



## MICROBIOLOGICAL CHARACTERISTICS AND ANTIMICROBIAL RESISTANCE IN DIABETIC FOOT ULCERS

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### ABSTRACT

Diabetic foot ulcers (DFUs) are among the most severe complications of diabetes mellitus, contributing significantly to morbidity, prolonged hospitalization, and lower-extremity amputations. Infection plays a critical role in the progression of DFUs, with diverse bacterial involvement and increasing antimicrobial resistance posing major challenges to effective treatment. This study aimed to synthesize current evidence on bacterial identification and antimicrobial resistance patterns in diabetic foot ulcers. A semi-systematic literature review was conducted using PubMed, Scopus, ScienceDirect, and Google Scholar, following PRISMA guidelines. A total of 130 articles were identified, and 20 studies met the inclusion criteria after screening. The findings revealed that diabetic foot infections are predominantly polymicrobial, with Gram-negative bacteria being more prevalent than Gram-positive organisms. Common pathogens include *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*. High resistance was observed against commonly used antibiotics, while multidrug-resistant organisms were increasingly reported. These findings highlight the importance of accurate bacterial identification and antimicrobial susceptibility testing to guide appropriate therapy and improve clinical outcomes.

### ABSTRAK

Ulkus kaki diabetik merupakan salah satu komplikasi serius dari diabetes melitus yang berkontribusi terhadap peningkatan morbiditas, lama rawat inap, serta risiko amputasi. Infeksi memegang peranan penting dalam memperburuk kondisi ulkus, dengan keterlibatan berbagai jenis bakteri serta meningkatnya resistensi antimikroba yang menjadi tantangan dalam terapi. Penelitian ini bertujuan untuk mensintesis bukti ilmiah terkait identifikasi bakteri dan pola resistensi antimikroba pada ulkus kaki diabetik. Metode yang digunakan adalah literature review semi-sistematis dengan mengikuti pedoman PRISMA melalui database PubMed, Scopus, ScienceDirect, dan Google Scholar. Sebanyak 130 artikel teridentifikasi, dan 20 artikel memenuhi kriteria inklusi untuk dianalisis. Hasil menunjukkan bahwa infeksi ulkus diabetikum umumnya bersifat polimikrobial dengan dominasi bakteri Gram-negatif dibandingkan Gram-positif. Bakteri yang sering ditemukan meliputi *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, dan *Pseudomonas aeruginosa*. Tingkat resistensi yang tinggi ditemukan terhadap antibiotik lini pertama, serta meningkatnya kejadian bakteri multidrug-resistant. Temuan ini menegaskan pentingnya identifikasi bakteri dan uji sensitivitas antibiotik untuk menentukan terapi yang tepat dan meningkatkan luaran klinis pasien.

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## INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from impaired insulin secretion, insulin action, or both. The global burden of diabetes continues to increase significantly, with recent estimates indicating that hundreds of millions of individuals are affected worldwide, and projections suggest a substantial rise in prevalence over the coming decades (Zambelli et al. 2025) (Manihuruk and Gultom 2024). This condition is associated with a wide range of complications, among which diabetic foot ulcers (DFUs) represent one of the most severe and clinically challenging outcomes.

Diabetic foot ulcers are a major cause of morbidity, hospitalization, and lower-extremity amputation. It has been reported that approximately 19% to 34% of individuals with diabetes will develop a foot ulcer during their lifetime, with high recurrence rates and significant mortality associated with these conditions (Mcdermott et al. 2023). The development of DFUs is multifactorial, involving peripheral neuropathy, peripheral arterial disease, and impaired wound healing, all of which contribute to tissue breakdown and increased susceptibility to infection (Ramirez-acuña et al. 2019).

Infection is a critical factor that complicates the clinical course of diabetic foot ulcers. The immunocompromised state associated with diabetes, including impaired neutrophil function, reduced cytokine response, and altered cellular immunity, significantly increases the risk of bacterial colonization and infection (Darwitz, Genito, and Thurlow 2024). Additionally, hyperglycemia creates a favorable environment for bacterial growth by providing an abundant nutrient source, thereby enhancing microbial proliferation and virulence (Ramirez-acuña et al. 2019).

Microbiologically, diabetic foot infections are often polymicrobial and involve a wide range of bacterial species. Earlier studies suggested that Gram-positive organisms, particularly *Staphylococcus aureus*, were the predominant pathogens in these infections. However, more recent evidence indicates a shift toward the predominance of Gram-negative bacteria, especially in chronic or severe infections (Soldevila-boixader et al. 2025). Commonly isolated Gram-negative pathogens include *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, which are frequently associated with hospital-acquired infections and chronic wound environments (Puca et al. 2021) (Spagnolo, Sartini, and Cristina 2021).

The presence of polymicrobial communities in diabetic wounds further complicates the infection process. These microorganisms can interact synergistically, forming structured biofilms that enhance bacterial survival and resistance to antimicrobial agents. Biofilm formation has been identified as a key factor in the persistence of infection and delayed wound healing, as it limits antibiotic penetration and protects bacteria from host immune responses (Rajab and Hegazy 2023).

One of the most concerning aspects of diabetic foot infections is the increasing prevalence of antimicrobial resistance. Numerous studies have reported high levels of resistance to commonly used antibiotics, including penicillin, amoxicillin, and trimethoprim-sulfamethoxazole. In particular, Gram-negative bacteria have demonstrated extensive resistance mechanisms, such as the production of extended-spectrum beta-lactamases (ESBLs) and carbapenemases, which significantly reduce treatment options (Saleem et al. 2025). The emergence of multidrug-resistant (MDR) organisms further complicates clinical management and is associated with poorer outcomes, including prolonged hospitalization and higher amputation rates (Liu et al. 2024).

In addition, variations in bacterial profiles and resistance patterns have been observed across different geographical regions and healthcare settings. These variations highlight the importance of local epidemiological data in guiding empirical antibiotic therapy. Without

accurate knowledge of the prevailing microbial patterns, inappropriate antibiotic use may occur, contributing to the acceleration of antimicrobial resistance (Wang et al. 2024).

The urgency of this study is further emphasized by the rapid increase in antimicrobial resistance observed in diabetic wound infections worldwide. Inappropriate and empirical use of antibiotics without microbiological confirmation has contributed significantly to the emergence of resistant strains, particularly in low- and middle-income countries where access to diagnostic facilities may be limited. Moreover, variations in bacterial profiles and resistance patterns across different regions highlight the need for updated and comprehensive evidence to support clinical decision-making. Without a clear understanding of current microbial trends, treatment strategies may become ineffective, leading to prolonged infection, increased healthcare burden, and higher risk of complications such as amputation.

Despite the growing body of research on diabetic foot infections, there remains a need for a comprehensive synthesis of current evidence focusing on both bacterial identification and antimicrobial resistance patterns. Understanding these aspects is essential for improving clinical decision-making, optimizing antibiotic therapy, and reducing the burden of complications associated with diabetic wounds. Therefore, this study aims to systematically review the existing literature on bacterial identification and antimicrobial resistance in diabetic foot ulcers, with the goal of identifying dominant pathogens, resistance trends, and their clinical implications.

## **METHODS**

This study employed a semi-systematic literature review approach to synthesize existing evidence on bacterial identification and antimicrobial resistance in diabetic foot ulcers. The review aimed to provide a comprehensive understanding of the microbiological profile and resistance patterns associated with diabetic wound infections.

A systematic search of the literature was conducted across several electronic databases, including PubMed, Scopus, ScienceDirect, and Google Scholar. The search strategy combined relevant keywords using Boolean operators, such as “diabetic foot ulcer,” “bacterial identification,” “antimicrobial resistance,” and “diabetic wound infection.” These terms were adapted according to each database to ensure a broad yet focused retrieval of relevant studies.

The selection of studies followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Initially, a total of 130 records were identified, consisting of 120 articles retrieved from database searches and an additional 10 articles identified through other sources. After removing duplicates, 110 unique articles remained for further screening.

The screening process was conducted by reviewing titles and abstracts, resulting in the exclusion of 70 articles that were not relevant to the research topic. The remaining 40 full-text articles were then assessed for eligibility. Of these, 20 articles were excluded due to reasons such as lack of antimicrobial resistance data, limited relevance to diabetic foot ulcer infections, or unavailability of full-text access.

Ultimately, 20 studies met all inclusion criteria and were included in the final analysis.

Data extraction was performed systematically from each selected study, including information on authorship, publication year, study design, geographical setting, bacterial isolates, Gram classification, and antimicrobial resistance patterns. The collected data were then analyzed using a qualitative descriptive approach with narrative synthesis, allowing the identification of common trends, dominant pathogens, and resistance profiles across different studies.

To ensure the reliability of the findings, only peer-reviewed articles from reputable scientific journals were included. Cross-comparison between studies was also performed to identify consistent patterns and minimize potential bias in interpretation.

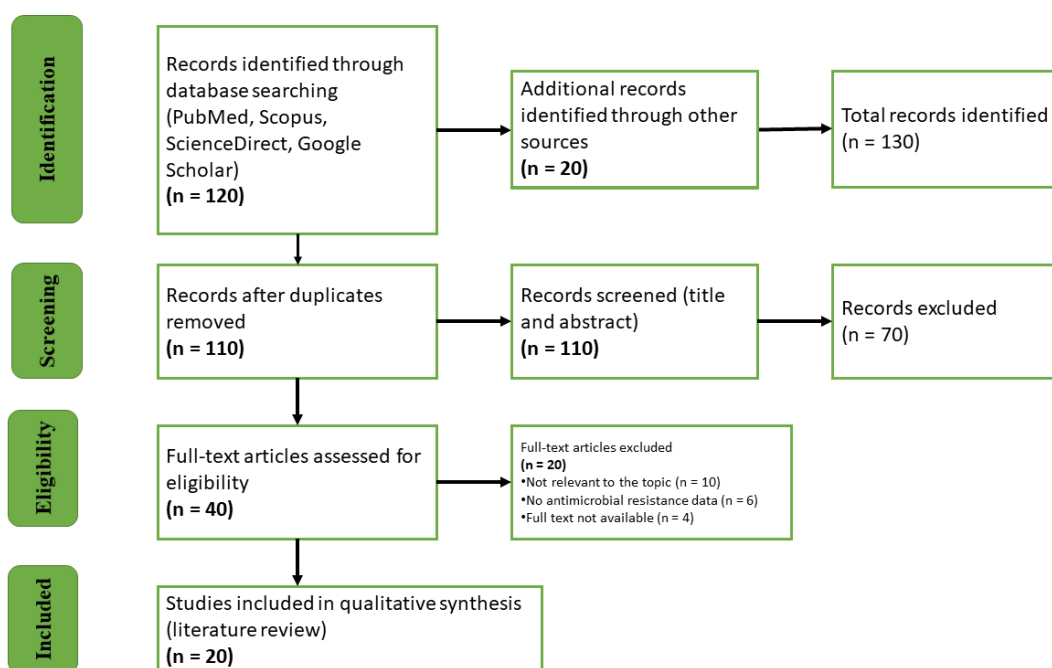
**Inclusion and Exclusion Criteria**

Inclusion criteria were as follows:

1. Original research articles and review papers
2. Studies focusing on bacterial identification in diabetic foot ulcers
3. Studies reporting antimicrobial resistance patterns
4. Articles published in English or Indonesian
5. Publications between 2019 and 2025
6. Articles with accessible full text

Exclusion criteria included:

1. Irrelevant studies not related to the research topic
2. Duplicate publications
3. Articles lacking microbiological or antibiotic resistance data
4. Abstract-only publications without full-text access



**Figure 1.** Prisma Flow

The study selection process was conducted in accordance with the **PRISMA guidelines**. A total of **130 records** were initially identified through database searching and additional sources. After duplicate removal, **110 articles** were screened based on titles and abstracts, of which **70 were excluded** due to irrelevance. Subsequently, **40 full-text articles** were assessed for eligibility. Among these, **20 articles were excluded** for not meeting the inclusion criteria, primarily due to insufficient data on antimicrobial resistance, lack of specific focus on diabetic foot ulcer infections, or limited access to full-text content. Finally, **20 studies** were included in the qualitative synthesis and formed the basis of this review.

## RESULTS AND DISCUSSION

The characteristics of the included studies are summarized in Table 1. A total of 20 studies were analyzed, showing that diabetic foot infections are predominantly polymicrobial, with more than one microorganism identified within a single lesion. Gram-negative bacteria were found to be more prevalent than Gram-positive organisms, accounting for approximately 60%–80% of total isolates across several studies.

**Table 1.** Summary of Bacterial Identification and Antimicrobial Resistance in Diabetic Foot Ulcers

No	Author (Year)	Study Design	Dominant Bacteria	Gram Type	Antimicrobial Resistance
1	Patricia et al. (2023)	Descriptive	<i>S. aureus</i> , <i>E. coli</i>	GP & GN	Resistance to penicillin
2	Hitam et al. (2019)	Cross-sectional	Polymicrobial	GP & GN	Increased resistance patterns
3	Alhumaid et al. (2021)	Retrospective	<i>E. coli</i> , <i>Klebsiella</i>	GN	High resistance to beta-lactams
4	Soldevila-Boixader et al. (2025)	Review	<i>P. aeruginosa</i>	GN	MDR reported
5	Qona'ah et al. (2024)	Observational	<i>S. aureus</i>	GP	Moderate resistance
6	Khan et al. (2023)	Molecular	<i>E. coli</i>	GN	Resistant to common antibiotics
7	Munyemana et al. (2022)	Cross-sectional	Gram-negative dominant	GN	High resistance rate
8	Santos et al. (2024)	Observational	Mixed bacteria	GP & GN	Sensitive to meropenem
9	Zambelli et al. (2025)	Cohort	MDR bacteria	GN	MDR prevalence high
10	Saleem et al. (2025)	Molecular	<i>Klebsiella</i> , <i>Acinetobacter</i>	GN	ESBL & carbapenemase
11	Husna et al. (2023)	Review	ESBL-producing bacteria	GN	Beta-lactam resistance
12	Darwitz et al. (2024)	Review	<i>S. aureus</i>	GP	Biofilm-related resistance
13	Touaitia et al. (2025)	Review	<i>S. aureus</i>	GP	Virulence & resistance
14	Maity et al. (2024)	Review	Mixed bacteria	GP & GN	Complex resistance
15	Salam et al. (2023)	Review	Global AMR	-	Increasing resistance
16	Li et al. (2025)	Review	MDR bacteria	GN	Multidrug resistance
17	Afonso et al. (2021)	Review	Biofilm bacteria	-	Resistance via biofilm
18	Spagnolo et al. (2021)	Review	<i>P. aeruginosa</i>	GN	High resistance
19	Puca et al. (2021)	Observational	Mixed bacteria	GP & GN	Variable resistance
20	Wang et al. (2024)	Observational	Mixed pathogens	GP & GN	Resistance variation

The most frequently identified pathogens included *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*. High resistance rates were observed against commonly used antibiotics such as penicillin and amoxicillin. In contrast, antibiotics such as meropenem and amikacin showed relatively higher sensitivity rates. Multidrug-resistant (MDR) organisms were also commonly reported, along with the presence of extended-spectrum beta-lactamase (ESBL)-producing and carbapenemase-producing bacteria.

These findings indicate that diabetic foot infections are microbiologically complex and influenced by multiple factors. The polymicrobial nature of these infections reflects the chronic condition of diabetic wounds, which provides a favorable environment for the colonization and

growth of diverse microorganisms (PATRICIA et al. 2023) (Hitam et al. 2019). This condition may contribute to increased infection severity and complicate treatment outcomes.

The predominance of Gram-negative bacteria observed in this study suggests a shift from the classical pattern of skin infections, which are typically dominated by Gram-positive organisms. This shift may be associated with chronic wound conditions, repeated exposure to hospital environments, and inappropriate antibiotic use. Gram-negative bacteria possess more complex resistance mechanisms, including beta-lactamase production and efflux systems, which contribute to their persistence and reduced susceptibility to antibiotics (Maity et al. 2024).

Despite the dominance of Gram-negative organisms, *Staphylococcus aureus* remains a key pathogen due to its virulence factors, including its ability to form biofilms and evade host immune responses (Darwitz et al. 2024)(Touaitia et al. 2025). Biofilm formation plays a crucial role in chronic infections by protecting bacteria from antibiotics and host immune defenses, resulting in persistent infection and delayed wound healing (Liu et al. 2024).

On the other hand, Gram-negative bacteria such as *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* were consistently identified as dominant pathogens across multiple studies (Soldevila-boixader et al. 2025)(Qona`ah et al. 2024)(Holmes, Anderson, and Mobley 2021). These organisms are commonly associated with chronic wounds and hospital environments, which may explain their increased prevalence in diabetic foot infections. Their dominance is clinically significant, as Gram-negative bacteria are known to possess more complex resistance mechanisms, including the production of beta-lactamase enzymes, efflux pumps, and structural modifications in their outer membrane, all of which contribute to reduced antibiotic susceptibility (Maity et al. 2024).

The antimicrobial resistance profile observed in the reviewed studies raises significant clinical concern. A large proportion of bacterial isolates demonstrated resistance to commonly used first-line antibiotics such as penicillin, amoxicillin, and trimethoprim-sulfamethoxazole. In some studies, resistance among Gram-negative isolates approached 100%, highlighting the limited effectiveness of these antibiotics in current clinical settings (Khan et al. 2023) (Munyemana et al. 2022). This finding underscores the risk of empirical antibiotic therapy without prior microbiological confirmation, which may lead to treatment failure and prolonged infection.

In contrast, several studies reported that antibiotics such as meropenem, amikacin, and gentamicin retained relatively high levels of effectiveness against both Gram-positive and Gram-negative bacteria (Santos et al. 2024). However, the increasing reliance on these broad-spectrum antibiotics raises concerns regarding the potential emergence of further resistance, particularly in the context of inappropriate or excessive antibiotic use (Salam et al. 2023).

Another important finding is the high prevalence of multidrug-resistant (MDR) organisms in diabetic foot infections. The proportion of MDR isolates varied across studies but was consistently reported to be substantial, ranging from approximately 15% to more than 50% (Zambelli et al. 2025). This trend is further supported by the detection of extended-spectrum beta-lactamase (ESBL)-producing bacteria and carbapenemase-producing strains, which represent a growing challenge in clinical management (Saleem et al. 2025)(Husna et al. 2023). The presence of these resistant organisms significantly limits therapeutic options and is associated with poorer clinical outcomes, including delayed wound healing and increased risk of amputation (Ilyas et al. 2024).

The development of antimicrobial resistance in diabetic wounds is multifactorial. Chronic inflammation, impaired immune response, and repeated antibiotic exposure create a selective environment that favors the survival of resistant strains (Li et al. 2025). In addition, biofilm formation further complicates treatment by providing a protective barrier that shields bacteria from both antibiotics and host immune defenses. This combination of factors

contributes to the persistence of infection and the difficulty in achieving complete eradication of pathogens (Sahoo and Meshram 2024).

Furthermore, the polymicrobial and biofilm-associated nature of diabetic foot infections suggests that bacterial interactions may also play a role in enhancing virulence and resistance. Within biofilms, bacteria can engage in metabolic cooperation and genetic exchange, including the transfer of resistance genes, which accelerates the spread of antimicrobial resistance within the microbial community (Afonso et al. 2021).

Overall, the findings of this review emphasize that diabetic foot infections should not be approached as simple monomicrobial infections but rather as complex, dynamic microbial ecosystems. Effective management requires not only accurate bacterial identification but also routine antimicrobial susceptibility testing to guide targeted therapy. Such an approach is essential to improve clinical outcomes, reduce the risk of complications, and limit the progression of antimicrobial resistance in diabetic wound infections.

## KESIMPULAN

Diabetic foot infections represent a complex and multifactorial clinical condition characterized by polymicrobial involvement and a predominance of Gram-negative bacteria. The most frequently identified pathogens include *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, reflecting both community- and hospital-associated microbial profiles. The findings of this study highlight a concerning increase in antimicrobial resistance, particularly against commonly used first-line antibiotics. The presence of multidrug-resistant organisms, including ESBL- and carbapenemase-producing bacteria, further complicates treatment strategies and limits available therapeutic options.

These results emphasize the importance of accurate microbiological identification and routine antimicrobial susceptibility testing in the management of diabetic foot infections. Empirical antibiotic therapy without laboratory confirmation may lead to suboptimal outcomes and contribute to the progression of resistance. In addition, the polymicrobial nature and biofilm-forming capacity of pathogens in diabetic wounds play a significant role in infection persistence and therapeutic failure. Therefore, a comprehensive and targeted approach, including appropriate antibiotic selection and continuous monitoring of resistance patterns, is essential to improve clinical outcomes and reduce the burden of complications such as prolonged infection and amputation. Future research should focus on region-specific microbial surveillance and the development of more effective antimicrobial strategies to address the growing challenge of resistance in diabetic wound infections.

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