Content available at: https://www.ipinnovative.com/open-access-journals

IP International Journal of Medical Microbiology and Tropical Diseases

Journal homepage: https://www.ijmmtd.org/

Review Article

# Evaluating diagnostic approaches for diabetic foot infections: A systematic review

**J Bindhu[1]*, R Umashankar[2], Ramesh Vasudevan[3], B. Mahalakshmi[4], Sovan Bagchi[5], Wethroe Kapfo[6], Abida Khan[7], Suria Prabha[8], Muthu Prasanna[9]**

[1]Dept. of Biotechnology, Sri Shakthi Institute of Engineering and Technology, Coimbatore, Tamil Nadu, India
[2]Dept. of General Medicine, Sree Balaji Medical College Hospital, Chennai, Tamil Nadu, India
[3]Dept. of General Surgery, Apollo Institute of Medical Sciences, Jubilee Hills, Hyderabad, Telangana, India
[4] Dept. of Child Health Nursing, Nootan College of Nursing, Sankalchand Patel University, Visnagar, Gujarat, India
[5]Dept. of Biomedical Sciences, Gulf Medical University, United Arab Emirates
[6]Dept. of Biochemistry, MMK and SDM Mahila Mahavidyalaya Krishnamurthypuram, Mysuru, Karnataka, India
[7]Center for Health Research, Northern Border University, Arar, Saudi Arabia
[8]Dept. of Pharmaceutical Sciences, Chettinad School of Pharmaceutical Sciences, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education, Kelambakkam, Tamil Nadu, India
[9]Dept. of Pharmaceutical Biotechnology, Surya College of Pharmacy, Vikiravandi, Villupur, Tamil Nadu, India

## Abstract

Diabetic neuropathy, a major complication of diabetes mellitus, encompasses disorders affecting the somatic and autonomic nervous systems. Among its clinical manifestations is diabetic foot (DF), characterized by structural and functional foot changes, including ulceration, infection, and gangrene. These issues often arise from prolonged hyperglycemia, neuropathy, and peripheral vascular disease and can progress to severe complications such as foot ulcers, Charcot osteoarthropathy, and limb amputation. Diabetic foot infections (DFIs), a serious complication, impose a significant burden on global healthcare systems. Peripheral neuropathy and arterial disease contribute to ulceration, impaired wound healing, and infection. *Staphylococcus aureus* is a common pathogen, though microbial profiles vary with geography, patient characteristics, and local resistance patterns. Effective management of DFIs relies on prompt diagnosis, guided by imaging and deep tissue cultures, to inform surgical and antimicrobial strategies. Surgical debridement and, in cases of osteomyelitis, excision of infected bone is critical for reducing recurrence and amputation risk. Antibiotic therapy should be tailored to culture results to optimize outcomes and curb resistance. Preventative measures, such as patient education, regular foot care, and specialized clinics, are essential in mitigating DFI risk. This systematic review consolidates findings from early reported studies, analyzing microbial profiles, antibiotic resistance trends, and clinical practice guidelines for diabetic foot management. It highlights the need for integrated approaches to improve patient outcomes and reduce the global burden of DFIs.

**Keywords:** Diabetes, Diabetic foot infections, Foot ulcers, Systematic review.

**Received:** 26-12-2024; **Accepted:** 20-02-2025; **Available Online**: 26-03-2025



## 1. Introduction

Diabetes is a condition impacting millions globally, with its prevalence rising significantly over the past three decades. Diabetic neuropathy encompasses a diverse group of disorders affecting both the somatic and autonomic nervous systems. Among its clinical manifestations is diabetic foot (DF), characterized by structural or functional changes in the foot, including ulceration, infection, and gangrene.[1] These issues often result from prolonged hyperglycemia and pre-existing trauma, combined with varying degrees of peripheral vascular disease. Prevention and early intervention are key to avoid the development of DF. Consistently checking blood sugar levels, maintaining proper foot hygiene, and using suitable footwear are crucial for lowering the risk of diabetic foot (DF). People with diabetes should collaborate closely with their healthcare teams to prevent and address complications related to DF. Even without noticeable

*Corresponding author: J Bindhu
Email: bindhuraviedu0412@gmail.com

http://doi.org/10.18231/j.ijmmtd.2025.003

symptoms, DF can lead to severe issues such as foot ulcers, Charcot osteoarthropathy, and, in extreme cases, amputation.[2] Diabetic foot infections (DFIs) represent a challenging and severe complication of diabetes mellitus, placing significant strain on healthcare systems worldwide. These infections, typically stemming from diabetes-related neuropathy and vascular issues, can result in serious consequences, including tissue destruction, limb amputations, prolonged hospitalizations, and increased risk of death.'[3] Early detection and treatment of DFIs are crucial in preventing these consequences. Patients with diabetes should be educated on the importance of daily foot inspections, proper foot care, and seeking medical attention at the first sign of infection. Healthcare providers should be diligent in conducting thorough foot exams and promptly treating any wounds or infections that may arise.

A thorough knowledge of the microbiological characteristics and antibiotic resistance patterns of pathogens responsible for diabetic foot infections (DFIs) is crucial for successful treatment and better patient outcomes. DFIs involve a wide variety of microorganisms, with Staphylococcus aureus often recognized as a primary pathogen in numerous studies.[4] The composition of microbes differs greatly based on geographical region, individual patient factors, and the prevalence of antimicrobial resistance in the area. Therefore, healthcare providers must conduct thorough assessments and obtain appropriate cultures to diagnose and treat DFIs accurately. Prompt and effective treatment with antibiotics tailored to the specific pathogens present is essential to prevent the spread of infection and avoid serious complications such as cellulitis or osteomyelitis.[5] This knowledge helps healthcare providers choose the most appropriate antibiotic therapy to target the specific pathogens causing the infection. In addition, proper wound care and management are essential in preventing the spread of infection and promoting healing. In severe cases, surgical intervention may be necessary to remove infected tissue and promote healing. A multidisciplinary approach involving healthcare professionals, patients, and caregivers is essential to effectively manage DFIs and prevent long-term consequences in individuals with diabetes. By implementing preventative measures and staying vigilant in monitoring for signs of infection, patients with diabetes can significantly decrease their risk of serious complications and improve their overall quality of life. The onset of diabetic foot infections (DFIs) is closely linked to the microvascular and neuropathic complications associated with diabetes. Peripheral neuropathy, marked by sensory impairments and motor dysfunction, contributes to an increased risk of foot deformities, abnormal biomechanics, and pressure-related injuries or ulcers. The presence of peripheral arterial disease adds complexity by reducing blood flow, hindering wound healing, and fostering conditions favorable for infection. Preventative measures such as daily foot washing, moisturizing, thorough inspections, appropriate footwear, and maintaining good hygiene can help minimize the risk of DFIs and associated complications. Additionally, managing blood glucose levels through proper medication, diet, and physical activity plays a crucial role in preventing DFIs and promoting foot health in individuals with diabetes. Healthcare providers often rely on advanced imaging modalities like magnetic resonance imaging (MRI) and computed tomography (CT), along with deep tissue cultures, to inform and optimize treatment strategies.[6] Timely and accurate diagnoses is essential for initiating effective treatment, preventing complications, and lowering the risk of limb amputation or systemic infection. Surgical debridement plays a crucial role in addressing deep or severe infections by removing necrotic tissue and ensuring proper source control.[7]

For osteomyelitis, removing the infected bone is often a definitive treatment that greatly reduces the chances of recurrence and the need for amputation. Tailored antimicrobial therapy, informed by culture and sensitivity testing, is essential for improving treatment success and minimizing antibiotic resistance. Implementing preventive measures is vital for lowering the incidence and severity of diabetic foot infections (DFIs).[8] This involves patient education, encouraging routine foot checks, and facilitating prompt medical interventions. Recognizing high-risk individuals and launching focused strategies, like dedicated diabetic foot care clinics and structured treatment plans, can significantly reduce the occurrence of DFIs and related complications. Emerging research highlights the critical need to thoroughly examine the microbial profiles linked to DFIs and their patterns of antibiotic resistance. Numerous studies, including this systematic review, have explored the complex interplay between DFIs and antimicrobial resistance. This study aims to systematically review the evaluation and treatment strategies recommended in clinical practice guidelines for managing diabetic foot and related complications. This review consolidates data from relevant articles from PubMed and other reputable databases. Its goal is to provide an integrated overview of the microbial profiles in DFIs and emerging patterns in antibiotic resistance while also evaluating clinical practice guidelines addressing diabetic foot care and associated infections.

## 2. Materials and Methods

### *2.1. Search strategy*

The search and selection process was independently conducted by two blinded reviewers, with conflicts resolved by a third. Searches covered multiple databases, including PubMed, EMBASE, and Cochrane sources, for English-language studies published between 2017 and 2023. The search strategy was collaboratively developed using MeSH terms like "Diabetic Foot" and "Drug Resistance, Microbial." The query used was ("Diabetic Foot" [Mesh]) AND "Drug Resistance, Microbial" [Mesh]. The snowball method was also applied by reviewing reference lists of selected articles.

### *2.2. Data extraction*

The researchers collected and verified the relevant data, meticulously recording key details in a blank Microsoft Excel sheet. These details included the year of publication, authorship, geographic region, patient age range, total number of patients, predominant pathogens, resistance patterns of Gram-positive and Gram-negative bacteria, and the primary focus of each study. Data extraction from all eligible controlled studies was performed by one researcher and organized into an evidence table. This table summarized the population and study characteristics, intervention and control information, and the primary and secondary outcomes. A second researcher reviewed the extracted data to ensure accuracy and clarity. Lastly, the evidence tables were collaboratively reviewed and discussed by all authors.

### *2.3. Inclusion and exclusion criteria*

We included studies focusing on patients diagnosed with diabetic foot that addressed at least one predefined intervention and reported relevant outcomes. Excluded studies involved healthy individuals, those with non-diabetic conditions, or diabetic patients either without risk of foot ulcers or with active ulcers unless the latter reported on ulcer recurrence post-healing. Systematic reviews were excluded, but their references were checked to validate search results. Eligible studies addressed the prevention, assessment, diagnosis, and management of diabetic foot, compared clinical practice guidelines with strong internal validity, and evaluated the quality of evidence and strength of recommendations.

### *2.4. Quality assessment*

Two researchers, who were blinded to each other's assessments, evaluated the quality of the selected clinical practice guidelines (CPGs) using the Appraisal of Guidelines for Research and Evaluation (AGREE II) tool. This tool includes 23 items grouped into six domains, each assessing a specific aspect of guideline quality, as well as two global evaluation items to assess the overall guideline quality and recommendation status. Domain scores were calculated by summing the individual item scores and converting them into a percentage of the maximum possible score for that domain. The overall quality of the guidelines was rated on a scale from 1 (lowest) to 7 (highest), with guidelines scoring above 4 categorized as “quality CPGs.” Following the AGREE II evaluation, the final guidelines were chosen, and the results were synthesized. The quality of the studies included was assessed using the JBI Critical Appraisal Tool for Analytical Cross-Sectional Studies, with all 10 studies meeting the criteria of at least five “YES” responses, qualifying them for inclusion in the systematic review synthesis.

## 3. Discussion

After searching the databases, we identified 10 articles on diabetic foot infection and antibiotic resistance patterns in the systematic review conducted between 2017 and 2023. The reasons for excluding certain articles were as follows:

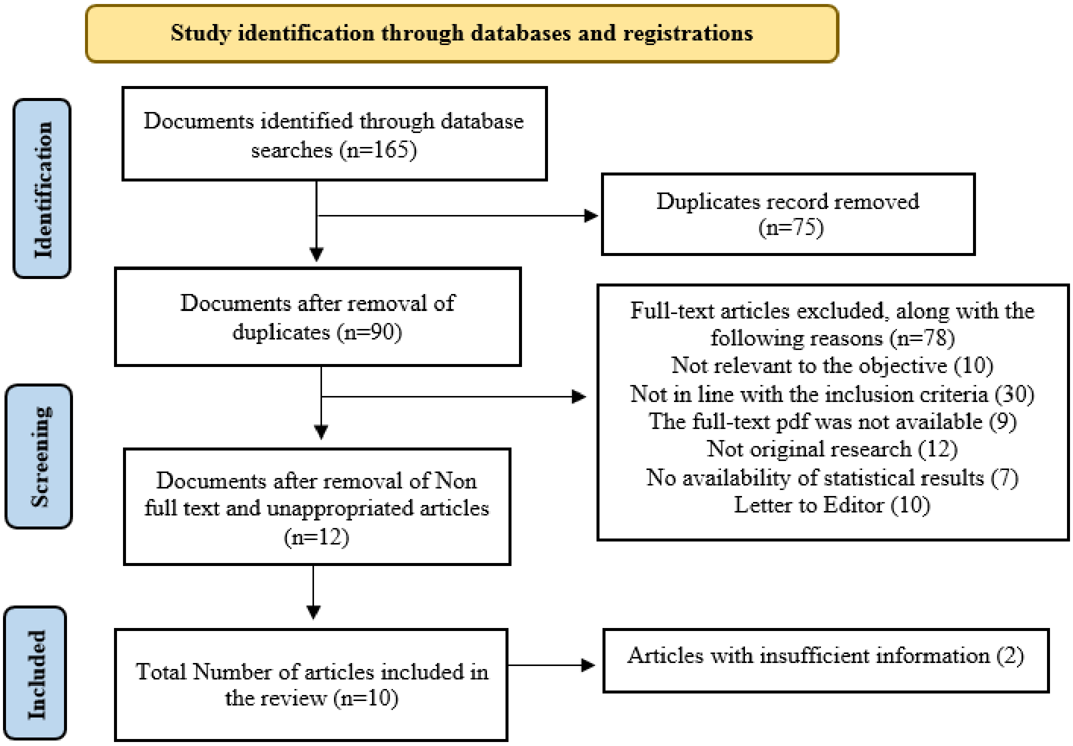


**Figure 1:** Flow chart

**Table 1:** Demographic distribution of patients by region, age range, and gender

| Study | Region | Age/Range | Gender | Total patients |
|---|---|---|---|---|
| Emaneini 2022[9] | The study was conducted in Iran | The mean age of the patients was 59.3 | 83 males and 32 females. | 115 patients were included in the study. |
| Jessica 2017[10] | The study was conducted in the Maule Region of Chile, specifically at the Regional Hospital of Talca. | The participants in the study were between 18 and 80 years of age, focusing on individuals with type 2 diabetes. | The control group consisted of 5 men and 3 women.<br>The Propolis group consisted of 16 men and 4 women. | A total of 31 patients were eligible for the study, with 20 in the propolis group and 11 in the control group. |
| Qingfeng 2022[11] | The study was conducted in China, specifically at the First Affiliated Hospital of Chongqing Medical University. | The mean age of the patients was 60.86 ± 11.08 years for type 2 diabetes patients, with 49 (50.0%) of these patients being over 60 years old. For the 3 patients with type 1 diabetes, the mean age was 42.67 ± 17.50 years | 67 men and 34 women. | 101 patients were included in the study. |
| Nese 2021[12] | The study was conducted across five centers in Turkey. | Mean age: 59.90 years<br>Age range: 30 to 90 years | 193 males, | 284 patients with diabetic foot infections (DFI). |
| Vickie 2012[13] | The study was conducted in the USA. | Mean Age for Group 1: 52.6 years (SD = 3.8)<br>Mean Age for Group 2: 64.8 years (SD = 8.7)<br>Mean Age for Group 3: 50.8 years (SD = 8.5) | NR | 12 patients with diabetic<br>foot ulcers(DFU) |
| Hikmat 2022[14] | The study focuses on Indonesia, specifically at Hasan Sadikin General Hospital in Bandung. | The study included patients with diabetes mellitus aged over 18 years. | Groups: Group A:<br>Gram (-):18 Females<br>Gram (+):3 Females<br>mixed gram (-) and gram (+):1 Female<br>Group B: Gram (-):16 Males Gram (+):5 Males<br>Mixed gram (-) and gram (+): 2 Males | The total number of patients in the study was 45 |
| Muhammad 2021[15] | The study was conducted in Mayo Hospital, Lahore, Pakistan | The mean age of the patients was 53.05 ± 10.70 years | 134 (66.7%) male | 201 patients |
| Igor 2021[16] | The study was conducted in Ukraine. | The average age of the patients was 56.8 ± 2.5 years. | NR | 210 patients with sepsis due to complicated diabetic foot syndrome. |
| Rajasekar 2019[17] | The study was conducted in India. | The mean age of the patients was 53.04 ± 12.12 years | Male patients were predominant (34, 68%)<br>Female patients (16, 32%). | The total number of patients in the study was 50. |
| Yu-Yao 2021[18] | The study was conducted at Chang Gung Memorial Hospital, located in Taiwan. | The average age of patients with limb preservation was 62.9 years (± 14.0).<br>The average age of patients with poor outcomes was 63.5 years (± 12.1) | Limb preserved<br>60.2% males<br>Poor outcome<br>65.0% males | The total number of patients analyzed in the study was 558 |

NR: Not reported

**Table 2:** Prevalence of pathogens in foot evaluations and screening outcomes

| Study | Most prevalent pathogens | Foot evaluation | Screening |
|---|---|---|---|
| Emaneini 2022[9] | *Staphylococcus spp., Escherichia coli, Klebsiella spp.* | Assessment of foot ulcers, infections, and overall foot health in diabetic patients, including examination for neuropathy and peripheral arterial disease. | Regular checks for foot complications in diabetic patients, focusing on identifying early signs of ulcers, infections, and other foot-related issues. |
| Jessica 2017[10] | The study provides a supplementary table for determining microorganisms in diabetic foot wounds, but specific and most prevalent pathogens are not listed. | A comprehensive assessment of the foot's condition, including inspection for ulcers, deformities, and signs of infection, and evaluation of blood flow and nerve function. | The process of identifying individuals at risk for foot complications, particularly in diabetic patients, through regular examinations and assessments. |
| Qingfeng 2022[11] | *Staphylococcus aureus* (most common)<br>*Enterococcus faecalis*<br>*Streptococcus agalactiae*<br>*Gram-negative bacteria such as Pseudomonas aeruginosa, Klebsiella pneumoniae,* and *Proteus mirabilis.* | The study involved a retrospective evaluation of patients diagnosed with diabetic foot ulcers and necrotizing fasciitis, following the diagnostic criteria set by the International Working Group on the Diabetic Foot (IWGDF). | NR |
| Nese 2021[12] | *Staphylococcus aureus and Escherichia coli*<br>Other notable pathogens included *Klebsiella* spp. and various Gram-negative and Gram-positive bacteria. | The study made a comprehensive foot evaluation, including assessing wound depth, infection presence, and underlying complications like neuropathy or vascular insufficiency. | Regular foot screening for diabetic patients to detect potential issues like infection, ulceration, or abnormalities early and manage them effectively. |
| Vickie 2012[13] | *Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, Streptococcus* species, and fungal pathogens like Candida can cause wound infections, leading to severe complications and affecting wound healing. | The study reported managing and treating diabetic sensorimotor polyneuropathy, emphasizing standardized clinical assessments, early detection of issues, and therapeutic footwear use to prevent complications. | Screening involves testing individuals for specific diseases or conditions to identify those at risk or needing further evaluation. |
| Hikmat 2022[14] | The pathogens identified included *Klebsiella pneumoniae, Acinetobacter baumannii, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, and Enterococcus faecalis* | Foot evaluation included assessing ulcer size, depth, presence of infection, and vascular status to determine appropriate treatment for diabetic foot infections | The study stressed regular foot screening is essential for the early detection of diabetic foot complications and for preventing severe outcomes |
| Muhammad 2021[15] | Bacterial Isolates: 389 total<br>- Gram-negative organisms: 238 (61.11%)<br>- Gram-positive organisms: 151 (38.89%)<br>- Common Pathogens: *Staphylococcus aureus, β-haemolytic streptococci*, and gram-negative bacteria. | Most Common Site of DFUs:<br>- Forefoot: 129 (64.2%)<br>- Hindfoot: 49 (24.4%)<br>- Midfoot: 23 (11.4%)<br>DFU Grades:<br>- Grade 3: 104 (51.7%)<br>- Grade 1: 62 (30.8%) | Deep-seated tissue samples from the ulcer bed were tested for culture and sensitivity. |
| Igor 2021[16] | *Staphylococcus aureus, Enterococcus faecalis, Pseudomonas aeruginosa, Staphylococcus epidermidis, Escherichia coli, Acinetobacter baumannii.* | Assessed infection severity and complications in patients with diabetic foot syndrome. | Involved in microbiological studies of blood and wound discharge to identify pathogens. |

| | | | |
|---|---|---|---|
| Rajasekar 2019[17] | The study identified pathogens, including *Staphylococcus aureus, Bacillus subtilis, Enterococcus faecalis*, and Gram-negative bacteria in diabetic foot infections. | Foot evaluation in diabetic patients assessed for ulcers, infections, neuropathy, and vascular issues to prevent complications and promote healing. | Regular assessments to identify diabetic foot complications early, preventing severe outcomes. |
| Yu-Yao 2021[18] | Common pathogens include *Streptococcus spp., Staphylococcus aureus, E. coli, Proteus spp., Pseudomonas spp., Peptostreptococcus spp., and Bacteroides spp.* | Assessing foot condition to identify complications and prevent further issues in diabetic patients | Regular checks for foot problems to ensure early detection and management of diabetic foot complications |

NR: Not reported

### *3.1. Screening and evaluation*

A comprehensive evaluation of diabetic foot health has emphasized the assessment of ulcers, infections, and complications such as neuropathy and vascular insufficiency. Several studies have highlighted the diagnostic criteria established by the International Working Group on the Diabetic Foot (IWGDF) for identifying and managing diabetic foot ulcers (DFUs). The research noted the prevalence of DFUs, with the forefoot being the most common site (64.2%) and Grade 3 ulcers (51.7%) representing the most severe cases. Other studies have focused on early detection, standardized assessments, and therapeutic interventions, emphasizing the critical role of evaluating infection severity and vascular health to promote healing and prevent complications. The importance of a multidisciplinary approach to managing DFUs was also stressed, involving podiatrists, wound care specialists, infectious disease experts, and vascular surgeons. Additionally, the significance of patient education on foot care and self-management strategies to prevent recurrent ulcers was underscored. Overall, the findings highlight the complex nature of DFUs and the necessity for comprehensive assessment and treatment strategies to improve outcomes and minimize the risk of amputation in diabetic patients.(**Table 2**)

### *3.2. Most prevalent pathogens*

The most common pathogens identified in diabetic foot infections (DFI) include *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella spp*., and both Gram-negative and Gram-positive bacteria. Research has confirmed that *Staphylococcus spp*., *E. coli*, and *Klebsiella spp*. are frequently implicated as causative organisms. Additionally, studies have reported the presence of *Staphylococcus aureus*, *Enterococcus faecalis*, and Streptococcus agalactiae, emphasizing the importance of proper wound care and targeted antibiotic therapy in managing these infections. Understanding the specific pathogens involved allows healthcare providers to tailor treatments to effectively target the bacteria causing the infection. Other research highlights *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and Proteus mirabilis as significant contributors, while *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and Candida fungi have also been identified as key pathogens. These findings underscore the diverse range of microorganisms that may contribute to diabetic foot infections, stressing the need for a targeted treatment approach. By identifying the bacteria or fungi responsible, healthcare providers can prescribe the most effective antibiotics or antifungal medications, leading to improved patient outcomes and reduced risk of complications. Gram-negative bacteria like *Acinetobacter baumannii* and Gram-positive bacteria such as *Enterococcus faecalis* and *Staphylococcus epidermidis* have been frequently observed. Additional studies have noted the presence of β-haemolytic streptococci, Bacillus subtilis, Proteus spp., and *Peptostreptococcus spp*., further highlighting the diversity of pathogens in DFIs. These findings emphasize the critical role of precise pathogen identification in optimizing treatment regimens for diabetic foot infections.

### *3.3. Pathogenesis and diagnosis*

The onset of diabetic foot infections (DFIs) is driven by several factors, primarily linked to diabetes-related complications like peripheral neuropathy, peripheral arterial disease, and impaired immune function. Peripheral neuropathy leads to a loss of sensation and motor control, raising the risk of undetected injuries and skin damage. Additionally, high blood glucose levels in diabetes promote bacterial growth and impair immune responses, creating favorable conditions for infections.[20] Collectively, these factors greatly increase the likelihood of diabetic foot infections (DFIs) in individuals with diabetes. Diagnosing DFIs involves a thorough clinical assessment, looking for symptoms such as redness, warmth, swelling, and discharge. Imaging tools, including X-rays and more advanced methods, are used to evaluate soft tissue damage and possible osteomyelitis. Laboratory tests, like elevated inflammatory markers (e.g., C-reactive protein and erythrocyte sedimentation rate), help confirm the presence of infection.[21] Molecular diagnostic techniques enable the identification of various bacteria, including those that are challenging to culture and anaerobic, assisting in the selection of targeted antimicrobial therapies. Advanced imaging methods, such as contrast-enhanced MRI and PET-CT scans, enhance the detection of soft tissue infections, osteomyelitis, and deep abscesses. These technologies allow clinicians to tailor treatment strategies according to the specific infection characteristics, resulting in more effective interventions and improved patient outcomes. The use of these advanced diagnostic tools enables healthcare providers to make earlier and more accurate diagnoses, leading to more precise and individualized treatments for complex diabetic foot infections (DFIs).

### *3.4. Risk factors for DFIs*

The increased likelihood of antibiotic resistance in diabetic foot infections (DFIs) is associated with factors like higher BMI, elevated HbA1c, higher fasting blood glucose, and the size and progression of the ulcer. These factors highlight the complex interaction between the host's characteristics and the microbes' resistance to antibiotics. Excess body weight promotes chronic inflammation and a weakened immune response, fostering conditions that support microbial growth and resistance. Additionally, the surplus adipose tissue in individuals with a high BMI can provide a favorable environment for pathogens, contributing to prolonged infections and decreased antibiotic efficacy.[23] High blood glucose levels encourage bacterial proliferation and biofilm development, which in turn contribute to increased resistance. The extent and persistence of the ulcer, as reflected by its size and progression, are often linked to the presence of various microbial communities, including antibiotic-resistant strains. Host-related factors, such as immune function, coexisting health conditions, and anatomical characteristics, also play a role in shaping the microbial makeup of polymicrobial infections and can impact the virulence of the involved microorganisms.[24] Recent research on diabetic foot infections (DFIs) has highlighted several risk factors, including previous hospitalizations, ulcer size, surgical interventions, and increased C-reactive protein levels. Hospital-acquired infections, often linked to poor hygiene and insufficient infection control measures, play a significant role in the issue. Notably, larger ulcers are considered a key prognostic indicator.[25] Common pathogens in severe infections include *Staphylococcus aureus*, Enterococcus, facultative gram-negative bacilli, and group B streptococci, with hospital ward conditions often exacerbating these infections.[26] Research indicates that, despite these challenges, treating diabetic foot infections (DFIs) does not contribute to an increase in antibiotic resistance, and recurrent infections do not necessarily lead to higher antimicrobial resistance in future episodes.

**Table 3:** Debridement and treatment strategies

| Study | Debridement | Dressings | Treatment strategies | Neuropathic pain |
|---|---|---|---|---|
| Emaneini 2022[9] | The study emphasizes the significance of debridement in managing diabetic foot infections, involving wound cleaning, tissue removal, microbiological analysis, and patient healing to enhance infection control. | Protective coverings are applied to wounds to maintain a moist environment, absorb exudate, and prevent infection, aiding in the healing process of diabetic foot ulcers. | Comprehensive approaches combining medication, lifestyle changes, and wound care to manage diabetic foot complications effectively enhanced patient treatment outcomes. | The study found that neuropathic pain is linked to diabetic foot ulcers, classified as Neuropathic (N) by the Meggitt-Wagner classification system. This classification helps understand foot ulcer causes and influences treatment strategies and patient outcomes. |
| Jessica 2017[10] | NR | Protective materials were applied to wounds to protect them, absorb exudate, and promote a moist healing environment. The choice of dressing varied based on the wound's characteristics. | The study compared propolis treatment for diabetic foot wounds to standard care, emphasizing the need for consistent pharmacological treatment and specialized care protocols. | A study by Jessica Zuñiga-Hernandez and colleagues found that propolis significantly reduced wound area in diabetic foot ulcers, highlighting the importance of addressing neuropathic pain and inflammation in wound management, |

| | | | | |
|---|---|---|---|---|
| | | | | especially in patients with type 1 or 2 diabetes. |
| Qingfeng 2022[11] | The study highlights that surgical intervention is crucial for treating necrotizing fasciitis, often involving debridement to remove necrotic tissue and control the infection. | NR | The study advocates for prompt, aggressive surgical treatment and appropriate antibiotic therapy for managing DNF, emphasizing the importance of understanding microbial distribution for effective treatment. | NR |
| Nese 2021[12] | Debridement is a crucial procedure in managing DFI, involving removing necrotic tissue and foreign material to promote healing and reduce infection risk. | NR | Diabetic foot infections require a multidisciplinary approach, including antibiotic therapy, regular foot evaluations, therapeutic footwear, wound care, and surgical interventions like debridement when necessary. | A study on 284 diabetic foot infections revealed rheopathic pain, osteomyelitis, and the need for broad-spectrum antibiotic regimens and de-escalation despite limitations like small sample size and smoking status exclusion. |
| Vickie 2012[13] | Regular de Abridgment and advanced treatment modalities like NCLF-US can significantly improve wound healing and reduce inflammation in diabetic foot ulcers, highlighting the importance of regular debridement in patient outcomes. | This study found that non-contact low-frequency ultrasound treatment reduced wound area by 86% over five weeks, potentially enhancing tissue regeneration by modulating inflammatory responses. | Treatment strategies implemented are planned approaches to manage diseases, incorporating medications, therapies, lifestyle changes, and patient education for optimal health outcomes. | NCLF-US can effectively treat diabetic foot ulcers by reducing pro-inflammatory cytokines, reducing wound area by 86%, and promoting healing. |
| Hikmat 2022[14] | This study suggests debridement is crucial for managing diabetic foot infections, which have a high prevalence of Gram-negative bacteria. | This study emphasizes the importance of proper wound care, including cleaning ulcers with sterile saline and using aseptic techniques. Advanced wound care products, such as hydrocolloids, alginates, and antimicrobial dressings, are typically used. | Effective treatment strategies for diabetic foot infections included timely antibiotic administration, wound care, and addressing underlying conditions. | NR |

| | | | | |
|---|---|---|---|---|
| Muhammad 2021[15] | The study emphasizes the significance of debridement in managing diabetic foot ulcers, which involves removing slough and necrotic tissue, washing thoroughly, and sending samples for culture and sensitivity testing. | Dressings protect wounds, absorb exudate, and promote healing. Hydrocolloid, foam, alginate, transparent film, and antimicrobial dressings were used. | Antimicrobial Susceptibility: Determined according to Clinical and Laboratory Standards Institute guidelines.<br><br>Empirical Treatment: Early identification of infections for timely initiation of treatment. | Neuropathy significantly affects 89.1% of diabetic foot ulcers, necessitating targeted treatment strategies to alleviate the underlying pain in affected individuals. |
| Igor 2021[16] | A study of 210 diabetic foot syndrome patients underwent surgical intervention to address purulent-necrotic lesions, aiming to improve outcomes and reduce mortality rates. | Protective coverings were applied to wounds to maintain moisture, prevent infection, and facilitate healing in diabetic foot injuries. | Comprehensive approaches combining medication, lifestyle changes, and wound care to manage diabetic foot complications. | The study revealed diabetic neuropathy, a common complication of diabetes, can cause neuropathic pain, exacerbated by foot lesions, affecting 86 patients with diabetic foot syndrome. |
| Rajasekar 2019[17] | This study reported multiantibiotic-resistant bacteria in wound swabs from 50 patients, emphasizing the need for new strategies to clean and disinfect ulcers. | Specialized coverings were used for wounds to promote healing and protect against infection in diabetic foot ulcers. | Comprehensive approaches included medication, wound care, and lifestyle modifications to manage diabetic foot complications effectively. | The study highlights chronic pain in diabetic foot ulcers due to neuropathy, high pressures, vascular insufficiency, and impaired neutrophil function, causing infection persistence and prolonged treatment. |
| Yu-Yao 2021[18] | The study emphasizes the significance of debridement in ulcer management, removing necrotic tissue for accurate diagnosis and treatment, and collecting bacterial and fungal cultures for broad-spectrum antibiotic therapy. | NR | Comprehensive approaches to managing diabetic foot infections included wound care, antibiotics, and surgical interventions. | NR |

NR: Not reported

**Table 4:** Use of antibiotics and adjuvant treatments

| Study | Most Effective Antibiotics Against Microbial Infection | Therapeutic Footwear | Antibiotherapy | Adjuvant Treatments |
|---|---|---|---|---|
| Emaneini 2022[9] | Imipenem, piperacillin-tazobactam, amikacin was used. | Specialized shoes designed to provide support, reduce pressure, and | The study highlighted the need for personalized antibiotic therapy for | Additional therapies, such as growth factors, are used alongside primary |

| | | | | |
|---|---|---|---|---|
| | | accommodate foot deformities, helping prevent ulcers and promote healing in diabetic patients were provided. | diabetic foot infections, emphasizing the ineffectiveness of standard treatments like clindamycin and ciprofloxacin due to high resistance rates. | treatments to enhance healing, reduce infection risk, and improve outcomes in diabetic foot care. |
| Jessica 2017[10] | NR | Specialized shoes designed to provide support, reduce pressure, and prevent foot injuries in individuals with diabetes or other foot conditions were provided | NR | Additional therapies, such as topical agents like propolis or other natural products, are used alongside primary treatments to enhance healing. |
| Qingfeng 2022[11] | Effective antibiotics include linezolid, vancomycin, tigecycline, and daptomycin for Gram-positive bacteria and various options for Gram-negative pathogens. | Therapeutic footwear is designed to provide support, reduce pressure, and prevent ulcers in patients with diabetes or foot deformities. | The study emphasizes the need for appropriate antibiotic therapy for diabetic foot infections involving necrotizing fasciitis, recommending levofloxacin, moxifloxacin, vancomycin, teicoplanin, tigecycline, linezolid, carbapenems, and amikacin for Gram-negative bacteria. | NR |
| Nese 2021[12] | The most common initial antimicrobial regimens include beta-lactam/beta-lactamase inhibitor combinations, fluoroquinolones, and daptomycin. Vancomycin was identified as an independent predictor of reinfection/death when treatment was inappropriate. | Therapeutic footwear is recommended for diabetic patients to offer adequate foot support and protection, thereby reducing the risk of ulcers and injuries. | The study found that beta-lactam/beta-lactamase inhibitor combinations are the most commonly used initial regimens for treating DFI based on clinical findings and local epidemiological data. | Adjuvant treatments for neuropathic pain include medications like gabapentin and duloxetine, which can alleviate pain and enhance patient comfort. |
| Vickie 2012[13] | Effective antibiotics include amoxicillin, ceftriaxone, azithromycin, ciprofloxacin, doxycycline, vancomycin, clindamycin, gentamicin, and linezolid for various infections. | Therapeutic footwear supports and protects feet, reducing pressure and preventing ulcers, especially for individuals with diabetes or foot deformities. | NR | The study found that non-contact low-frequency ultrasound (NCLF-US) effectively treated diabetic foot ulcers, reducing wound area and improving tissue regeneration. |
| Hikmat 2022[14] | Antibiotics effective against microbial infections included carbapenems, amikacin, tigecycline, vancomycin, | Therapeutic footwear was provided to support and protect feet, reducing the risk | The study highlights antibiotic therapy challenges due to local bacterial | Adjuvant treatments, such as analgesics and topical agents, were used to enhance |

| | | | | |
|---|---|---|---|---|
| | ampicillin-sulbactam, and cephalosporins. | of ulcers and injuries in people with diabetes. | susceptibility. Common antibiotics for Gram-negative bacteria are poor, while effective options include carbapenems, gentamicin, tigecycline, and vancomycin. The authors call for a re-evaluation of empirical antibiotic choices. | the effectiveness of primary therapies for diabetic foot infections. |
| Muhammad 2021[15] | Methicillin-resistant *Staphylococcus aureus*: Found in 62 (64.58%) isolates. | Therapeutic footwear provides support and protection for diabetic patients, featuring extra depth, cushioning, stability, and custom orthotics to prevent ulcers. | The study outlines antibiotic therapy guidelines for diabetic foot infections based on severity. Grade I infections require no antibiotics, while Grade II require narrow-spectrum oral antibiotics. Grade III infections require double intravenous therapy with cephalosporins and oral agents. | Adjuvant treatments enhanced healing through offloading, physical therapy, nutritional support, and advanced therapies like negative pressure wound therapy. |
| Igor 2021[16] | Daptomycin, linezolid, teicoplanin, vancomycin, tigecycline, aminoglycosides, fluoroquinolones, and macrolides. | Specialized shoes are designed to support, reduce pressure, accommodate foot deformities, and prevent injuries in individuals with diabetes or foot conditions. | Studying timely antibiotic therapy reduces mortality and complications, particularly for Gram-positive bacteria like *Staphylococcus aureus*, emphasizing the need for tailored approaches. | Additional therapies, such as physical therapy or medications, are used alongside primary treatments to enhance effectiveness. |
| Rajasekar 2019[17] | Antibiotics tested included amikacin, amoxicillin, cefotaxime, ciprofloxacin, gentamycin, penicillin, tetracycline, and vancomycin against microbial infections in DFUs. | Specialized shoes are designed to reduce pressure and support diabetic patients, preventing ulcers. | This study revealed that Gram-negative bacteria exhibit 100% resistance to amoxicillin and cotrimoxazole and varying resistance rates to erythromycin, penicillin, and vancomycin. | Additional therapies, such as physical therapy and alternative medicine, are used alongside primary treatments to enhance healing outcomes. |
| Yu-Yao 2021[18] | Broad-spectrum antibiotics included third-generation cephalosporins, extended-spectrum penicillins, fluoroquinolones, carbapenems, metronidazole, | Specialized shoes designed to provide support and prevent injuries in patients with diabetic foot issues | The study examined diabetic foot infections in patients and utilized broad-spectrum antibiotic therapy, including cephalosporins, | The study suggested adjuvant treatments for limb-threatening diabetic foot infections, including adjunct angiography, |

| | | | | |
|---|---|---|---|---|
| | and glycopeptides for MRSA treatment. | | penicillins, fluoroquinolones, and carbapenems, with additional MRSA coverage based on wound cultures. | wound cultures, and surgical interventions, to improve infection management and patient outcomes. |

**Table 5:** Challenges and recommendations in developing and adopting standard guidelines: limitations and strengths

| Study | Challenges in developing and adopting Standard Guidelines | Recommendations | Limitations and strengths |
|---|---|---|---|
| Emaneini 2022[9] | Creating and implementing effective clinical guidelines is difficult due to varying patient needs, resistance to change, and resource limitations in healthcare settings. | Implement tailored treatment plans, regular monitoring, and patient education to improve outcomes in diabetic foot care and management. | Study limitations include sample size; strengths include comprehensive data collection and insights into local bacterial resistance patterns. |
| Jessica 2017[10] | The study highlights the growing issue of chronic wounds in healthcare systems, highlighting the need for improved therapies and understanding of their molecular and cellular environment. | Recommendations included best practices, patient education, research directions, and new therapy implementation. | Limitations of the study include small sample size, short duration, potential biases, and external variables, while strengths include robust design, comprehensive data collection, well-defined population, and clinical practice impact. |
| Qingfeng 2022[11] | The study highlights the need for more research on the distribution and drug sensitivity of pathogenic bacteria in DNF patients, which hinders the creation of comprehensive treatment guidelines. | The study recommends using broad-spectrum antibiotics initially, considering the high risk of multi-drug resistant bacteria and the potential for amputation in DNF patients. | The study offers valuable insights into microbial distribution and drug sensitivity in DNF patients, potentially informing empirical treatment strategies due to its retrospective nature and single-center design. |
| Nese 2021[12] | Challenges in healthcare include local practice variability, resource disparities, ongoing provider education, and antibiotic resistance's rapid emergence, complicating standardized treatment protocols. | Regular foot health screening, early antibiotic therapy, multidisciplinary care, and patient education on foot care and glycemic control are recommended for managing diabetic foot infections. | The study has limitations like small sample size and potential biases, but its strengths include its multicenter design and comprehensive assessment of factors influencing diabetic foot infection outcomes. |
| Vickie 2012[13] | Challenges in developing and adopting guidelines include varying evidence quality, stakeholder consensus, resource limitations, and resistance to change among practitioners. | Treatment recommendations must be tailored to patient needs, regularly updated, and include multidisciplinary collaboration to enhance treatment effectiveness and adherence. | Strengths include robust methodology and clear outcomes; limitations involve small sample size, short duration, and potential biases in participant selection. |
| Hikmat 2022[14] | Challenges include varying bacterial patterns, resistance issues, and the need for localized guidelines tailored to specific populations. | Recommendations emphasized the importance of individualized treatment plans based on local microbiological data and patient-specific factors. | Limitations include potential antibiotic resistance and variability in patient responses, while strengths involve comprehensive management approaches and multidisciplinary care. |
| Muhammad 2021[15] | The geographic diversity of organisms and evolving local antibiotic resistance patterns emphasize the clinical | Emphasized for timely treatment to prevent amputations. | The study's single-center design limits generalizability but offers a comprehensive analysis of |

| | | | |
|---|---|---|---|
| | significance of regional data for effective treatment. | | microbial patterns and antibiotic sensitivity in many patients. |
| Igor 2021[16] | Barriers include variability in patient populations, resistance patterns, and resource limitations affecting implementation. | Evidence-based suggestions for managing diabetic foot conditions, emphasizing prevention, early intervention, and multidisciplinary care. | Limitations include study variability; strengths involved comprehensive data supporting effective management practices for diabetic foot care. |
| Rajasekar 2019[17] | Variability in patient populations, resistance patterns, and resource availability complicate standardization of care protocols. | Implementing evidence-based practices, regular screenings and patient education is recommended to improve outcomes in diabetic foot care. | Limitations included variability in studies; strengths involve comprehensive data supporting effective interventions for diabetic foot management. |
| Yu-Yao 2021[18] | Difficulties in creating and implementing effective protocols for diabetic foot care due to variability in patient needs | Evidence-based suggestions for managing diabetic foot infections to improve patient outcomes and reduce complications | Strengths included focus on gram-negative bacteria and funding; limitations are small sample size, lack of longitudinal data, and identification constraints. |

*3.5. Treatment strategies*

The reviewed studies highlight various treatment strategies for managing diabetic foot complications and infections. Comprehensive approaches that integrate medication, lifestyle changes, and wound care were emphasized. The importance of timely surgical intervention and understanding microbial distribution was also stressed. Multidisciplinary methods incorporating antibiotics, therapeutic footwear, and wound care were recommended. The effectiveness of propolis alongside standard care was noted, and planned, patient-centered strategies combining education and therapy were identified as essential for improving outcomes. To continue, innovative techniques such as the use of bioengineered skin substitutes and advanced dressings were shown to promote wound healing effectively. The role of negative pressure wound therapy in managing complex cases was highlighted, as was the potential of growth factors and stem cell therapies in enhancing tissue regeneration. Telemedicine and digital tools for monitoring diabetic foot ulcers were also identified as promising approaches to ensure consistent patient follow-up and early detection of complications. Additionally, the integration of psychosocial support into treatment plans was emphasized to address the mental health challenges often associated with chronic diabetic foot conditions.(**Table 3**)

*3.6. Most effective antibiotics against microbial infection*

Studies on effective antibiotics for microbial infections have highlighted various options based on the pathogen and clinical context. For Gram-positive bacteria, linezolid, vancomycin, tigecycline, and daptomycin are frequently recognized as effective. Broad-spectrum treatments often involve carbapenems, cephalosporins, fluoroquinolones, and beta-lactam/beta-lactamase inhibitor combinations. Specific regimens, such as amikacin, imipenem, and piperacillin-tazobactam, have demonstrated efficacy in multiple cases. Additionally, newer antibiotics like teicoplanin and aminoglycosides have shown potential against resistant strains. Effective treatments for Methicillin-resistant *Staphylococcus aureus* (MRSA) often include glycopeptides and carbapenems. However, the rise of multidrug-resistant pathogens underscores the importance of antibiotic stewardship and thorough susceptibility testing. Notably, inappropriate use of vancomycin has been associated with higher risks of reinfection and mortality, highlighting the need for targeted therapies and meticulous clinical monitoring to achieve optimal patient outcomes.(**Table 4**)

## 4. Challenges in Developing and Adopting Guidelines

Developing and implementing standardized guidelines for diabetic foot infections (DFIs) presents numerous challenges, as highlighted by various studies. These challenges include significant variation in the clinical presentation and severity of DFIs, the absence of universally accepted diagnostic criteria, and difficulties in distinguishing infections from other common diabetic foot complications. The diverse nature of the diabetic population and the presence of multiple comorbidities further complicate the establishment of standardized protocols. Despite these obstacles, ongoing efforts focus on improving the management of DFIs through collaborative research and evidence-based strategies. Resistance to change, limited resources, and variability in patient needs have been identified as significant barriers. Additionally, there is a need for greater understanding of the chronic wound environment and more research on the distribution of pathogenic bacteria and drug sensitivity. Addressing these barriers is crucial for advancing treatment methods and enhancing outcomes for patients with DFIs. Overcoming resistance to change, securing adequate resources, and improving knowledge of chronic wound dynamics can help healthcare providers develop more effective treatment strategies, ultimately improving care quality. Local practice variability, antibiotic resistance, and region-specific guidelines also pose challenges. Geographic diversity and resistance patterns must be considered in clinical practices to ensure effective management. Patient population variability further impacts the development of protocols, emphasizing the necessity of tailored approaches for successful implementation. These insights underscore the importance of addressing regional differences in practice, resistance trends, and patient demographics. Collaboration among researchers, clinicians, and policymakers is essential for creating comprehensive guidelines that address the complexities of managing DFIs across diverse regions and populations.(**Table 5**)

## 5. Recommendations

Studies have provided evidence-based recommendations for managing diabetic foot infections (DFIs), emphasizing prevention, early intervention, and multidisciplinary care. Researchers highlight the importance of tailored treatment plans, regular updates to guidelines, and patient education to address the complexities of chronic wound environments. A comprehensive approach to managing DFIs is widely regarded as essential for preserving limb function and quality of life in diabetic patients. By staying informed on the latest findings and guidelines, healthcare providers can deliver effective, individualized care. Experts advocate for timely intervention with broad-spectrum antibiotics to reduce the risks of multi-drug resistance and amputations. Individualized treatments based on local microbiological data and resistance patterns are also recommended. Regular screenings and collaboration among healthcare professionals from various disciplines are emphasized to address the challenges of managing DFIs effectively. Preventive measures and early management strategies are considered critical for improving patient outcomes. By implementing evidence-based practices, healthcare providers can significantly enhance the quality of care for DFIs, reduce complications, and alleviate the burden on healthcare systems by preventing costly outcomes such as amputations.[27] This collaborative and informed approach underscores the importance of ongoing education and teamwork in improving the management of diabetic foot infections.

## 6. Conclusion

Diabetic foot infections (DFIs) are complex clinical conditions requiring a multifaceted diagnosis, management, and prevention approach. Predominantly isolated Gram-positive microbes in DFIs include *Staphylococcus aureus*, *Enterococcus faecalis*, *Streptococcus pyogenes*, *Streptococcus agalactiae*, and *Staphylococcus epidermidis*. At the same time, Gram-negative species often involve *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Pseudomonas aeruginosa*. Risk factors contributing to antimicrobial resistance in DFIs include elevated BMI, HbA1c levels, blood glucose, ulcer characteristics, neuropathy, and vascular disease. A multidisciplinary team (MDT) approach is critical in DFI prevention and management, particularly involving podiatrists. Future research should prioritize understanding antibiotic resistance mechanisms, developing new agents, and advancing stewardship programs alongside collaborations and clinical trials to address management limitations. Key recommendations include judicious antibiotic use, enhanced surveillance, and promoting interventions like debridement (highly evidence-backed and strongly recommended), regular foot evaluations, and therapeutic footwear (moderately supported and fairly recommended) to optimize outcomes despite variations in clinical guidelines.

## 7. Source of Funding

None.

## 8. Conflict of Interest

Conflict of interest declared none.

## References

1. Duff M, Demidova O, Blackburn S, Shubrook J. Cutaneous manifestations of diabetes mellitus. *Clin Diabetes*. 2015;33(1):40–8. doi: 10.2337/diaclin.33.1.40.
2. Schmidt BM, Holmes CM. Updates on diabetic foot and Charcot osteopathic arthropathy. *Curr Diab Rep*. 2018;18(10):74. doi: 10.1007/s11892-018-1047-8.
3. Costa RH, Cardoso NA, Procópio RJ, Navarro TP, Dardik A, de Loiola Cisneros L. Diabetic foot ulcer carries high amputation and mortality rates, particularly in the presence of advanced age, peripheral artery disease and anemia. *Diabetes Metab Syndr*. 2017;11(Suppl 2):S583–7. doi: 10.1016/j.dsx.2017.04.008.
4. Shettigar K, Murali TS. Virulence factors and clonal diversity of Staphylococcus aureus in colonization and wound infection with emphasis on diabetic foot infection. *Eur J Clin Microbiol Infect Dis*. 2020;39(12):2235–46.
5. Mandell JC, Khurana B, Smith JT, Czuczman GJ, Ghazikhanian V, Smith SE. Osteomyelitis of the lower extremity: pathophysiology, imaging, and classification, with an emphasis on diabetic foot infection. *Emerg Radiol*. 2018;25(2):175–88. doi: 10.1007/s10140-017-1564-9.
6. Komarraju A, Chhabra A. Advanced cross-sectional radiology-ultrasound, computed tomography and magnetic resonance imaging of the diabetic foot. The Foot in Diabetes. John Wiley & Sons Ltd. 2020 Apr 24:169–85. 10.1002/9781119445821.ch10
7. Tom LK, Wright TJ, Horn DL, Bulger EM, Pham TN, Keys KA. A skin-sparing approach to the treatment of necrotizing soft-tissue infections: thinking reconstruction at initial debridement. *J Am Coll Surg*. 2016;222(5):e47–60. doi: 10.1016/j.jamcollsurg.2016.01.008.
8. Hatipoglu M, Mutluoglu M, Turhan V, Uzun G, Lipsky BA, Sevim E et al. Causative pathogens and antibiotic resistance in diabetic foot infections: a prospective multi-center study. *J Diabetes Complications*. 2016;30(5):910–6.
9. Taki E, Jabalameli F, MR MT, Feizabadi MM, Beigverdi R, Emaneini M. Microbial profile and antibiotic susceptibility pattern in diabetic patients with mild, moderate, and severe foot infections in Tehran. *Arch Razi Inst*. 2022;77(5):1925–33. doi: 10.22092/ARI.2022.359759.2476.
10. Mujica V, Orrego R, Fuentealba R, Leiva E, Zúñiga-Hernández J. Propolis as an adjuvant in the healing of human diabetic foot

wounds receiving care in the diagnostic and treatment centre from the regional hospital of Talca. *J Diabetes Res*. 2019:2019:2507578.
11. Li X, Du Z, Tang Z, Wen Q, Cheng Q, Cui Y. Distribution and drug sensitivity of pathogenic bacteria in diabetic foot ulcer patients with necrotizing fasciitis at a diabetic foot center in China. *BMC Infect Dis*. 2022;22(1):396. doi: 10.1186/s12879-022-07382-7.
12. Saltoglu N, Surme S, Ezirmik E, Kadanali A, Kurt AF, Sahin Ozdemir M et al. The effects of antimicrobial resistance and the compatibility of initial antibiotic treatment on clinical outcomes in patients with diabetic foot infection. *Int J Low Extrem Wounds*. 2023;22(2):283–90.
13. Yao M, Hasturk H, Kantarci A, Gu G, Garcia-Lavin S, Fabbi M et al. A pilot study evaluating non-contact low-frequency ultrasound and underlying molecular mechanism on diabetic foot ulcers. *Int Wound J*. 2014;11(6):586–93. doi: 10.1111/iwj.12005.
14. Permana H, Saboe A, Soetedjo NN, Kartika D, Alisjahbana B. Empirical antibiotic for diabetic foot infection in Indonesian tertiary hospital, is it time to rethink the options?. *Acta Medica Indonesiana*. 2022;54(2):247–54.
15. Siddiqui MA, Naeem H, Ali MM, Randhawa FA, Nazir S, Farooqui F. Microbiological and antimicrobial pattern of diabetic foot ulcers (DFUs) at a tertiary care center in North East, Punjab. *J Pak Med Assoc*. 2021;71(6):1566–9. doi: 10.47391/JPMA.1180.
16. Savon IL, Shapoval SD, Maksymova OO, Sofilkanych MM, Sheremet MI, Shidlovskyi OV et al. Alternative antibacterial therapy of methicillin-resistant Staphylococcus aureus in patients with diabetic foot and sepsis. *Rom J Diabetes Nutr Metab Dis*. 2021;28(1):11–7.
17. Thanganadar Appapalam S, Muniyan A, Vasanthi Mohan K, Panchamoorthy R. A study on isolation, characterization, and exploration of multiantibiotic-resistant bacteria in the wound site of diabetic foot ulcer patients. *Int J Low Extrem Wounds*. 2021;20(1):6–14. doi: 10.1177/1534734619884430.
18. Hung SY, Chiu CH, Huang CH, Lin CW, Yeh JT, Yang HM et al. Impact of wound microbiology on limb preservation in patients with diabetic foot infection. *J Diabetes Investig*. 2022;13(2):336–43. doi: 10.1111/jdi.13649.
19. Xin H, Fu Y, Feng M, Wang S, Sui C, Gao Y et al. Altered intrinsic brain activity related to neurologic and motor dysfunction in diabetic peripheral neuropathy patients. *J Clin Endocrinol Metab*. 2023;108(4):802–11. doi: 10.1210/clinem/dgac651.
20. Ohara-Nemoto Y, Nakasato M, Shimoyama Y, Baba TT, Kobayakawa T, Ono T et al. Degradation of incretins and modulation of blood glucose levels by periodontopathic bacterial dipeptidyl peptidase 4. *Infect Immun*. 2017;85(9):e00277–17. doi: 10.1128/IAI.00277-17.
21. Sproston NR, Ashworth JJ. Role of C-reactive protein at sites of inflammation and infection. *Front Immunol*. 2018;9:754. 10.3389/fimmu.2018.00754
22. Tuttolomondo A, Maida C, Pinto A. Diabetic foot syndrome: Immune-inflammatory features as possible cardiovascular markers in diabetes. *World J Orthop*. 2015;6(1):62–76. doi: 10.5312/wjo.v6.i1.62.
23. Chiricozzi A, Raimondo A, Lembo S, Fausti F, Dini V, Costanzo A et al. Crosstalk between skin inflammation and adipose tissue-derived products: pathogenic evidence linking psoriasis to increased adiposity. *Expert Rev Clin Immunol*. 2016;12(12):1299–308.
24. Laudisio A, Marinosci F, Fontana D, Gemma A, Zizzo A, Coppola A et al. The burden of comorbidity is associated with symptomatic polymicrobial urinary tract infection among institutionalized elderly. *Aging Clin Exp Res*. 2015;27(6):805–12. doi: 10.1007/s40520-015-0364-x.
25. Khan HA, Baig FK, Mehboob R. Nosocomial infections: Epidemiology, prevention, control and surveillance. *Asian Pacific J Trop Biomed*. 2017;7(5):478–82. 10.1016/j.apjtb.2017.01.019
26. Huang L, Zhang R, Hu Y, Zhou H, Cao J, Lv H et al. Epidemiology and risk factors of methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococci infections in Zhejiang China from 2015 to 2017. *Antimicrob Resist Infect Control*. 2019:8:90. doi: 10.1186/s13756-019-0539-x.
27. Nikoloudi M, Eleftheriadou I, Tentolouris A, Kosta OA, Tentolouris N. Diabetic foot infections: update on management. *Curr Infect Dis Rep*. 2018;20(10):40. doi: 10.1007/s11908-018-0645-6.

**Cite this article:** Bindhu J, Umashankar R, Vasudevan R, Mahalakshmi B, Bagchi S, Kapfo W et al. Evaluating diagnostic approaches for diabetic foot infections: A systematic review. *IP Int J Med Microbiol Trop Dis.* 2025;11(1):9-23.