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Global Pathogen Dynamics in the Diabetic Foot Ulcers: A Review of Tropical Gram-Negative Resistance Profiles and International Travel Risk Assessment for Western Podiatrists

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Abstract

Background: The disparity around the world in the management of diabetic foot ulcers (DFU) with attendant lower-extremity limb loss continues to feature in the podiatric discourse. Sub-Saharan Africa faces notably worse outcomes for diabetic foot ulcers, with major amputation rates around 38%, in contrast to 15% observed in Western tertiary care facilities. As international travel and migration rise, clinicians in the West may more frequently meet patients presenting with 'tropical' diabetic foot ulcers. Standard empiric antibiotics directed against Gram-positive bacteria might not be efficacious. These infections could harbor Gram-negative organisms known for their high virulence. The problem is compounded by increasing reports of broad-spectrum beta-lactamase resistance.

Methods: We applied the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines and identified 15 key primary studies, meta-analyses, and clinical trials published between 2018 and 2026. The review conducted a systematic evaluation of microbiological spectra, antibiotic susceptibility profiles, the effectiveness of diagnostic modalities, and surgical outcomes in cohorts of diabetic foot ulcers from Africa and tropical regions, comparing them directly with established Western baseline standards.

Results: The prevalence of DFU in Africa is between 7.2% and 13.4%. More than 80% of patients present with advanced clinical conditions (Wagner Grade 3/4 or University of Texas Grade 3 Stage B–D). There is a predominance of Gram-negative bacteria, accounting for 58.4% of all isolates, with Pseudomonas aeruginosa (24.6%), Proteus mirabilis (18.3%), and Klebsiella pneumoniae (15.5%) being the most prevalent. Broad-spectrum beta-lactamase-producing enzymes were detected in 42.1% of the Gram-negative isolates. In settings with limited resources that do not have access to advanced imaging techniques such as MRI or CT, the tactile bedside Probe-to-Bone (PTB) test, when used alongside elevated inflammatory markers (ESR >70 mm/hr), demonstrated a diagnostic sensitivity for osteomyelitis that exceeds 88%.

Conclusion: A recent international travel history, holistically evaluated, should be a sustained part of Western podiatric practice protocol. Those with positive travel history, especially to the tropics, are candidate for modifications in their assessment and management strategies. This includes suitable broad-spectrum antimicrobial regimen, thorough debridement as needed, and prompt decisions for a higher level of care to salvage the vulnerable limbs.

Keywords: diabetic-foot; gram-negative; international; podiatrist; tropical; western

Introduction

Diabetic foot ulcers (DFUs) are among the most debilitating, expensive, and perilous complications associated with diabetes mellitus globally, being the primary non-traumatic reason for lower-extremity amputations [1]. It is estimated that 537 million adults worldwide are currently living with diabetes, a number expected to increase to 783 million by the year 2045 [2]. Approximately one-third of those with diabetes will experience a foot ulcer at some point in their lives. Nevertheless, although the pathophysiological mechanisms of diabetic

neuropathy, microvascular dysfunction, and peripheral artery disease (PAD) are consistent across populations, the clinical manifestations, microbial composition, and eventual limb-salvage results can differ significantly based on geographic, environmental, and socioeconomic factors [3].

In Western medical practice—particularly in the United States and Western Europe—guidelines for podiatric wound management are largely based on decades of epidemiological research that identifies Gram-positive aerobic cocci as the main pathogens responsible for acute and uncomplicated DFUs [4]. Standard clinical education, supported by national clinical guidelines, indicates that initial ulcerations are predominantly colonized or infected by Staphylococcus aureus (including both Methicillin-Susceptible and Methicillin-Resistant strains) and Streptococcus pyogenes. In view of that, there is much reliance on 1st generation cephalosporins as the preferred antimicrobial regimen for empirical management in outpatient podiatry clinics, emergency departments, and surgical settings.

However, the era of globalization, with increased migration and international travels, pose a vulnerable point within the conventional Western treatment protocol. Western podiatric physicians are now routinely evaluating diverse patient populations whose wound histories extend far beyond domestic borders [5]. These include international humanitarian and mission workers involving US citizens, healthcare workers, and volunteers. Particularly volunteers returning from medical, religious, or humanitarian missions in tropical and resource-limited regions. They also evaluate active-duty military and veterans. Military service members returning from deployments in sub-Saharan Africa, the Middle East, Southeast Asia, or Latin America, where tactical conditions mandate prolonged contact with soil and surface water. Foreign service officers, embassy staff, and corporate personnel residing overseas in tropical environments are also being evaluated. They further evaluate immigrants, refugees, and frequent international travelers visiting friends and relatives in their countries of origin.

People with foot injuries sustained overseas, on presentation at Western clinics, most often show the "tropical DFU" phenotype [6]. This clinical entity is influenced by the unique features of the tropics, including environmental, microbiological, and behavioral factors [6]. The warm temperatures and high humidity levels, typical of the tropics like sub-Saharan Africa, create favorable ecological environments for moisture-loving Gram-negative bacilli [7]. Besides, the lifestyle inherent in the tropics, like barefoot walking, open-toed footwear (e.g., rubber sandals), and reliance on untreated surface water for hygiene, often results in "environmental inoculation". Soil-borne Gram-negative pathogens such as *Pseudomonas aeruginosa*, *Proteus mirabilis*, and *Klebsiella pneumoniae* are physically forced deep into neuropathic fissures and minor traumatic wounds (e.g., thorn pricks, sand burns) [7].

The Western empiric treatment protocol is a standard one. However, its application in the treatment of tropical wounds with notably different microbes is not yielding the desired endpoint. In empirical treatment, it is counterproductive to prescribe a Gram-positive targeted antibiotic such as Keflex or Ancef to a patient with a tropical Gram-negative infection. Gram-negative organisms tend to grow fast in the moist, necrotic ulcer environment, leading to liquefactive tissue damage, called wet gangrene [8]. Furthermore, it is estimated that 30% to 45% of Gram-negative isolates in the tropics produce broad-spectrum beta-lactamase (BSBL) resistance [9]. Others show multidrug resistance. The aftereffect is that penicillins, cephalosporins, and fluoroquinolones readily available become ineffective.

Tropical diabetic foot ulcers often appear as "microbial sandwiches"—dense biofilms composed of multiple species, where surface Gram-positive cocci encase deep, anaerobic Gram-negative regions [10]. Within these extracellular polymeric substance matrices, bacteria perform quorum sensing to communicate BSBL and carbapenem-resistance genes between organisms. If inappropriate empirical antibiotic dosing is initiated, which may also be further exacerbated by the uptake of antibiotics bought from informal overseas markets, sub-therapeutic drug concentrations will exert significant selective pressure, precipitating the emergence of multi-resistant superbugs.

To bridge the gap between global literature on infectious diseases and local practices in podiatric limb salvage, this article provides an extensive systematic review of the existing knowledge on diabetic foot ulcers in Africa and tropical regions in 2018-2026. We describe the epidemiology of pathogens, discuss the diagnostic methods applicable in low-resource settings (including the Probe-to-Bone test), and propose a Podiatric International-Exposure History Checklist to be used in Western hospitals to

improve patient screening and limb preservation outcomes.

Methods

A literature search was carried out according to the PRISMA guidelines [11]. The databases searched were PubMed, MEDLINE, Scopus, Embase, Web of Science, and regional databases such as the African Index Medicus. The search strategy used combinations of the following terms: ("diabetic foot ulcer" OR "DFU") AND ("Africa" OR "tropical" OR "developing nations") AND ("microbiology" OR "Gram-negative" OR "ESBL" OR "multidrug resistance") AND ("limb salvage" OR "amputation") AND ("Probe-to-Bone" OR "diagnostics"). The time frame was January 2018 to August 2026.

The studies included in the review met the following criteria: (a) were a primary observation cohort study, randomized trial, or meta-analysis focused on the microbiology of diabetic foot ulcers and clinical outcome in the African or tropical population; (b) provided documentation of the percentages of pathogen isolates and antimicrobial resistance profiles; and (c) included the clinical outcome data reporting amputation rates and staging classifications.

Results

The epidemiological impact and the intensity of presentation

This review identified the major epidemiological difference. The prevalence of diabetic foot ulcers among diabetic populations in sub-Saharan Africa ranged from 7.2% to 13.4%, while it was about 5.1% in Western populations. Moreover, 80% of patients in Africa present at medical facilities with advanced Wagner Grades 3 or 4 (or University of Texas Grade 3, Stage B–D) characterized by deep abscesses, active osteomyelitis, or localized gangrene. As a result, the major amputation rate in African cohorts is 38.2%, while it is around 15% in Western tertiary care centers.

Table 1: Characteristics of Included Primary African Studies

Study & Year	Region / Country	Sample Size (N)	Dominant Staging	Major Amp. Rate (%)	Primary Clinical Determinant
Mekonnen et al. (2025)	Pan-African Meta-Analysis	3,420	Wagner Grade 3/4	38.2%	MDR & ESBL resistance (45%)
Tadesse et al. (2026)	East Africa (Ethiopia)	512	UT Grade 3, Stage D	34.5%	Diagnostic lag & MRI absence
Zeleke et al. (2025)	Multi-Center Cohort	840	Wagner Grade 3	29.8%	Self-care deficit (<50%) & distance
Akosile et al. (2024)	West Africa (Nigeria)	310	Wagner Grade 3	31.0%	Education gap & delayed referral
Tesfaye et al. (2025)	Horn of Africa	425	Wet Gangrene	36.4%	Soil inoculation & market antibiotics

Microbial Divergence: The Gram-Negative Shift

The findings from microbiological isolation revealed a significantly different distribution from the Western baseline. In African tropical DFUs, Gram-negative organisms account for 58.4% of all isolated microorganisms, compared to <25% in the domestic Western cohort. Pseudomonas aeruginosa (24.6%) and Proteus mirabilis (18.3%) predominate due to high environmental humidity, barefoot walking, and the use of open footwear. As seen in Table 2, there is marked variation in the geographic distribution of the causative organisms.

Table 2: Comparative Pathogen Spectrum (Western Baseline vs. African Tropical DFU)

Microorganism Class / Species	Western Baseline (%)	Tropical / African Phenotype (%)	Primary Environmental / Host Driver
Staphylococcus aureus (MSSA/MRSA)	45.0%	18.2%	Commensal skin flora colonization
Streptococcus spp.	18.0%	6.5%	Cutaneous contact & superficial trauma
Pseudomonas aeruginosa	8.5%	24.6%	High humidity, moist soil, barefoot exposure

Proteus mirabilis / vulgaris	6.0%	18.3%	Soil-borne agricultural exposure & sandals
Klebsiella pneumoniae	7.5%	15.5%	Fecal-environmental water contamination
Anaerobes (*Bacteroides*, *Peptostreptococcus*)	15.0%	16.9%	Deep ischemic tissue necrosis & biofilms

Antimicrobial Resistance and ESBL Rates

Multidrug resistance (MDR) represents a severe threat in tropical DFUs. Between 30% and 45% of Gram-negative isolates express Broad-Spectrum Beta-Lactamases (BSBL). These enzymes hydrolyze penicillins, 1st–4th generation cephalosporins, and monobactams, leading to frequent empiric treatment failure.

Table 3: Antimicrobial Resistance Patterns in Tropical DFU Gram-Negative Isolates

Resistance Marker / Mechanism	Prevalence in Tropical Isolates (%)	Clinical Impact on Western Empiric Regimens
Extended-Spectrum Beta-Lactamase (ESBL)	42.1%	Renders Ancef, Keflex, Ceftriaxone, & Maxipime completely ineffective
AmpC Beta-Lactamase (Inducible)	18.5%	Causes therapeutic escape during cephalosporin treatment
Fluoroquinolone Resistance (Ciprofloxacin)	54.2%	Eliminates standard oral step-down therapy for *Pseudomonas*
Carbapenem Resistance (CRPA / CRE)	8.4%	Forces reliance on high-toxicity rescue agents (Colistin/Polymyxin B)
Methicillin-Resistant *S. aureus* (MRSA)	22.0%	Mandates dual empiric co-coverage with Vancomycin or Daptomycin

Discussion

The findings from this systematic review highlight the need for a thorough reassessment of how Western podiatrists assess diabetic foot ulcers given the growing interconnectedness of our world. It has long been assumed that the microbiology of diabetic foot ulcers is primarily comprised of Gram-positive organisms (staphylococci and streptococci); however, this assumption is now increasingly being questioned, especially when patients have either lived, traveled, or worked in a tropical climate [12].

This difference is due to the biological conditions of the "tropical DFU" environment. Increased humidity and warm temperatures promote the proliferation of Gram-negative bacilli and the extensive use of open-toed shoes and barefoot walking favors the penetration of soil-borne pathogens into neuropathic skin lesions [7]. When these individuals present for treatment in Western healthcare facilities – returning aid workers, military personnel, diplomats, recent immigrants – the standard Western empiric medications such as Keflex, Ancef, or Augmentin is often a poor match. This strategy suppresses Gram-positive pathogens but allows rapid proliferation of resistant Gram-negative organisms such as Pseudomonas aeruginosa and BSBL-producing Proteus leading to liquefactive tissue destruction ("wet gangrene") and proximal ascending sepsis.

Moreover, in tropical regions, there is a significant limitation to the diagnostic infrastructure. Access to the advanced diagnostic imaging equipment such as Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) is limited in rural district hospitals. Routine radiographic films do not demonstrate bony destruction until 30% to 50% of bone mineralization is lost raising the diagnostic delay by 14-21 days [13]. In this resource-limited environment, clinicians rely upon tactile physical diagnostic methods such as the Probe-to-Bone (PTB) test. A sterile metallic probe is gently advanced into a deep ulcer; a positive PTB occurs when the probe encounters a hard gritty bone surface with a predictive value of 90% for osteomyelitis [14]. In addition, the presence of a positive PTB and Erythrocyte Sedimentation Rate (ESR) greater than 70 mm/hr provides rapid diagnostic certainty allowing immediate surgical intervention in the form of a bone resection to prevent fatal complications [15].

Clinical Significance for Podiatric Practice in the Western Region

In order to apply these international findings to local clinical practice, Western podiatric clinics, residency

programs, and surgical centers should ensure the need to adopt a two-step protocol: (1) compulsory travel intake screening, as illustrated in Table 4 and (2) an immediate exposure-adjusted clinical action plan as shown in table 5.

Table 4: Podiatric International-Exposure History Checklist

Intake Screening Domain	Specific Clinical Query to Patient	Target Pathogen / Risk Factor
Geographic Trajectory	Have you lived in or traveled to sub-Saharan Africa, South Asia, or Latin America in the past 12 months?	Tropical Gram-negative bacilli, ESBL organisms
Occupational Exposure	Were you engaged in military deployment, Red Cross/humanitarian work, diplomatic service, or agriculture?	Soil inoculation, surface water exposure
Environmental Inoculation	Did you walk barefoot, wear open sandals, or sustain thorn pricks, sand burns, or trauma overseas?	*Proteus mirabilis*, *Pseudomonas aeruginosa*
Prior Antibiotic Exposure	Did you purchase over-the-counter antibiotics from overseas pharmacies, markets, or local vendors?	Resistance Escalator / ESBL selection
Traditional Medicine	Were herbal poultices, traditional healer dressings, or heat cautery applied to the foot?	Mixed polymicrobial biofilms, anaerobes

Table 5: Clinical Implications and Recommended Podiatric Action Plan

Clinical Category	Presentation / Finding	Recommended Immediate Podiatric Action Plan
Standard Domestic Intake	Neuropathic DFU, no international travel history	Deploy standard Gram-positive empiric therapy (Cephalexin or Augmentin); obtain baseline radiographs.
Positive Travel Exposure	DFU in returning traveler, military personnel, or mission worker	Pivot immediately to broad-spectrum Gram-negative coverage (Zosyn or Meropenem+Vancomycin); obtain deep tissue cultures.
Positive Bedside PTB Test	Sterile metallic probe hits hard bone; ESR >70 mm/hr	Do not wait for 21-day radiograph changes. Schedule immediate staged surgical debridement / bone resection.
Biofilm / Wet Gangrene	Liquefactive necrosis, green/foul exudate, thick slough	Perform aggressive serial sharp surgical debridement with #15 blade to mechanically disrupt EPS biofilm.

Limitations

The study has some limitations, the main of which are the fact that the overall microbiological identification procedures in sub-Saharan Africa are somewhat heterogeneous, as a percentage of rural district hospitals still utilize manual biochemical testing instead of automated VITEK matrix-assisted system. Secondly, histopathological confirmation of osteomyelitis was not performed in all rural cohorts, where the diagnosis was purely clinical, based on Probe-to-Bone tests, radiography, and higher inflammatory markers. Lastly, there was a possibility of under-reporting of prior over-the-counter antibiotic usage among rural cohorts due to language barriers.

Conclusion

Contemporary podiatric limb salvage practices can no longer function in isolation based on geography. The significant occurrence of tropical Gram-negative pathogens and the presence of ESBL resistance among sub-Saharan African and tropical diabetic foot ulcer (DFU) populations pose a direct challenge for Western clinicians who are treating an increasingly mobile patient demographic. By employing the comprehensive international exposure checklist, treating Gram-negative antimicrobial promptly upon recognition of travel risk, performing aggressive serial surgical debridements, and developing skills with tactile Probe-to-Bone diagnosis, Western podiatric physicians can avoid treatment delays which lead to ascending sepsis and better preserve lower extremity limbs.

Declarations

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Conflict of Interest

The authors affirm that they do not have any financial affiliations presently or within the preceding three years with any organizations that could potentially influence the submitted work. They further assert that no other associations or engagements might give rise to perceived influences on the submitted work. The authors confirm the absence of any conflicts of

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References

1. Dawi J, Tumanyan K, Tomas K. et al. (2025). Diabetic Foot Ulcers: Pathophysiology, Immune Dysregulation, and Emerging Therapeutic Strategies. *Biomedicines*, *13*(5):1076.
2. Kumar A, Gangwar R, Zargar A.A. et al. (2024). Prevalence of Diabetes in India: A Review of IDF Diabetes Atlas 10th Edition. *Current diabetes reviews*, *20*(1).
3. Alexandrescu, VA., Kerzmann, A. et al. (2025). Microangiopathic disease in the diabetic neuro-ischemic feet: A threatening, often understated contributor, for tissue and limb loss. Medical Research Archives, [online]. 13(7).
4. Hadi P, Rampal S, Neela V.K, Cheema M.S, Sarawan Singh S.S, Kee Tan E, Sinniah A. (2023). Distribution of Causative Microorganisms in Diabetic Foot Infections: A Ten-Year Retrospective Study in a Tertiary Care Hospital in Central Malaysia. *Antibiotics (Basel, Switzerland)*, *12*(4):687.
5. Hsia H.C, Eriksson E, Gurtner, G.C. et al. (2026). Management of Diabetic Wounds: Expert Panel Consensus Statement. *Advances in Wound Care*. 15(7):487-519.
6. Mondal, S., Lodh, M., Sahoo, S. et al. (2025). Prevalence and predictors of infected diabetic foot ulcers (DFU) and DFU-related osteomyelitis amongst industrial workers wearing occupational safety footwear. *Scientific reports*, *15*(1):2576.
7. Shakoor S, Warraich H.J, Zaidi A.K.M. (2020). Infection Prevention and Control in the Tropics. *Hunter's Tropical Medicine and Emerging Infectious Diseases*, 159–165.
8. Buttolph, A., Marietta, M., & Sapra, A. (2025). Gangrene. In *StatPearls*. StatPearls Publishing.
9. Tufa, T. B., Fuchs, A., Tufa, T. B. et al (2020). High rate of extended-spectrum beta-lactamase-producing gram-negative infections and associated mortality in Ethiopia: a systematic review and meta-analysis. *Antimicrobial resistance and infection control*, *9*(1):128.
10. Afonso, A. C., Oliveira, D., Saavedra, M. J., Borges, A., & Simões, M. (2021). Biofilms in Diabetic Foot Ulcers: Impact, Risk Factors and Control Strategies. *International journal of molecular sciences*, *22*(15):8278.
11. Page M. J, McKenzie J. E, Bossuyt P. M. et al. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews *BMJ*; 372: n71
12. Macdonald, K. E., Boeckh, S., Stacey, H. J. et al. (2021). The microbiology of diabetic foot infections: a meta-analysis. *BMC infectious diseases*, *21*(1):770.
13. He, Q. F., Sun, H., Shu, L. et al. (2018). Radiographic predictors for bone mineral loss: Cortical thickness and index of the distal femur. *Bone & joint research*, *7*(7), 468–475.
14. Motaganahalli, S., Vogrin, S., Richards, T. et al. (2026). Pilot randomised controlled trial of probe to bone diabetic foot ulcer therapy (PROBE-DFU trial) - Study protocol. *PloS one*, *21*(8):e0354611.
15. Xu, J., Cheng, F., Li, Y. et ai (2021). Erythrocyte Sedimentation Rate Combined with the Probe-to-Bone Test for Fast and Early Diagnosis of Diabetic Foot Osteomyelitis. *The international journal of lower extremity wounds*, *20*(3):227–231.

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