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ORIGINAL ARTICLE

Diabetic Foot Infection: An Indian Scenario

[1]Ashu Rastogi, [2]Anil Bhansali

ABSTRACT

Introduction: Diabetes mellitus is assuming epidemic proportions and with that an increasing burden of diabetic foot complications. Diabetic foot infections (DFIs) contribute not only to morbidity, amputation, and increased health-care costs but also to mortality.

Aim: To review the literature regarding the epidemiology and management of DFIs in India.

Results: The socioepidemiology of diabetic foot and its complications in India is different from the West. There is a considerable delay in seeking a physician for foot problems, as patients continue invalidated and indigenous methods of treatment. At presentation, most of the foot ulcers are chronic, harbor infection, and neuropathic in origin compared to the West with predominantly neurovascular ulcers. A predominance of Gram-negative bacterial species is reported in DFIs, with *Pseudomonas aeruginosa* as the most common isolated organism. An initial empirical antibiotic choice covering Gram-negative bacteria is suggested.

Conclusion: There are very few studies on the countrywide prevalence of foot complications from India. In India, DFIs behave differently from the West because of sociocultural and economic differences. We need indigenous ways for prevention and management of DFIs in India.

Keywords: Amputation, Antibiotics, Diabetic foot, Diabetic foot infection, Foot ulcer, IWGDF, Osteomyelitis, Peripheral arterial disease.

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INTRODUCTION

According to an estimate by International Diabetes Federation (IDF), 80% of people with diabetes live in low- to middle-income countries including India, a country with the second largest number of diabetic patients in the world after China.[1] India is home to 69.1 million patients with diabetes mellitus with an overall prevalence of 9.3%. The regional prevalence of diabetes varies from as low as 5.3% in Jharkhand to 10.4% in Tamil Nadu and 13.6% in Chandigarh.[2] The age standardized prevalence of diabetes and prediabetes were 11.2 and 13.2% respectively in a community-based study from North India.[3] It is also estimated that still majority of the population – that is, 52.1% – remain undiagnosed, amounting for another 36.1 million people. The World Health Organization took a note of the magnanimity of the disease, and the theme of "World Health Day" on April 7, 2016, was made "Beat Diabetes" to create awareness.

An increasing number of patients with diabetes translate into an increased burden of diabetic complications including microvascular and lower extremity complications. Lower extremity diseases, including peripheral neuropathy, peripheral arterial disease (PAD), and foot ulceration, is twice as common in diabetic subjects as compared with nondiabetic persons and affects 30% of diabetic people older than 40 years. The annual incidence of diabetic foot ulcer (DFU) in population-based studies is 1.0 to 4.1% and prevalence of 4.5 to 10%, with an overall lifetime incidence of up to 25%.[4,5] Foot wounds not only add to morbidity but also to health-care cost, and are attributed as the most frequent cause for diabetes-associated hospitalization.

The foot ulcer itself is worrisome; however, the most feared consequence of it is limb amputation, which is seen 10 to 30 times more often in persons with diabetes than in general population. It is known that diabetes account for 8 of 10 nontraumatic amputations, of which 85% are due to DFU. The age-adjusted annual incidence for nontraumatic lower limb amputations in persons with diabetes ranges from 2.1 to 13.7 per 1,000 persons. Therefore, it is believed that in every 30 seconds a lower limb is lost somewhere in the world as a consequence of diabetes.[5] After a unilateral amputation, rates for mortality are also very high, ranging from 13 to 40% in 1 year, 35 to 65% in 3 years, and 39 to 80% in 5 years, which is worse than most malignancies.[4-6]

Diabetic foot does not occur spontaneously, and there are many premonitory signs that may be used to predict those "at risk." In the words of Dr. Elliott Joslin, who recognized this more than 75 years ago, "Diabetic gangrene is not heaven-sent but is earth-born."[7] Recognizing infection in DFU is important as infection is the precipitating event for nearly 90% of the amputations and about one-half of the diabetic foot wounds become clinically infected during the course of disease. Though diabetic foot has been well described over the years, unfortunately little information has been available to assist the clinician in diagnosing and treating these difficult infections. Some

[1]Assistant Professor, [2]Professor and Head

[1,2]Department of Endocrinology and Metabolism, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Corresponding Authors: Anil Bhansali, Professor and Head Department of Endocrinology and Metabolism, Post Graduate Institute of Medical Education and Research, Chandigarh, India, e-mail: anilbhansaliendocrine@gmail.com

recent studies along with Infectious Disease Society of America (IDSA)/International Working Group for Diabetic Foot (IWGDF) guidelines have provided data to scientifically base decisions for appropriate foot care and managing diabetic foot infections (DFIs).[8-10]

WHY FOOT IS PRONE TO INFECTIONS?

Foot ulcer and infection in persons with diabetes occurs as a consequence of hyperglycemia and several other comorbidities prevalent in diabetes, especially neuropathy, vasculopathy, sight-threatening retinopathy, and defects in immunity and wound healing. Other risk factors include peripheral edema and increasing duration of diabetes. An increased susceptibility to foot trauma due to the presence of vision-threatening retinopathy; small- and large-fiber peripheral neuropathy; limited joint mobility; and presence of foot deformity, particularly claw toes, hallux valgus, bunion, and prominent metatarsal heads are a proven risk factor for ulceration in a patient with diabetes. Plantar callus accumulation due to abnormal dynamics of foot is known to cause 77-fold increase in risk for ulceration in one cross-sectional study.[11] Furthermore, persons with diabetes are 2.5 times more likely to have onychomycosis and Toe-web tinea infection that can lead to skin disruption and ulcers.[12] Smoking, hypertension, and hyperlipidemia are other factors that are prevalent in patients with diabetes and contribute to the development of PAD and susceptibility for DFU.

Once a foot wound occurs, it is less likely to heal in patient with diabetes person because of several intrinsic wound-healing disturbances, including impaired collagen cross-linking and matrix metalloproteinase function, and immunologic perturbations, especially in polymorphonuclear leukocyte function.[13]

EPIDEMIOLOGY OF DIABETIC FOOT INFECTIONS IN INDIA

There is a dearth of countrywide data for the prevalence of risk factors for DFU and DFIs among patients with diabetes in India. There have been various single-center and few multicenter reports with heterogenous study population (hospitalized, outpatients, or community based), as well as use of varying assessment tools for the diagnosis of DFI. In a multicentric study from India, on patients with diabetes, the prevalence of neuropathy was found to be 15% and peripheral vascular disease (PVD) as 5%.[14] The data from North India suggest that one-third of patients with diabetes have prevalent peripheral neuropathy. More importantly, two-thirds of the patients were "at risk" for foot ulcers and 9% had prevalent ulcer, out of which 20.2% required amputation.[15] Among newly diagnosed patients of diabetes mellitus, the prevalence of DFU was 4.5 and 3% in general clinic population, which is much lower than reported in the Western world.[16] A possible reason for the low prevalence in Indians could be under-reporting, younger age, and shorter duration of diabetes.

The prevalence of DFIs is estimated to be 6 to 11%, and neuropathy is considered to be the most important determinant for occurrence of infection in diabetic foot wound.[14] Among newly diagnosed patients of diabetes with DFU, almost half of the ulcers were neuropathic, 19.7% ischemic, 34.2% neuroischemic, and nearly 3% of subjects had history of minor or major amputation of extremities.[16] In a multicentric study of 1985 diabetic patients with prior amputation from 31 centers across India, prevalence of neuropathy was 85% and PVD was 35%. Infection was considered to be the major cause of amputation in 90% of the patients.[17] Most of the study subjects (65–80%) in the studies from India were found not to follow any foot care procedures, in spite of having "foot at risk."[15-17] Diabetic foot and related sepsis was found out to be the second most common form of infection-related mortality (8.3%) in hospitalized patients, despite of supposedly lower reported prevalence of foot problems in India.[18] Therefore, it is prudent to identify infections in DFU early and treat appropriately.

Similarly, the prevalence of PVD among persons with diabetes and prevalent DFU has been found to be low among the Indians, that is, 3 to 6%[19,20] as against 25 to 45% reported from the West[21-23] or some recent studies from North India (12.6–31.6%).[15,24] The prevalence of PVD otherwise is known to increase with advancing age and with increased duration of diabetes. It is 3.2% in below 50 years of age and rises to as high as 55% in those above 80 years of age. The prevalence of PVD is 15% at 10 years and 45% after 40 years of diabetes.[25] The lower reported prevalence of foot problems in India may be just an eyewash as most of the studies have an inherent bias, being clinic-based data, rather than epidemiological community surveys or population-based studies. In developing world, most of the patients either do not seek medical advice and continue self-treatment with home-based remedies or delay seeing health care personnel because of poor awareness. They either consider foot problems as nonsignificant or are discouraged by lack of financial resources.

WHEN TO SUSPECT INFECTION IN DIABETIC FOOT ULCER?

Diagnosing a DFI begins with clinical suspicion through a comprehensive history and physical examination, validated with a complete laboratory evaluation, microbiology assessment, and diagnostic imaging. Patients may present

with a varying complaints related to local signs or less commonly systemic signs of infections. These signs include erythema, edema, purulent drainage, local pain/tenderness, new-onset malodor or anorexia, vomiting, fever, chills, change in mental status, and a recent worsening of glycemic control and renal functions because of sepsis. According to the IDSA guidelines, infection is present in DFU, if there is an obvious purulent drainage and/or the presence of two or more signs of inflammation (erythema, pain, tenderness, warmth, or induration).[8] Local signs of infection in foot may not always be present in a diabetic patient and a clinician has to be aware of secondary signs of infection, viz., foul odor, serous exudates, undermined wound edge, and discolored or friable wound edges. In these circumstances, infection may be suspected, if the wound size is more than 2 cm, duration more than 2 weeks, or depth more than 3 mm; renal insufficiency; loss of protective sensations; and history of prior amputation or walking bare foot. People in India are from predominantly agrarian background, have poor foot hygiene, and walk bare foot; therefore, a high index of suspicion is required for infection in DFU.

HOW TO APPROACH A PATIENT WITH DIABETIC FOOT INFECTION?

A thorough history related to diabetes should be obtained, including duration of disease, previous foot complications, prior ulcerations or amputations, and assessment of recent glycemic control. Any diabetes-related complications of neuropathy and retinopathy along with comorbidities, such as renal, hepatic, or cardiovascular disease should be enquired in detail. A current medication list, including past or current antibiotic usage, should be obtained. Social history must not be overlooked, including home support network, access to nearby health care facility, use of tobacco or alcohol, quantity of weight-bearing and ambulation level, diet, and exercise. Objective physical examination should begin by acquiring vital signs, weight, height, body mass index (BMI), and assessment of patient's general well-being.

A thorough systemic examination should be done to evaluate the severity of a potential infectious process, including features of systemic inflammatory response syndrome (SIRS), hypothermia (< 36.8°C) or fever (38.8°C), hypotension, tachycardia, and tachypnea.[8] A significant number of patients may not have *sine quo non* signs of inflammation because of impaired neuroinflammatory response due to neuropathy or vasculopathy. Thus clinician might underestimate the severity of infection.[26] Foot wound should be described as length, width, and depth of the wound, color, and consistency of drainage and character of wound base (granular, fibrous, or necrotic). Foot deformities like hallux valgus, claw toe or hammertoe, osseous prominences, loss of plantar arches, range of motion, and gait abnormalities should also be noted.

The neurological examination should include testing for sensory, motor, and autonomic neuropathy including evaluation of the Achilles reflex. A simple bedside evaluation including 10 gm Semmes-Weinstein monofilament, vibration testing with 128 Hz tuning fork or vibration perception threshold (VPT) > 25 (by Vibrotherm), temperature perception, and ankle reflex is useful for assessing peripheral diabetic neuropathy. When compared with VPT, ankle reflex was the most sensitive (90.7%) but least specific (37.3%) modality for diagnosing peripheral neuropathy. The tuning fork and monofilament tests respectively had lower sensitivity (62.5 and 62.8%) but better specificity (95.3 and 92.9%) and accuracy (78.9 and 7.9%).[27] In addition, use of simple clinical scores like Diabetic Neuropathy Symptom (DNS) and Diabetic Neuropathy Examination (DNE) are useful as a sensitive but less specific measure to diagnose peripheral neuropathy.

An assessment of vascularity is critical in diabetic foot examination. The extent and nature of edema and capillary fill time should be documented. The documentation of lower extremity pulses, including dorsalis pedis, posterior tibial, and popliteal artery, is mandatory. Ankle-brachial index (ABI) should be a part of routine examination in all patients with diabetes as it is a noninvasive and simple modality for vascularity assessment with a portable hand-held Doppler. In patients with faint or nonpalpable pedal pulses, ABI has proven to be a reliable and simple examination to evaluate PAD in outpatient settings. Falsely elevated ABI values may warrant more detailed vascular studies, such as peripheral arterial duplex Doppler.

Diagnosing osteomyelitis (OM) always remains a challenge in diabetic foot. As a rule, bone infection in diabetes is contiguous from overlying soft tissue, rather than systemic spread. Positive results on both microbiological and histopathology examination of aseptically obtained bone specimen remains the gold standard for diagnosis. However, bone sampling and processing is not always possible at many centers in India. Thus, clinicians use surrogate diagnostic tools, including clinical, laboratory, and imaging findings for the diagnosis of OM.

Clinically, OM should be considered in chronic wounds, or if ulcer lies over a bony prominence, bone is visible or palpable in the base of an ulcer when it fails to heal despite appropriate off-loading or when a toe is erythematous and indurated (sausage toe). The presence of exposed bone and large ulcers (size > 2 cm) has a positive likelihood ratio (LR) of 9.2 and 7.2 respectively for OM.[28,29] Probe-to-bone test (PTB) is a simple

bedside diagnostic tool, where a blunt sterile metal probe is gently inserted through a wound and noticed whether it strikes the bone or not. Probe-to-bone test is considered as a stronger predictor for the absence of bone infection because a negative PTB in a patient at low risk (<20%) essentially rules out OM and has a negative predictive value of 98% and positive predictive value of 57%.[30-32]

HOW TO CLASSIFY DIABETIC FOOT INFECTIONS?

A systematic grading of DFIs is needed to assess the severity of infections, identifying treatment strategies, level of care needed, and patient outcome. The severity of DFIs needs to be assessed and graded appropriately for selecting an antibiotic regimen, route of drug administration, need for hospitalization, or need for emergent surgical procedures including the likelihood of amputation. Once a DFI is graded, mild DFI may be treated with oral antibiotic therapy in an outpatient setting, whereas a moderate-to-severe infection, which can be limb- or life-threatening, may require inpatient antibiotic therapy, fluid resuscitation, and control of metabolic derangements. Wagner–Meggitt grade is traditionally used to classify the ulcer based on the depth of the wound. But it has several limitations including the lack of details regarding the general condition of the patient, severity of infection, and the vascular status of the foot. University of Texas staging/grading is another classification of foot wound which takes into account infection and vascularity, but the severity of infection is not graded.

Recently, IDSA and the IWGDF (the "infection" part of the Perfusion, Extent, Depth, Infection and Sensation (PEDIS) classification) elaborately describe both the presence and severity of infection.[8,33,34] The IDSA classification scheme proposes four levels of infection based upon severity correlated to clinical findings.[8] Mild infections are characterized by 2 cm of erythema while moderate infections have >2 cm of erythema, and severe infections are usually associated with systemic and/or metabolic instability. As this classification describes the wound and the general condition of the patient in detail, and validated to predict clinical outcomes, it is widely accepted.[35,36] In a prospective observational study by Lavery et al[36] of 1,666 patients with DFI, there was a trend toward significant increase in hospitalization rates for lower extremity amputation with increasing severity of infection. However, DFIs in Indian scenario may behave differently because of epidemiological and sociocultural differences and a validated Indian classification for DFIs is the need of hour.

WHAT LABORATORY AND RADIOLOGICAL INVESTIGATIONS ARE REQUIRED TO DIAGNOSE DFI?

Laboratory supports essential to establish a baseline diagnosis and assess the response to treatment in DFI. A complete hemogram and metabolic panel should be ordered including renal function, electrolytes, blood glucose level, and Hemoglobin A1C (HbA1c). Armstrong et al[26] found that fewer than 50% of DFI patients mounted the leukocytosis response to infection, with the mean WBC count being 11,995 cells/mm^3.

Acute phase reactants, including erythrocyte sedimentation rate (ESR), C-reactive protein level (CRP), and pro-calcitonin, have been measured for the evaluation of infection including OM in DFU. An ESR >70 mm/hour and CRP >3.2 mg/dL increases the probability of OM and are a useful marker for differentiating OM from cellulitis.[28,37] Studies have demonstrated that lower serum albumin levels (3.8 gm/dL compared to 3.5 gm/dL) were predictive of treatment failure and most patients required amputation.[38,39] Combining clinical findings with laboratory parameters significantly improves the diagnostic accuracy for DFIs and OM.

Plain X-ray of the foot is a readily available tool for the initial evaluation of infection. It provides valuable information regarding involvement of soft tissue and osseous structures, deformity, foreign bodies, soft tissue emphysema, and Charcot's neuroarthropathy changes in the foot. Osteomyelitis is considered on plain films by the presence of bony destructive changes, periosteal reaction, and permeative radiolucency. The sensitivity and specificity of plain radiograph for OM is 60 and 67% respectively. However, X-ray changes may take >3 week to be apparent, as they follow 30 to 50% loss of mineralized bone.[40]

Magnetic resonance imaging (MRI) is more specific and sensitive noninvasive test to evaluate OM and also provides excellent soft tissue details including an overlying sinus tract formation. Diagnostic sensitivity of MRI for osteomyelitis has generally been accepted as 90 to 100% with negative predictive values of 93 and 100%.[41] Magnetic resonance imaging may be less specific in distinguishing osteomyelitis from other causes of marrow edema, including acute neuropathic osteoarthropathy (CN). In these situations, three phase bone scans or WBC labeled Indium-111, Technetium-99m HMPAO, and sulfur colloid marrow scan may be useful in distinguishing acute and chronic foot infections, with the latter useful for identifying OM from CN. But their sensitivity is limited in an ischemic foot, and their performance characteristics is inferior to MRI for OM. Recently, F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (FDG PET/CT) and Labeled white blood cells (WBC PET/CT) have been shown to be very specific (author

experience) in distinguishing OM from CN with excellent spatial resolution and anatomic details.[42]

For PAD, if there is a high degree of clinical suspicion of PAD, CT angiography or MR angiography should be considered, as an intervention may be warranted in patients with ischemic infections. Nevertheless, all these modalities except plain X-ray are not readily available in resource-constraint settings and may not be needed always. A plain X-ray would suffice clinical evaluation in most circumstances, if there were high probability for osteomyelitis.

HOW TO TREAT DFI IN RESOURCE-CONSTRAINT SETTINGS?

Patients with severe foot infection, some patients who have moderate infection with complicating features (e.g., severe PAD, coexisting renal failure), and any patient unable to comply with the required outpatient treatment regimen for psychological or social reasons be hospitalized. A thorough sharp debridement, preferably in single sitting, should be performed and appropriate tissue specimen be collected and send for culture-sensitivity analysis.

An initial empirical antibiotic regimen should be chosen primarily on the basis of infection severity and likely pathologic agents, and later the definitive therapy should be based upon tissue-specific culture and antimicrobial sensitivity analysis. However, treatment centers in our country lack the specific information of prevalent microorganisms and their antibiotic susceptibility. The initial antibiotic regimen may include an agent active against Gram-positive cocci, if wound is of shorter duration (< 1 week). Previously treated or severe DFIs require an extended coverage for Gram-negative bacilli and *Enterococcus* species, a more common scenario in Indian context. Gangrenous and foul-smelling wounds may require antianaerobic therapy.

The microbial profile from DFIs vary widely among studies from different parts of the country, but all of them show a Gram-negative preponderance.[43-50] In a study by Parvez et al,[24] from North India, Gram-negative organisms were isolated in 66.2% of patients and enterobacteriacae family accounted for almost 50% of bacterial isolates in DFI. This Gram-negative preponderance has been shown to be similar over a span of two decades by Ramakant et al.[48] Parenteral therapy may be chosen initially for most severe infections and some moderate infections, for those who are unable to tolerate oral agents and who are infected with pathogens insensitive to available oral agents followed by a switch to oral therapy when the infection is responding. After the patient's clinical condition has stabilized and the infection is responding, most can switch to oral therapy.

In resource-constraint settings, cost of therapy is an important factor for selecting a treatment regimen, as compliance to treatment may be affected if expensive medicines are offered. Compared with parenteral therapy, treatment with oral antibiotic agents is more convenient, not associated with infusion-related complications, and is generally less expensive. Bioavailability of some oral antibiotics, such as fluoroquinolones, clindamycin, rifampicin, trimethoprim/sulfamethoxazole, linezolid, and doxycycline is excellent. Unfortunately, resistance to the above said antibiotics is rampant, especially fluoroquinolones. In addition, potential side effects of the drug, its pharmacokinetics, bioavailability, and frequency and route of administration should also be considered before starting the treatment. A significant antibiotic dose modification may also be required in a patient with diabetes because of existing comorbidities like chronic kidney disease.

Applying a total contact cast makes it difficult for the clinician and patient to visualize the wound for evaluation of response to treatment between changes, and is generally not appropriate for infected wounds. However, a modified cast with a window may be used for offloading in specific conditions, if the wound is small and not heavily exudating.

WHAT IS THE ROLE OF TOPICAL THERAPY AND WOUND DRESSINGS IN DFI?

The use of any specific wound dressings or topical antimicrobials is not supported by the evidence which may suggest that any of these therapies are better in wound healing. In general, DFUs with heavy exudate need a dressing that absorbs moisture, whereas dry wounds need topical treatments that add moisture.

Topical antimicrobial agents as well as antimicrobial impregnated wound dressings (e.g., those containing silver and iodine) might be useful for preventing, or even treating, mild infections; however, current data is too limited to recommend topical antimicrobial therapy.[50] A factor that impair response to antibiotic therapy in DFI is the presence of biofilm. Eradicating the bacteria in a biofilm may require physical removal and is often combined with topical agents, such as hypochlorous acid, cadexomer iodine, and systemic agents, such as fluoroquinolones and rifampicin.[51] The use of other adjunctive therapies like negative pressure wound therapy (NPWT), systemic hyperbaric oxygen therapy (HBOT), granulocyte colony stimulating factors (G-CSF), and larval (maggot) therapy are not recommended. Moreover, their prohibitive cost discourages their use in resource poor settings.

HOW LONG TO TREAT WITH ANTIMICROBIALS?

Data on optimum duration of therapy for predominant Gram-negative foot infection is lacking. In general,

moderate, and severe DFI are typically treated from 2 to 4 weeks of antibiotic therapy, initially intravenous (IV) followed by oral. Mild-to-moderate skin and soft tissue infections need antimicrobials for 1 and 2 weeks. Antibiotic therapy should be discontinued once signs and symptoms of infection have resolved, even if the wound has not healed. The antibiotics are administered to treat infection and not to heal wounds, as wound healing depends on numerous other factors, infection being one of them. Antibiotic therapy should be continued for 6 weeks for patients with diabetic foot osteomyelitis who do not undergo resection of infected bone, and no more than a week if all infected bone is surgically resected.

WHEN SHOULD A SURGEON BE INVOLVED FOR MANAGEMENT OF DFI?

Surgical management of moderate-to-severe DFI is often required when an aggressive incision, drainage, and debridement of nonviable soft tissue and bone is required. Multiple debridements may be necessary to provide adequate drainage and control of infection. In a study from South India, surgical debridement was the commonest surgical procedure performed in 65.8% of patients hospitalized for DFI. Emergent surgical intervention is necessary in most cases of deep abscesses, compartment syndrome, and virtually all cases of necrotizing soft tissue infections. A recent trial has shown that treatment outcomes with either antibiotics alone or predominantly surgical treatment (with some antibiotic therapy) are similar in patients who have neuropathic forefoot ulcers complicated by osteomyelitis, but without ischemia or necrotizing soft tissue infections.[52]

ARE DIABETIC FOOT INFECTIONS IN INDIA DIFFERENT FROM WEST?

The socioepidemiology of diabetic foot and its complications in India is entirely different from the West. Diabetic foot infections in India are often a consequence of wounds caused by the person wearing footwear that is not sufficiently protective (e.g., sandals) or poor fit, or wearing none at all. Poor hygiene may be associated with risk of rat bites and increases the risk of ulcer infection and may enable maggot infestation. There is a considerable delay by the patients in approaching the physician for foot problems, and in the meantime, they resort to many nonvalidated and indigenous methods of treatment, including home and herbal remedies and easily available over-the-counter antibiotics and drugs without proper prescription. The delay in seeking proper health care is also because of lack of health-related education, nearby health care services, or financial resources. An acute shortage of trained personnel, multidisciplinary teams, and dedicated diabetic foot centers compound the problem.

The prevalence of risk factors for foot ulcer and infections, viz., neuropathy and vasculopathy, are different from the Western literature. Studies from India, suggest predominantly neuropathic ulcers in 50 to 70%[14,15,25] unlike the West where neuroischemia is the most important predisposing factor. Prevalence of vasculopathy in patients being followed for DFIs has been documented to be 10 to 30% as compared to the West suggesting presence of PVD in 46 to 60%. However, the diagnostic criteria for vasculopathy have not been uniform in the studies.

Health infrastructure in our country lack appropriate diagnostic facilities and microbiological laboratories, which hampers isolation of causative organisms and antimicrobial susceptibility testing. Similarly, simple imaging modalities like X-ray facility are not available at many centers limiting the diagnostic capabilities. Therefore, antibiotics are prescribed without prior tissue culture, for inappropriate duration and doses, leading to widescale antimicrobial resistance. An appropriate culture and culture-sensitive specific antibiotic is a prerequisite for management of DFI. Unfortunately, with the paucity of dedicated diabetic foot units and trained personnel in India, more often than not, antibiotic treatment is empirical and not based on an appropriate prior tissue culture. Even if cultures are taken, wound swab is more commonly obtained which misrepresents the underlying soft tissue or bone infections.

As compared to the West, which have predominant Gram-positive infections, centers throughout India have reported a consistent Gram-negative bacterial preponderance in DFI.[25,43-49] The predominance of Gram-negative in studies from Indian subcontinent, as compared to the West, is attributed to a longer duration of ulcer, prior exposure to inadvertent antibiotics, or some unique environmental factors, such as sanitary habits. In addition, Gram-positive organisms were also isolated in the studies, but a low hemoglobin, high leukocyte, and neutrophil count at presentation were found to be significantly associated with the presence of Gram-negative bacilli. Gram-positive infections account for one-thirds of all DFIs but are milder ones, and incidence of MRSA is suggested to be 10%.[24,46]

The common bacterial isolates in various studies from different parts of India is shown in Table 1. *Pseudomonas aeruginosa* has been consistently shown to be the most common organism isolated form diabetic foot wounds in our country.[43-46,48,49] However, few others have shown *Escherichia coli* as the most common organism followed by *Staphylococcus aureus*.[24,47] Regarding, antimicrobial susceptibility for *P. aeruginosa*, the organism was found to be 100% resistant to ampicillin or quinolones; > 80%

Table 1: Organisms isolated from diabetic foot ulcers among different studies from India

Organism (%)	*Parvez et al*[24]	*Ramakant et al*[48]	*Vishwanathan et al*[45]	*Bansal et al*[44]	*Shankar et al*[46]	*Gadepalli et al*[47]	*Elamurgan et al*[43]
Escherichia coli	19	16.1	–	18	22	12	14
Pseudomonas aeruginosa	5.9	16.9	17	22	29.8	9.8	18.8
Proteus spp.	16.7	8.8	–	11	11.5	12.6	9.5
Klebsiella spp.	5.9	6.7	–	21	11.6	6.6	7.2
Acinetobacter spp.	3.6	3.7	–	4	–	9.3	13.3
Citrobacter spp.	2.3	3.2	–	1	2.4	0.5	–
Staphylococcus aureus	29.7	13.8	18.2	19	24.5	13.7	31.1
Enterococcus spp.	4.8	9.5	–	5	3.8	11.5	–
Streptococcus spp.	1.2	3.0	16.8	–	–	–	3
Anaerobes	23.8	0.7	33.2	–	6.3	15.3	–

resistant to piperacillin or ticarcillin; >65% resistant to ceftazidime, imipenem, or aminoglycosides; and 50% resistant to cefoperazone. IDSA guidelines suggest that the initial antibiotic regimen should include an agent active against Gram-positive cocci with special attention for MRSA in high-risk patients. However, studies from India suggest that third-generation cephalosporins and piperacillin are an appropriate empirical antibiotic of choice until definitive culture reports are available, because of predominant Gram-negative bacterial isolates.

In India factors, such as lack of adherence to foot care practices, noncompliance to recommended dose and duration of antibiotics, offloading devices, and inept follow-up at desirable intervals because of economic or social reasons lead to treatment failures. The lack of purchasing power for the health needs in the absence of health insurance in our country leads to out-of-pocket expenditure through undesirable means, viz., personal savings, getting loans, selling houses or land. A patient with diabetes and foot problems has to spend four times more as compared to a patient without foot disease.

CONCLUSION

Diabetes and its associated complications, including foot diseases, are increasing at an alarming pace in India and putting enormous burden on our limited health care resources. Diabetic foot ulcer and DFI have long-term implications for persons living with diabetes in the form of morbidity and mortality. Early recognition, classification, diagnosis, and treatment of foot complications are needed to optimize outcomes in patients with diabetes. We need a different and indigenous ways for preventing and treating foot complications, as DFIs in India behave differently from the West because of sociocultural and economic differences. It is not only the patients but also physicians and surgeons at primary and secondary care levels who need to be sensitized, educated, and trained regarding foot care. Therefore, a conscious effort by the health care providers and professional bodies to challenge this upcoming epidemic of diabetes and DFIs in India is needed.

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