[57] It helps in wound healing by forming epithelialization.

Pexiganin is a synthetic host defense peptide having antibacterial activity against gram-positive and gram negative aerobic bacteria by interfering with the permeability of the cell wall and membrane of pathogens.[58,59]

Hyaff is a semi-synthetic derivative of hyaluronic acid, which facilitates growth and movement of fibroblasts.[58] Hyaff membrane is placed in contact with the wound; its characteristic selective permeability to aqueous vapor keeps the wound moist and allows a natural drainage of excess exudates, thus avoiding maceration of tissues. [59]

12.Prevention of Foot Infection

- Wearing well-fitting shoes at all times.
- Meticulous attention to foot care and proper management of minor foot injuries.
- Daily foot inspection by the patient.
- Gentle cleansing of minor wounds with soap and water and application of topical antibiotic, moisturizers – emulsifying ointment to maintain moist wound environment.[60]
- Inspection of foot wear for areas of inadequate support or improper fit.
- Avoidance of hot soaks, heating pads and harsh topical agents such as tincture iodine, astringents , detergents and avoidance of prolonged washing.[61]
- Maintain euglycemic state.

13.Conclusion

Preventing the diabetic foot using the multidisciplinary team approach is a noble step in the right direction. Early recognition of lesions and prompt initiation of appropriate antimicrobial therapy as well as surgical debridement of necrotic tissue and bone are essential for controlling the infection and preventing additional morbidity.

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