narra j

Original Article

Antimicrobial resistance and empirical antibiotic use in diabetic foot infections: A retrospective study from Indonesia

Menang B. Tarigan[1], Rama M. Saragih[2*], Kevin A. Tarigan[3] and Franciscus Ginting[4]

[1]Division of Metabolic, Endocrinology and Diabetic, Department of Internal Medicine, Faculty of Medicine, Universitas Methodist Indonesia, Medan, Indonesia; [2]Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia; [3]Faculty of Medicine, Universitas Methodist Indonesia, Medan, Indonesia; [4]Division of Tropical Medicine and Infectious Disease, Department of Internal Medicine, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

*Corresponding author: ramamalachi@gmail.com

Abstract

Diabetic foot infection (DFI) represents a major complication of diabetes mellitus with significant morbidity, frequently leading to amputation if not optimally managed. The aim of this study was to analyze clinical, microbiological, and antibiotic susceptibility data from patients with type 2 diabetes who presented with foot infections in Indonesia. The retrospective study, conducted at St. Elisabeth Hospital in North Sumatra, Indonesia, predominantly comprised male farmers with a mean diabetes duration of 8.6 years, most of whom exhibited advanced ulcer severity (64.5% at Wagner grade III). Surgical debridement was performed in 79.0% cases, and amputation in 21.0% of cases. Laboratory investigations revealed poor glycemic control (mean HbA1c 10.12%) and biochemical markers indicative of systemic inflammation and renal impairment. Microbial cultures identified a predominance of Gram-negative bacteria (58.1%), primarily *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Escherichia coli*, whereas Gram-positive isolates (41.9%) were dominated by *Staphylococcus aureus*, including methicillin-resistant strains. Empirical outpatient and inpatient antibiotic regimens commonly included amoxicillin, ciprofloxacin, metronidazole, and ceftriaxone; however, in vitro susceptibility testing demonstrated limited efficacy of β-lactams such as ampicillin and amoxicillin (<10% sensitivity). In contrast, linezolid, amikacin, vancomycin, carbapenems, and fosfomycin exhibited superior activity against the isolated pathogens. These findings emphasize the critical need for empirical antibiotic guidelines tailored to local microbial ecology and resistance profiles, integrated with early surgical management, stringent glycemic control, and multidisciplinary care. This comprehensive approach is essential to reduce the risk of amputation and improve clinical outcomes in tropical, resource-limited settings.

Keywords: Diabetic foot infection, antimicrobial susceptibility, empirical antibiotic guideline, multidrug resistance, surgical debridement

Introduction

Diabetic foot infection (DFI) represents one of the most devastating and economically burdensome complications of diabetes, affecting approximately 6.3% of diabetic patients globally, with lifetime ulcer development risks ranging from 19% to 34%; frequently necessitating hospitalization, prolonged antibiotic therapy, and lower extremity amputation [1,2]. Its pathophysiology involves a complex interplay of peripheral neuropathy affecting approximately 70% of DFI patients, peripheral arterial disease present in 50% of cases, and compromised wound

Received: August 1, 2025 - Accepted: September 11, 2025 - Published online: September 17, 2025

healing mechanisms that collectively predispose patients to ulceration and subsequent polymicrobial bacterial invasion [3,4]. The epidemiological data demonstrate that approximately 50–60% of diabetic foot ulcers (DFUs) subsequently develop secondary infections, creating a cascade of complications with *Staphylococcus aureus* (17.7–19.9%), *Escherichia coli* (10.9–12.2%), and *Pseudomonas aeruginosa* (8.3–10.5%) identified as predominant pathogens [1,5]. While traditionally classified within skin and soft tissue infections (SSTIs), DFIs possess unique characteristics that distinguish them from conventional SSTIs, including chronic infection patterns, substantial osteomyelitis risk (20% in mild-moderate infections, 50–60% in severe cases), and complex microbial patterns that necessitate specialized management approaches as recognized by the updated 2023 International Working Group of Diabetic Foot (IWGDF)/ Infectious Disease Society of America (IDSA) guidelines [6,7].

The emergence of antimicrobial resistance (AMR) in DFIs has created a global public health crisis, particularly affecting low- and middle-income countries where empirical antibiotic prescribing without microbiological confirmation remains commonplace and DFI patients exhibit 1.87 times greater hospitalization risk when treated with empirical versus culture-directed therapy [8]. In Indonesia, inappropriate antimicrobial use reflects wider regional challenges, with pooled data indicating that only 33.5% of hospital antibiotic prescriptions are appropriate [9]. Recent studies from Indonesian tertiary hospitals revealed that Gram-negative bacteria dominated DFI cases (83.07%), with multidrug-resistant organisms found in 27.7% of isolates, including extended-spectrum beta-lactamase (ESBL) carbapenemase-producing bacteria, and methicillin-resistant *Staphylococcus aureus* (MRSA) [9,10]. The absence of comprehensive local antimicrobial resistance surveillance data and region-specific treatment protocols contributes to suboptimal patient outcomes and accelerates resistance development, with contemporary resistance surveillance revealing alarming resistance rates, including limited susceptibility to empirical first-line antibiotics recommended by international guidelines [5,10]. Context-specific strategies are urgently needed to develop evidence-based, hospital-based empirical antibiotic guidelines that incorporate local microbiological data and resistance patterns, as international guidelines may not adequately reflect regional pathogen distribution and antimicrobial susceptibility profiles, with successful implementation of localized guidelines demonstrating potential for significant improvements in clinical outcomes and enhanced antimicrobial stewardship effectiveness [11,12]. The aim of this study was to characterize the microbiological spectrum, antimicrobial susceptibility patterns, and antibiotic prescription practices in patients with DFI, and to provide evidence for developing context-specific empirical antibiotic guidelines to improve clinical outcomes and reduce amputation risk.

Methods

Study design and settings

This retrospective study was conducted between October 2023 and May 2025 at St. Elisabeth Hospital, a general hospital in Medan, North Sumatra, Indonesia. Privately managed, this hospital facility offers an extensive capacity of 200 beds and accommodates approximately one hundred daily consultations. Of these, around a hundred consultations per month are related to type 1 and type 2 diabetes across all care departments. The hospital serves as an essential healthcare institution for the local community, playing a crucial role in meeting their medical needs.

Study sample and inclusion criteria

The study included adult patients diagnosed with type 2 diabetes by an endocrinologist according to the 2024 Indonesian Society of Endocrinology guideline for Diabetes [13]. Eligible patients also had a confirmed diagnosis of DFU, classified using the Wagner system, which ranges from grade 0 (no open lesion) and grade 1 (superficial ulcer) to grade 2 (deep ulcer), grade 3 (abscess or osteitis), grade 4 (gangrene of the forefoot), and grade 5 (gangrene of the entire foot). In addition, inclusion required the availability of a positive microbial culture obtained from a tissue swab of the DFU. Patients were excluded if their medical records were incomplete, if cultures yielded non-bacterial isolates, or if samples were obtained from anatomical sites other than the

foot. Individuals with type 1 diabetes, gestational diabetes, lower-limb amputations unrelated to diabetes, or ischemic limbs without viable tissue were also excluded.

Sample collection, identification, and sensitivity testing

Upon collection, tissue samples were promptly transported to the microbiology laboratory under controlled conditions to preserve specimen integrity. Bacterial cultures were performed on agar plates and incubated at 37°C for 24 hours under standardized conditions [14]. Following colony growth, Gram staining was conducted using standard methods to differentiate isolates into Gram-positive and Gram-negative groups [15]. Antimicrobial susceptibility testing was performed on Mueller–Hinton agar using the Kirby–Bauer disk diffusion method, in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines [16]. After 24 hours of incubation, inhibition zone diameters surrounding antibiotic discs were measured using a standardized zone scale, and results were interpreted according to CLSI criteria to classify isolates as susceptible, intermediate, or resistant [16].

Study variables

Clinical and laboratory information was extracted from medical records at the time of admission and throughout hospitalization. The following variables were included into the analysis: (1) demographic and clinical characteristics, including age, sex, occupation, Wagner's classification, and surgical interventions; (2) laboratory parameters, comprising hemoglobin, leukocyte count, platelet count, absolute lymphocyte count (ALC), serum albumin, uric acid, urea, creatinine, D-dimer, low-density lipoprotein cholesterol (LDL-C), triglycerides, and glycated hemoglobin (HbA1c); and (3) microbiological findings from infected tissue specimens, including bacterial species isolated, antimicrobial susceptibility profiles, and resistance patterns.

Statistical analysis

Descriptive analyses were conducted to present frequency distributions and percentages for categorical variables, and means with standard deviations for continuous variables. All statistical analyses were performed using SPSS Statistics version 26 (IBM Corp., Armonk, NY, USA)

Results

Characteristics of diabetic patients

A total of 62 patients with DFI were included in the study (**Figure 1**), and characteristics of the patients are presented in **Table 1**. A higher proportion of patients were male (54.8% vs. 45.2%), with 48.4% working as farmers, and the majority presented with Wagner grade III (64.5%) and grade IV (35.5%). Debridement was the most common surgical intervention (79.0%), while amputation was performed in 21.0% of cases. Microbiological analysis revealed that Gram-negative bacteria were more frequently isolated (58.1%) compared to Gram-positive bacteria (43.6%). The mean duration of diabetes onset among patients in this study was 8.6 years.

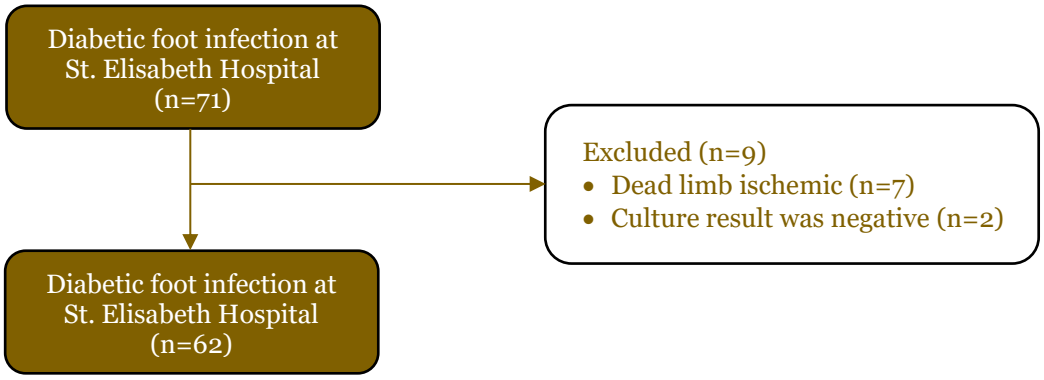

Figure 1. Flowchart of the study.

Table 1. Characteristics of the diabetic patients with diabetic foot infections (n=62)

Variable	Frequency	Percentage (%)
Age (years)		
<60	32	51.61
≥60	30	48.39
Sex		
Male	34	54.8
Female	28	45.2
Occupation		
Farmer	30	48.4
Housewife	14	22.6
Entrepreneur	6	9.7
Retired employee	6	9.7
General employee	5	8.1
Seller	1	1.7
Wagner's criteria		
III	40	64.5
IV	22	35.5
Surgical procedure		
Debridement	49	79.0
Amputation	13	21.0
Comorbid		
Yes	28	45.2
No	34	54.8
Comorbidities		
Cardiovascular	9	14.5
Renal disease	14	22.5
Pulmonary disease	7	11.3
Diabetes onset (years), mean (SD)	8.6 (5.14)	
Length of stay (days), mean (SD)	8.9 (2.31)	

The laboratory findings of patients with DFI are presented in **Table 2**. The mean hemoglobin level was 11.52 g/dL, leukocyte count of 11,766 mg/dL, and platelet count of 258,719 mg/dL. The mean Hemoglobin A1c (HbA1c) level was notably elevated at 10.12%, indicating poor glycemic control. Other important findings included a mean creatinine of 14.34 mg/dL, urea of 54.33 mg/dL, and D-dimer of 1,896 ng/mL, reflecting potential renal impairment and inflammation. The mean low-density lipid (LDL) and triglyceride levels were 100.56 mg/dL and 121.00 mg/dL, respectively (**Table 2**).

Table 2. Laboratory findings of diabetic patients with diabetic foot infections (n=62)

Variable	Mean (SD)
Hemoglobin (g/dL) (n=60)	11.5 (1.70)
Leukocyte (mg/dL) (n=60)	11,766 (8,926)
Platelet (mg/dL) (n=60)	258,719 (179,773)
Absolute lymphocyte count (cell/mm^3) (n=57)	1,644 (1,053)
Albumin (g/dL) (n=41)	6.3 (8.77)
Uric acid (mg/dL) (n=43)	12.5 (21.12)
Creatinine (mg/dL) (n=55)	14.3 (41.36)
Urea (mg/dL) (n=55)	54.3 (48.80)
D-Dimer (ng/mL) (n=51)	1,896 (1,370)
Low-Density Lipid (mg/dL) (n=62)	100.5 (39.69)
Triglyceride (mg/dL) (n=62)	121.0 (45.46)
Hemoglobin A1c (mg/dL) (n=60)	10.1 (2.42)

Microbial culture results of diabetic foot infection (DFI)

The microbial culture results from DFI cases in this study are summarized in **Table 3**. Among the 62 isolates identified, Gram-negative bacteria were more prevalent (58.1%), whereas Gram-positive bacteria accounted for 41.9%. Among the Gram-negative group, *Klebsiella pneumoniae* was the most frequently isolated organism (17.7%), followed by *Proteus mirabilis* (11.3%), *Escherichia coli* (8.1%), *Pseudomonas aeruginosa* (6.5%), *Acinetobacter baumannii* (4.8%), *Enterobacter cloacae* (3.2%), *Providencia stuartii* (3.2%), and others such as *Burkholderia pseudomallei, Serratia fonticola*, and *Pseudomonas luteola*, each at 1.6% (**Table 3**). In the Gram-positive group, *Staphylococcus aureus* was the most common isolate (19.4%), with MRSA

found in 3.2% of cases (**Table 3**). Other Gram-positive bacteria included *Staphylococcus pseudintermedius* (4.8%), *Staphylococcus haemolyticus* (4.8%), *Kocuria kristinae* (3.2%), *Staphylococcus lugdunensis* (1.6%), *Streptococcus agalactiae* (1.6%), and *Enterococcus faecalis* (1.6%). These findings indicate a predominance of Gram-negative bacteria in DFI, with a diverse range of both Gram-negative and Gram-positive organisms identified.

Table 3. Distribution of microbial culture isolates from diabetic foot infection (DFI)

Microbial culture	Frequency	Percentage (%)
Gram-negative	37	59.7
Klebsiella pneumoniae	11	17.7
Proteus mirabilis	7	11.3
Escherichia coli	5	8.1
Pseudomonas aeruginosa	4	6.4
Acinetobacter baumannii	3	4.8
Enterobacter cloacae	2	3.2
Providencia stuartii	2	3.2
Burkholderia pseudomallei	1	1.6
Seratia fonticola	1	1.6
Pseudomonas iuteola	1	1.6
Gram-positive	25	40.3
Staphylococcus aureus	12	19.3
Staphylococcus pseudintermedius	3	4.8
Staphylococcus haemolyticus	3	4.8
Methicillin-Resistant *Staphylococcus aureus*	2	3.2
Kocuria kristinae	2	3.2
Staphylococcus lugdunensis	1	1.6
Streptococcus agalactiae	1	1.6
Enterococcus faecalis	1	1.6

Antibiotic prescription patterns for diabetic foot infection (DFI)

The antibiotic prescription patterns for DFI at St. Elisabeth Hospital across three distinct contexts: prior outpatient history (n=51), empirical physician-initiated therapy (n=115), and culture-guided regimens (n=121) are presented in **Table 4**. In the outpatient setting, amoxicillin was the most frequently recorded prior prescription (n=24, 47.0%), followed by ciprofloxacin (n=13, 25.5%) and metronidazole (n=8, 15.7%). Less commonly used agents included chloramphenicol and ceftriaxone (each 3.9%), as well as amoxicillin–clavulanic acid and gentamicin (each 2.0%). Empirically, physicians predominantly administered metronidazole infusion (n=53, 46.1%) and intravenous ceftriaxone (n=48, 41.7%), with meropenem (4.3%), topical gentamycin (2.6%), and other broad-spectrum agents such as cefoperazone, ciprofloxacin, azithromycin, and amikacin each comprising fewer than 2% of empirical choices.

Table 4. Antibiotic prescription patterns for diabetic foot infection (DFI)

Variable	Frequency	Percentage (%)
Antibiotic prescriptions' history		
Amoxicillin	24	47.0
Ciprofloxacin	13	25.5
Metronidazole	8	15.7
Chloramphenicol	2	3.9
Ceftriaxone	2	3.9
Amoxicillin-clavulanic acid	1	2.0
Gentamycin	1	2.0
Empirical Antibiotic (n=115)		
Metronidazole (infusion)	53	46.1
Ceftriaxone (intravenous)	48	41.7
Meropenem (intravenous)	5	4.3
Gentamycin (ointment)	3	2.6
Cefoperazone (intravenous)	2	1.7
Ciprofloxacin (intravenous)	2	1.7
Azithromycin (oral)	1	0.9
Amikacin (intravenous)	1	0.9
Antibiotic combination (n=62)		
1 antibiotic	9	14.5
2 antibiotics	53	85.5

Antibiotic susceptibility patterns in isolates from DFIs demonstrated considerable variability in efficacy across tested agents (**Table 5**). Linezolid and amikacin achieved the highest sensitivity rates, with 90.9% and 90.6% of isolates susceptible, respectively, followed closely by vancomycin at 89.5%. These findings highlight the potential of these agents as key therapeutic options for managing diabetic foot infections in settings with comparable microbial profiles. Substantial activity was also observed for azithromycin (77.8%) and meropenem (72.2%). In contrast, agents frequently used in clinical practice, such as ampicillin and amoxicillin, showed very limited effectiveness, with sensitivity rates of only 10.0% and 9.6%, underscoring their restricted clinical utility in this context. Intermediate activity was documented for fosfomycin (68.4%), ertapenem (62.8%), and tigecycline (62.1%), suggesting a potential role for these drugs as alternative therapeutic options when first-line treatments are unsuitable (**Table 5**).

Table 5. Definitive antibiotic based on microbial culture sensitivity

Definitive antibiotic	Total isolate	Total sensitive	Sensitivity (%)
Linezolid	22	20	90.9
Amikacin	53	48	90.6
Vancomycin	19	17	89.5
Azithromycin	18	14	77.8
Meropenem	54	39	72.2
Fosfomycin	38	26	68.4
Ertapenem	43	27	62.8
Tigecycline	58	36	62.1
Levofloxacin	21	13	61.9
Gentamycin	57	34	61.4
Piperacillin-tazobactam	49	30	61.2
Cefepime	50	30	60.0
Trimethoprim-sulfamethoxazole	50	30	60.0
Erythromycin	21	12	57.1
Clindamycin	21	12	57.1
Cefotaxime	18	10	55.6
Aztreonam	34	16	47.1
Ceftriaxone	47	21	44.7
Kanamycin	45	20	44.4
Tetracycline	54	23	42.6
Ampicillin-sulbactam	49	20	40.8
Ciprofloxacin	56	22	39.3
Ceftazidime	46	18	39.1
Ampicillin	30	3	10.0
Amoxicillin	52	5	9.6

The antimicrobial susceptibility profiles of Gram-negative bacteria isolated from DFIs at St. Elisabeth Hospital demonstrated substantial heterogeneity in both prevalence and resistance patterns (**Table 6**). *Klebsiella pneumoniae* was the most frequently isolated species, followed by *Proteus mirabilis* and *Escherichia coli*, each displaying distinct susceptibility spectra. Carbapenems, particularly ertapenem and meropenem, together with fosfomycin, exhibited the greatest efficacy across most isolates, with both *K. pneumoniae* and *P. mirabilis* showing marked susceptibility. In contrast, ampicillin and amoxicillin were largely ineffective, reflecting widespread resistance among Gram-negative organisms. *Pseudomonas aeruginosa* and *Acinetobacter baumannii* demonstrated high levels of resistance to multiple antibiotic classes but retained activity against select agents such as ciprofloxacin, gentamicin, and tigecycline. Less common species, including *Enterobacter cloacae*, *Providencia stuartii*, and *Serratia fonticola*, generally showed high susceptibility to carbapenems and fosfomycin, although resistance to other antibiotics was variable.

The antimicrobial susceptibility profiles of Gram-positive bacteria isolated from diabetic foot infections showed marked heterogeneity across species and antibiotic classes (**Table 7**). *Staphylococcus aureus* was the most prevalent isolate and demonstrated high susceptibility to azithromycin, linezolid, vancomycin, tigecycline, and meropenem, while exhibiting only moderate sensitivity to erythromycin and clindamycin. MRSA isolates, although less frequent, remained fully susceptible to linezolid, vancomycin, tigecycline, and amikacin, confirming the reliability of these agents against resistant strains.

Table 6. Antimicrobial sensitivity profile of Gram-negative bacteria (n=37)

Gram-negative bacteria	n	%	GEN	CIP	TMX	AMI	TYG	AMO	APS	CFM	CFZ	CEF	ERT	MER	PTM	TET	KAN	FOS	AZA	AMP
K. pneumoniae	11	29.7	63.6	18.2	45.4	100	63.6	0	36.3	66.7	36.4	40.0	90.0	90.0	55.6	37.5	62.5	87.5	36.4	0
P. mirabilis	7	18.9	42.9	28.6	28.6	100	0	28.6	28.6	66.7	42.9	57.1	42.9	85.7	85.7	0	40.0	80.0	57.1	14.3
E. coli	5	13.5	60.0	20.0	20.0	100	100	0	60.0	100	80.0	60.0	80.0	80.0	80.0	20.0	75.0	80.0	40.0	0
P. aeruginosa	4	10.8	75.0	75.0	NT	100	0	0	0	NT	100	75	NT	100	75.0	0	50.0	50.0	75.0	NT
A. baumannii	3	8.1	NT	0	0	66.7	100	66.7	0	66.7	0	0	NT	66.7	0	33.3	33.3	100	NT	NT
E. cloacae	2	5.4	0	50.0	100	50	50	50	0	50.0	50.0	50.0	50.0	100	50.0	0	50.0	0	100	0
P. stuartii	2	5.4	0	0	0	50.0	100	0	0	0	50.0	50.0	50.0	50.0	50.0	0	50.0	0	100	0
B. pseudomalei	1	2.7	NT	NT	NT	NT	100	NT	0	NT	NT	NT	NT	100	NT	0	0	0	NT	NT
S. fonticola	1	2.7	0	0	0	0	100	0	0	0	NT	0	100	100	100	0	100	0	0	0
P. iuteola	1	2.7	NT	0	0	100	100	100	0	0	0	0	NT	0	NT	100	0	100	0	NT

Values highlighted in green indicate antibiotic sensitivity rates ≥80%

AMI: amikacin; AMO: amoxicillin; AMP: ampicillin; APS: ampicillin-sulbactam; AZA: aztreonam; AZI: azithromycin; CEF: ceftriaxone; CFM: cefepime; CFO: cefotaxime; CFZ: ceftazidime; CIP: ciprofloxacin; CLI: clindamycin; ERY: erythromycin; ERT: ertapenem; FOS: fosfomycin; GEN: gentamycin; KAN: kanamycin; LEV: levofloxacin; LIZ: linezolid; MER: meropenem; MRSA: methicillin-resistant *Staphylococcus aureus*; NT: not tested; PTM: piperacillin-tazobactam; TET: tetracycline; TMX: trimethoprim-sulfamethoxazole; TYG: tigecycline; and VAN: vancomycin.

Table 7. Antimicrobial sensitivity profile of Gram-positive bacteria (n=25)

Gram-positive bacteria	n	%	ERY	AZI	LEV	LIZ	CLI	CIP	TMX	VAN	AMY	TYG	AMO	APS	CFO	CEF	ERT	MER	PTM	TET
S. aureus	12	48.0	83.3	90.9	63.6	100	75.0	60.0	100	100	88.9	100	0	77.8	80	77.8	77.8	80	80	75
S. pseudointermedius	3	12.0	0	NT	66.7	33.3	0	66.7	100	33.3	100	100	NT	NT	NT	NT	NT	NT	NT	100
S. haemolyticus	3	12.0	50.0	66.7	50.0	100	50.0	50.0	100	100	50.0	100	0	0	0	0	0	0	0	100
MRSA	2	8.0	100	100	50.0	100	100	50.0	100	100	100	100	0	0	0	0	0	0	0	50.0
K. kristinae	2	8.0	NT	NT	NT	NT	NT	NT	NT	NT	100	0	50.0	NT	NT	NT	NT	50.0	NT	100
S. lungudensis	1	4.0	0	0	100	100	0	100	NT	NT	NT	NT	0	0	0	0	0	0	0	NT
S. agalactiae	1	4.0	0	0	0	100	0	NT	NT	100	0	100	100	100	100	100	100	100	NT	100
E. faecalis	1	4.0	0	NT	100	100	NT	100	NT	100	NT	100	100	100	NT	NT	NT	NT	100	0

Values highlighted in green indicate antibiotic sensitivity rates ≥80%

AMI: amikacin; AMO: amoxicillin; AMP: ampicillin; APS: ampicillin-sulbactam; AZA: aztreonam; AZI: azithromycin; CEF: ceftriaxone; CFM: cefepime; CFO: cefotaxime; CFZ: ceftazidime; CIP: ciprofloxacin; CLI: clindamycin; ERY: erythromycin; ERT: ertapenem; FOS: fosfomycin; GEN: gentamycin; KAN: kanamycin; LEV: levofloxacin; LIZ: linezolid; MER: meropenem; MRSA: methicillin-resistant *Staphylococcus aureus*; NT: not tested; PTM: piperacillin-tazobactam; TET: tetracycline; TMX: trimethoprim-sulfamethoxazole; TYG: tigecycline; VAN: vancomycin.

Less common organisms, including *Staphylococcus lugdunensis*, *Streptococcus agalactiae*, and *Enterococcus faecalis*, consistently retained susceptibility to linezolid, vancomycin, and tigecycline but demonstrated variable resistance to other drugs. Across nearly all Gram-positive isolates, ampicillin and amoxicillin exhibited minimal activity, reflecting the high prevalence of resistance and limiting their utility in the clinical management of DFIs.

Discussion

DFI represents one of the most serious and complex complications of diabetes mellitus, contributing substantially to morbidity, mortality, and healthcare expenditure worldwide [17]. The pathophysiology of DFI is multifactorial, involving a complex interplay of neuropathy, ischemia, nutritional dysfunction, and infection, with each component creating a cascade of pathological processes that predispose diabetic patients to foot ulceration and subsequent infection [18,19]. The diabetic environment fundamentally alters the normal wound healing process through multiple mechanisms, including hyperglycemia-induced impairment of immune function, peripheral neuropathy leading to loss of protective sensation, and peripheral arterial disease compromising tissue perfusion [20].

The demographic profile of DFI patients in Asia and Southeast Asia reveals distinct age-related patterns that differ from those of Western populations. In Malaysia, a comprehensive study of 434 diabetic foot infection patients demonstrated that individuals between the ages of 58 and 68 years had the highest infection rate at 35.3%, followed by those aged 69 and over at 30.0% [21]. The present study found patients aged <60 years constituted 51.6% (n=32) and those ≥60 years comprised 48.4% (n=30) of DFI cases. This near-even split contrasts with larger Indonesian series, which report DFI predominance in older adults. For instance, a multicenter study in Jakarta (n=158) found 55.1% of DFI patients were ≥60 years (mean age 59.3 ± SD), while a tertiary hospital study in Surabaya (n=123) documented 75.6% of patients aged over 50 years, with a median age of 53 years [22,23]. Similar age patterns appear in other Southeast Asian reports, indicating that while our cohort includes a substantial middle-aged proportion, national data skew older, likely reflecting referral bias and longer diabetes duration in larger centers.

The present study comprised 54.8% males (n=34) and 45.2% females (n=28). In Indonesia, gender distribution varies by region. The Jakarta *Jaminan Kesehatan Nasional* (JKN)-DFU registry reported a female predominance (55.1% female vs 44.9% male)[23], whereas Buleleng Regency (Bali) data indicate 56.8% males vs 43.2% females (n=162) [24]. The Surabaya tertiary center saw no clear sex predominance (≈50% each) [25]. These discrepancies may reflect differences in healthcare access, cultural gender roles influencing foot care practices, and regional referral policies. Nevertheless, a slight male predominance in our sample aligns with findings that male patients often exhibit higher foot pressure and lower preventive foot-care awareness [26].

Occupation shapes DFI risk through socioeconomic and exposure factors. In our dataset, farmers represented the largest group (48.4%), followed by housewives (22.6%), entrepreneurs and retired employees (9.7% each), general employees (8.1%), and sellers (1.7%). Indonesian studies similarly highlight high DFI prevalence among individuals with limited resources: the Jakarta registry noted 63.9% of patients were housewives, retirees, or unemployed [23], while the Ibnu Sina Hospital series (n= 88) found 40.9% were housewives and 44.3% had only elementary education [27]. Agricultural work, as observed in our farmer cohort, also carries heightened risk due to barefoot ambulation and delayed wound recognition. Thus, occupation-driven patterns underscore the need for targeted education and protective footwear interventions for both rural farmers and homemakers.

The relationship between glycemic control and DFU healing represents a complex interplay of acute glycemic management and long-term metabolic optimization that significantly impacts both infection control and tissue repair processes [28,29]. Contemporary evidence demonstrates that patients achieving improved glycemic control during DFU treatment experience 87% healing rates compared to 63% in those with persistently elevated glucose levels, with HbA1c reduction of 2% or greater associated with accelerated healing and reduced resource utilization [28,29]. Prospective cohort studies reveal that early and intensive glycemic control within the first 4 weeks of treatment initiation independently predicts DFU healing, with HbA1c levels above 8.15% at 4 weeks serving as a threshold that predicts delayed healing regardless of initial ulcer

characteristics [30]. The mechanisms linking glycemic control to wound healing involve multiple pathways, including enhanced neutrophil function, improved collagen synthesis, reduced inflammatory cytokine production, and optimized angiogenesis. These processes are particularly critical in the setting of DFI, where bacterial clearance and tissue repair must occur simultaneously [30,31]. Perioperative glycemic management assumes particular importance in diabetic foot surgery, with studies demonstrating that glycated hemoglobin levels above 7% significantly increase postoperative infection rates and delay bone healing in foot and ankle procedures. However, the complexity of glycemic optimization in hospitalized diabetic foot patients is highlighted by recent studies showing that while normalization of blood glucose levels reduces hospital length of stay and antibiotic duration, the rapidity of glycemic control achievement does not independently influence treatment failure rates in operated DFI [30–32]. Integrated diabetes specialist co-management with podiatric care represents an emerging model that demonstrates superior wound healing outcomes, with collaborative glycemic management protocols achieving median ulcer volume reduction from 170 mm^3 to 0 mm^3 compared to persistent elevation in patients without coordinated diabetes care [33].

The antimicrobial susceptibility patterns documented in our institutional study showed that linezolid (90.9%) and vancomycin (89.5%) retained high activity against Gram-positive organisms, whereas activity against Gram-negative pathogens was more variable. These findings should be interpreted within the contemporary paradigm, which considers antibiotic therapy as merely one component of a comprehensive, multidisciplinary approach to DFI management [33–35]. International evidence consistently demonstrates that antimicrobial therapy alone, regardless of its precision or potency, cannot achieve optimal clinical outcomes in DFI without concurrent attention to surgical intervention, glycemic optimization, pressure offloading, and vascular assessment [36,37]. The 2023 IWGDF/IDSA guidelines explicitly emphasize that successful diabetic foot infection management requires integration of antimicrobial therapy with aggressive surgical debridement, comprehensive wound care, and multidisciplinary collaboration [7]. Antibiotics primarily reduce bacterial burden, whereas other interventions address the fundamental pathophysiological abnormalities that perpetuate infection and impede healing [7]. Recent studies demonstrate that multidisciplinary diabetic foot teams achieve significantly superior outcomes compared to single-specialty approaches, with limb salvage rates improving from 65% to 85% when antimicrobial therapy is delivered within structured multidisciplinary protocols that prioritize early surgical intervention and comprehensive metabolic management [38,39].

The critical importance of early and aggressive surgical debridement in DFI extends far beyond simple antimicrobial considerations, representing the primary intervention for infection control and tissue preservation that directly impacts amputation prevention [33,36,37]. This study's finding that 79% of patients underwent debridement aligns with international evidence demonstrating that surgical intervention within the first 24–48 hours of infection diagnosis significantly reduces amputation rates and accelerates healing compared to delayed surgical management [29,40]. Contemporary studies demonstrate that each day of delay in surgical debridement increases the odds ratio for proximal amputation by 1.61 (95% confidence interval (CI): 1.10–2.36), emphasizing that timing represents a critical determinant of limb salvage independent of antimicrobial selection or resistance patterns [40]. The concept of "time is tissue" in DFI reflects the understanding that bacterial invasion, particularly in the setting of compromised immune function and vascular supply, creates a rapidly expanding zone of tissue necrosis that requires immediate surgical intervention to prevent progression to deeper structures [33]. International guidelines consistently recommend that surgical debridement should be performed emergently for severe infections and within 24 hours for moderate infections, with the extent of debridement guided by intraoperative assessment of tissue viability rather than preoperative imaging studies that may delay necessary intervention [7]. The synergy between early surgical debridement and antimicrobial therapy has been extensively documented, with studies showing that adequate surgical source control enables shorter antibiotic courses and reduces the development of antimicrobial resistance through elimination of bacterial biofilms and necrotic tissue that harbor resistant organisms [29,37].

The clinical risk factors observed in our patient population align extensively with international literature identifying key predictors for multidrug-resistant organism (MDRO) acquisition in DFI. Recent systematic analyses identify previous hospitalization, prior antibiotic exposure, ulcer chronicity, and severe infection as primary MDRO risk factors, patterns that our 54.8% male predominance and mean 8.6-year diabetes duration suggest may be prevalent in our cohort [41,42]. Studies from tertiary centers demonstrate MDRO prevalence ranging from 22.3% to 66% in DFI, with Indonesian data specifically showing high resistance rates among Enterobacteriaceae family members [42,43]. The association between glycemic control and resistance patterns, demonstrated by our mean HbA1c of 10.12, correlates with international data showing poor glucose control as an independent risk factor for MDRO acquisition [44,45]. Methicillin-resistant *Staphylococcus aureus* (MRSA) prevalence in our study (3.2%) falls below global estimates of 8.6-17%, potentially reflecting regional epidemiological differences or institutional infection control practices. Recent meta-analyses demonstrate declining MRSA prevalence in DFI globally, from 25% before 2010 to 9% thereafter, suggesting that our findings may reflect contemporary trends rather than regional anomalies [46,47].

Our documentation of empirical antibiotic prescribing patterns, with metronidazole (46.1%) and ceftriaxone (41.7%) predominating, reveals significant discordance with evidence-based recommendations and highlights critical opportunities for antimicrobial stewardship intervention. International guidelines emphasize culture-directed therapy over empirical broad-spectrum coverage, yet recent studies demonstrate 1.87-fold higher hospitalization rates when empirical therapy is used versus culture-guided treatment [7,8]. The frequent outpatient use of amoxicillin (47.0%) and ciprofloxacin (25.5%) in our cohort reflects prescribing patterns common across developing nations but contradicts our antimicrobial susceptibility data showing limited efficacy of these agents. Contemporary European studies implementing empirical protocols based on local resistance patterns demonstrate significantly improved clinical outcomes, supporting the urgent need for institutional guideline development incorporating our microbiological findings. The IWGDF/IDSA guidelines specifically recommend against empirical anti-pseudomonal coverage in temperate climates but suggest consideration in Asian populations with moderate-to-severe infections, directly supporting revised empirical protocols in light of the 6.5% prevalence of *Pseudomonas aeruginosa* in our cohort.

The role of patient education in DFI prevention and amputation avoidance has evolved from traditional didactic approaches to evidence-based, structured interventions that demonstrate measurable improvements in foot care knowledge and self-care behaviors, though with limited direct evidence for ulcer and amputation reduction [48,49]. Systematic reviews of randomized controlled trials revealed that while patient education consistently improves short-term foot care knowledge and self-reported behaviors, the evidence for clinically meaningful reductions in ulcer incidence and amputation rates remains insufficient when education is implemented as an isolated intervention [48,49]. However, when integrated within comprehensive multidisciplinary care programs, patient education becomes a critical component that enhances adherence to offloading devices, improves recognition of early warning signs, and facilitates timely presentation for professional care [48]. The Step-by-Step Diabetic Foot Project, implemented in Tanzania and India, demonstrates that comprehensive educational programs incorporating patient and healthcare provider training, combined with systematic foot care protocols and regular follow-up, achieve greater than 50% reduction in amputation rates when delivered within organized healthcare systems [50]. Contemporary educational interventions increasingly focus on risk stratification, with high-risk patients (those with previous ulceration or amputation history) receiving intensive, individualized education programs that emphasize daily foot inspection, appropriate footwear selection, and immediate healthcare seeking for new lesions [48]. The IWGDF prevention guidelines recommend structured education for all diabetic patients at risk of foot ulceration (IWGDF risk categories 1–3), with educational content specifically tailored to include foot ulcer consequences, preventive self-care behaviors, and recognition of situations requiring urgent professional evaluation [7].

Our study's findings illuminate critical gaps in current DFI research and highlight essential priorities for future investigation, particularly regarding longitudinal resistance surveillance, clinical outcome correlations, and therapeutic optimization strategies. The documented

antimicrobial resistance patterns require continuous monitoring through standardized surveillance protocols, as international studies demonstrate significant temporal variations in resistance prevalence, with some centers reporting 2–3 fold changes in ESBL prevalence over 5-year periods [45]. Implementation of rapid molecular diagnostic techniques, increasingly validated in international studies for DFI, could significantly improve empirical antibiotic selection and reduce inappropriate broad-spectrum usage documented in our prescribing analysis [7]. The integration of artificial intelligence and machine learning approaches to predict antimicrobial resistance patterns, successfully piloted in European diabetic foot centers, represents a promising avenue for optimizing therapeutic strategies based on patient-specific risk factors and local epidemiological data [17]. International collaborations focusing on resistance mechanism characterization, particularly carbapenemase and ESBL gene distribution across Southeast Asian populations, could inform regional treatment guidelines and antimicrobial stewardship programs. The urgent need for clinical outcome studies correlating microbiological findings with patient-centered endpoints including healing rates, amputation risk, and quality of life measures represents a critical research priority that our institutional data could support through prospective cohort development.

Conclusion

The present study provides critical insights into the microbiological spectrum and antimicrobial susceptibility patterns of DFI in a tropical Southeast Asian context, revealing a predominance of Gram-negative bacteria, with *Klebsiella pneumoniae* as the leading pathogen and notable resistance to commonly used β-lactam antibiotics, such as ampicillin and amoxicillin. Effective agents identified include linezolid, amikacin, vancomycin, carbapenems, and fosfomycin, highlighting the necessity for local susceptibility data to inform empirical therapy. The findings underscore the pressing need for tailored antibiotic guidelines that reflect regional pathogen profiles and resistance trends, alongside integrated multidisciplinary management encompassing early surgical intervention, glycemic control, and patient education, to optimize clinical outcomes and reduce the substantial risk of lower limb amputation in this high-burden population.

Ethics approval

The study was approved by the Health Research Ethics Commission, Faculty of Medicine Universitas Methodist Indonesia, Medan, North Sumatra, Indonesia (168/KEPK-FKUMI/EC/2025, July 17, 2025).

Acknowledgments

Acknowledgement is extended to St. Elisabeth Hospital, Indonesia, for providing access to medical records that supported this work.

Competing interests

There were no identified potential conflicts of interest related to this article.

Funding

This study received no external funding.

Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of artificial intelligence use

This study used artificial intelligence (AI) tool and methodology, in which AI-based language model, Chat GPT, was employed in the language refinement (improving grammar, sentence structure, and readability of the manuscript). We confirm that all AI-assisted processes were critically reviewed by the authors to ensure the integrity and reliability of the results. The final decisions and interpretations presented in this article were solely made by the authors.

How to cite

Tarigan MB, Saragih RM, Tarigan KA, Ginting F. Antimicrobial resistance and empirical antibiotic use in diabetic foot infections: A retrospective study from Indonesia. Narra J 2025; 5 (3): e2895 - http://doi.org/10.52225/narra.v5i3.2895.

Reference

1. Wernecke J, Wernecke M, Ebenau O, *et al.* Epidemiology and the medical burden of diabetic foot ulcers especially in patients with infection—A population-based analysis from Germany. Int Wound J 2025;22(4).
2. McDermott K, Fang M, Boulton AJM, *et al.* Etiology, epidemiology, and disparities in the burden of diabetic foot ulcers. Diabetes Care 2022;46(1):209-221.
3. Parveen K, Hussain MA, Anwar S, *et al.* Comprehensive review on diabetic foot ulcers and neuropathy: Treatment, prevention and management. World J Diabetes 2025;16(3).
4. Dawi J, Tumanyan K, Tomas K, *et al.* Diabetic foot ulcers: Pathophysiology, immune dysregulation, and emerging therapeutic strategies. Biomedicines 2025;13(5):1-17.
5. Copari-Vargas E, Copari-Vargas LE, Copari-Vargas TL, *et al.* Bacteriological profile and antibiotic susceptibility in patients with diabetic foot infections. Cureus 2025;17(4):e82809.
6. Lipsky BA, Silverman MH, Joseph WS. A proposed new classification of skin and soft tissue infections modeled on the subset of diabetic foot infection. Open Forum Infect Dis 2016;4(1).
7. Senneville É, Albalawi Z, van Asten SA, *et al.* IWGDF/IDSA guidelines on the diagnosis and treatment of diabetes-related foot infections (IWGDF/IDSA 2023). Diabetes Metab Res Rev 2024;40(3):e3687.
8. Schmidt BM, Kaye KS, Armstrong DG, *et al.* Empirical antibiotic therapy in diabetic foot ulcer infection increases hospitalization. Open Forum Infect Dis 2023;10(10).
9. Limato R, Lazarus G, Dernison P, *et al.* Optimizing antibiotic use in Indonesia: A systematic review and synthesis of current evidence to inform opportunities for intervention. Lancet Reg Health Southeast Asia 2022;2:100013.
10. Permana H, Saboe A, Soetedjo NN, *et al.* Empirical antibiotic for diabetic foot infection in Indonesian tertiary hospital, is it time to rethink the options? Acta Medica Indones 2022;54(2):247-254.
11. Aviatin M, Sauriasari R, Yunir E, *et al.* Evaluation of the use of antimicrobial therapy for treating diabetic foot infections in an Indonesia referral hospital: A retrospective cohort study. Infect Chemother 2023;55(1):80-89.
12. Wu S, Tannous E, Haldane V, *et al.* Barriers and facilitators of implementing interventions to improve appropriate antibiotic use in low- and middle-income countries: A systematic review based on the consolidated framework for implementation research. Implement Sci 2022;17(1):30.
13. Perkumpulan Endokrinologi Indonesia. Pedoman pengelolaan dan pencegahan diabetes melitus tipe 2 di Indonesia 2021. Jakarta: PB Perkeni; 2021.
14. Sanders ER. Aseptic laboratory techniques: Plating methods. J Vis Exp 2012;(63):e3064.
15. Tripathi N, Zubair M, Sapra A. Gram staining. Treasure Island: StatPearls Publishing; 2025.
16. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. Wayne: CLSI; 2020.
17. Maity S, Leton N, Nayak N, *et al.* A systematic review of diabetic foot infections: Pathogenesis, diagnosis, and management strategies. Front Clin Diabetes Healthc 2024;5:1393309.
18. Murphy-Lavoie HM, Ramsey A, Nguyen M, *et al.* Diabetic foot infections. Treasure Island: StatPearls Publishing; 2025.
19. Bandyk DF. The diabetic foot: Pathophysiology, evaluation, and treatment. Semin Vasc Surg 2018;31(2):43-48.
20. Rodríguez-Rodríguez N, Martínez-Jiménez I, García-Ojalvo A, *et al.* Wound chronicity, impaired immunity and infection in diabetic patients. MEDICC Rev 2021;24(1):44-58.
21. Hadi P, Rampal S, Neela VK, *et al.* Distribution of causative microorganisms in diabetic foot infections: A ten-year retrospective study in a tertiary care hospital in central Malaysia. Antibiotics 2023;12(4):687.
22. Yunir E, Tahapary DL, Tarigan TJE, *et al.* Non-vascular contributing factors of diabetic foot ulcer severity in national referral hospital of Indonesia. J Diabetes Metab Disord 2021;20(1):805-813.
23. Sauriasari R, Yunir E, Saptaningsih AB. Socioeconomic and clinical profile of diabetic foot ulcer patients with national health insurance during pandemic COVID-19 in Indonesia. J Kefarmasian Indones 2024;15(1):21-33.
24. Fitrianingsih, Veryanti PR, Yunir E, *et al.* Factors affecting mortality in diabetic foot ulcer infection patients in national referral hospital, Jakarta, Indonesia: 4-year cross-sectional study. J Appl Pharm Sci 2025;15,(4):262-273.
25. Dinata IGS, Udrayana O, Pratama AAGW. High ulcer severity and amputation prevalence of diabetic foot infection patients in Buleleng Regency General Hospital Bali. Intisari Sains Medis 2022;13(2):629-631.

26. Vikram M, Iskandar D, Ardiyanto A, *et al.* Prevalence of diabetic foot ulcers in patients with type 2 diabetes mellitus. J Medihealtico 2024;5(6):1215-1223.
27. Hariftyani AS, Novida H, Edward M. Profile of diabetic foot ulcer patients at tertiary care hospital in Surabaya, Indonesia. J Berk Epidemiol 2021;9(3):293-302.
28. McNulty JN, Lewis BJ, La Fontaine J, *et al.* Diabetes foot wound healing—A collaborative approach. Diabetes 2018;67(Suppl 1):645-P.
29. Troisi N, Ercolini L, Chisci E, *et al.* Diabetic foot infection: Preliminary results of a fast-track program with early endovascular revascularization and local surgical treatment. Ann Vasc Surg 2016;30:286-291.
30. Dutta A, Bhansali A, Rastogi A. Early and intensive glycemic control for diabetic foot ulcer healing: A prospective observational nested cohort study. Int J Low Extrem Wounds 2023;22(3):578-587.
31. Patil MD, Gunasekaran U, Fontaine JL, *et al.* Does improving glycemic control accelerate healing of diabetic foot ulcers? Diabetes 2018;67(Suppl 1):2218-PUB.
32. Moret CS, Schöni M, Waibel FWA, *et al.* Correction of hyperglycemia after surgery for diabetic foot infection and its association with clinical outcomes. BMC Res Notes 2022;15(1).
33. Capobianco CM, Stapleton JJ. Diabetic foot infections: A team-oriented review of medical and surgical management. Diabet Foot Ankle 2010;1:10.3402.
34. Whisstock C, Volpe A, Ninkovic S, *et al.* Multidisciplinary approach for the management and treatment of diabetic foot infections with a resorbable, gentamicin-loaded bone graft substitute. J Clin Med 2020;9(11).
35. Wang G, Wang L, Wang Y, *et al.* Multidisciplinary approach to scheduling surgery for diabetic foot: A case report. BMC Musculoskelet Disord 2019;20(1):168.
36. Sumpio BE, Armstrong DG, Lavery LA, *et al.* The role of interdisciplinary team approach in the management of the diabetic foot: A joint statement from the society for vascular surgery and the American Podiatric Medical Association. J Vasc Surg 2010;51(6):1504-1506.
37. Cabeza de Vaca FG, Macias AE, Ramirez WA, *et al.* Salvaging diabetic foot through debridement, pressure alleviation, metabolic control, and antibiotics. Wound Repair Regen 2010;18(6):567-571.
38. Vuorlaakso M, Karèn V, Kiiski J, *et al.* Multidisciplinary management of diabetic foot infection associated with improved 8-year overall survival. J Diabetes Complications 2024;38(5).
39. Setacci C, de Donato G, Tadiello M, *et al.* Evidence on the need for an integrated approach to the management of diabetes: The surgical perspective. Transl Med UniSa 2020;21:4-6.
40. Faglia E, Clerici G, Caminiti M, *et al.* The role of early surgical debridement and revascularization in patients with diabetes and deep foot space abscess: retrospective review of 106 patients with diabetes. J Foot Ankle Surg Off Publ Am Coll Foot Ankle Surg 2006;45(4):220-226.
41. Liu X, Ren Q, Zhai Y, *et al.* Risk factors for multidrug-resistant organisms infection in diabetic foot ulcer. Infect Drug Resist 2022;15:1627-1635.
42. Pessoa e Costa T, Duarte B, João AL, *et al.* Multidrug-resistant bacteria in diabetic foot infections: Experience from a portuguese tertiary centre. Int Wound J 2020;17(6):1835-1839.
43. Kathirvel M, Prabakaran V, Jayarajan J, *et al.* Risk factors for the diabetic foot infection with multidrug-resistant microorganisms in South India. Int Surg J 2018;5(2):675-682.
44. Yan X, Song J fang, Zhang L, *et al.* Analysis of risk factors for multidrug-resistant organisms in diabetic foot infection. BMC Endocr Disord 2022;22(1):46.
45. Zubair M, Malik A, Ahmad J. Study of plasmid-mediated extended-spectrum β-lactamase-producing strains of enterobacteriaceae, isolated from diabetic foot infections in a North Indian tertiary-care hospital. Diabetes Technol Ther 2012;14(4):315-324.
46. Stacey HJ, Clements CS, Welburn SC, *et al.* The prevalence of methicillin-resistant Staphylococcus aureus among diabetic patients: A meta-analysis. Acta Diabetol 2019;56(8):907-921.
47. Zhou S, Hu X, Wang Y, *et al.* The global prevalence of methicillin-resistant Staphylococcus Aureus in patients with diabetic foot ulcers: A systematic review and meta-analysis. Diabetes Metab Syndr Obes 2024;17:563-574.
48. Dorresteijn JA, Kriegsman DM, Assendelft WJ, *et al.* Patient education for preventing diabetic foot ulceration. Cochrane Database Syst Rev 2014;2014(12):CD001488.
49. Gershater MA, Pilhammar E, Apelqvist J, *et al.* Patient education for the prevention of diabetic foot ulcers: Interim analysis of a randomised controlled trial due to morbidity and mortality of participants. Int Diabetes Nurs 2011;8(3):102-107b.
50. Abbas ZG. Preventive foot care and reducing amputation: a step in the right direction for diabetes care. Diabetes Manag 2013;3(5):427-435.