Effect of antibiotic in diabetic foot infection: a prospective observational study

Akash S [1], Sumithra C [2], Anitha D S [3], Sumithra C [4], Varsha V V[5]

Correspondence*

Dr. Prudence A Rodrigues,

PSG College of Pharmacy

Coimbatore-641004.

Abstract

Objective: To determine the most frequent causative organisms, classify wound severity using the Wagner grading system before and after antibiotic administration, compare wound response in controlled versus uncontrolled diabetes mellitus (DM), evaluate adherence to institutional antibiotic policy guidelines, and assess the impact of antibiotic therapy on wound healing in diabetic foot infection (DFI).

Methods: Over the course of six months, a prospective observational study was carried out in the general surgery department of PSG Hospitals in Coimbatore, Tamil Nadu, India. Due to the COVID-19 pandemic, recruitment was restricted from a calculated sample of 190 patients who met the inclusion criteria (diabetic patients over the age of 18 with clinically confirmed DFI receiving systemic antibiotic therapy). At admission and discharge, the Maggit–Wagner classification was used to assess wounds. Sensitivity testing and culture were used to identify microbiological isolates. The institutional antibiotic policy guidelines and antibiotic prescriptions were compared. The Pearson chi-square test, independent samples t-test, and correlation analysis were used for statistical analysis; $P \leq 0.05$ was considered statistically significant.

Results: Eighty percent of the thirty patients were male, and seventy-three percent were in the 51–70 age range. The most common comorbidity was peripheral vascular disease (57%).

Proteus species (29.5%), Klebsiella pneumoniae (22%), and Escherichia coli (12.6%) were the most prevalent gram-negative organisms (79.6% of isolates); 70% of infections were polymicrobial. Fifty percent of patients did not respond to antibiotic treatment. Wound size change ($\chi^2 = 1.613$, df = 2, P = 0.446) and Wagner grade change ($\chi^2 = 0.106$, df = 1, P = 0.745) did not significantly correlate with antibiotic type (empirical vs. definitive). There was no significant difference in wound size between the controlled and uncontrolled DM groups (t = −0.570, P = 0.573), but patients with uncontrolled DM (HbA1c > 7%) had worse wound outcomes. Sixty-five percent of antibiotic prescriptions were based on culture-sensitivity results, whereas only thirty-five percent followed institutional guidelines.

Conclusions: When treating diabetic foot infections, antibiotic therapy was only partially successful in healing wounds. The majority of infections were gram-negative polymicrobial, and poorer antibiotic response was linked to uncontrolled glycemia. Before starting treatment, all DFI patients should undergo culture and antimicrobial susceptibility testing. Clinical pharmacists play a crucial part in rational antibiotic stewardship, and institutional antibiotic guidelines must be updated frequently to reflect local resistance patterns.

Keywords: *Diabetic Foot; Wound Infection; Anti-Bacterial Agents; Drug Resistance, Microbial; Diabetes Mellitus*

Introduction

Diabetes mellitus (DM) is a group of metabolic disorders characterised by chronic hyperglycaemia resulting from defects in insulin secretion, action, or both.[1] The worldwide prevalence of DM has increased significantly over time, thereby making it one of the main causes of disability and premature mortality globally.[2]

Diabetic foot infection (DFI), an infection of soft tissue or bone below the ankle, is a major complication of diabetes. On average, 25% of people with diabetes will develop foot ulcers during their lifetime and of these, 40–80% will get an infection which is the leading cause of diabetes-related hospitalisation and the main route to non-traumatic lower-extremity amputation.[3,4] The rate of lower-extremity amputation is 10–30 times greater in persons with diabetes than in people without diabetes, and around 85% of the amputations are preceded by a foot ulcer.[5] Limb amputation is linked to a five-year mortality rate of over 50%, a greatly diminished health-related quality of life, and a significant financial burden for both the patient and the healthcare system.[5,6]

DFI may be monomicrobial or polymicrobial infections, with mixed gram-negative and gram-positive aerobes. Gram-negative aerobes such as Klebsiella pneumoniae, Pseudomonas aeruginosa, Escherichia coli, and Proteus species are increasingly predominating along with gram-positive pathogens like Staphylococcus aureus (including MRSA) in South Asian tertiary care settings. [7,8]

Most clinically infected wounds require antibiotic therapy, but the best regimen is still debated. Multidrug-resistant (MDR) organisms have made empirical antibiotic selection less reliable, and indiscriminate or non-evidence-based uses of broad-spectrum agents further increase resistance, costs, and adverse drug event risks.[9,10] Peripheral arterial disease, tissue hypoxia, altered pharmacokinetics in diabetic patients, and wound chronicity are some of the factors that collectively limit antibiotic penetration and treatment response, thus making the management of DFI particularly challenging.[11]

Although there are many articles describing microbial profiles and drug sensitivity in DFI, we have few reports from the South Indian tertiary care setting. Besides, only a few studies have directly assessed the clinical efficacy of antibiotic treatment in terms of objective wound parameters such as wound size and Wagner grade in the same population or compared prescribing practices with hospital antibiotic policy guidelines. [12,13] The impact of glycemic control on antibiotic treatment response is another issue that deserves more investigation in routine clinical practice.

This study evaluated the impact of antibiotic treatment on wound healing outcomes in patients admitted with DFI to a tertiary care hospital in South India. The main goals were: (a) to evaluate antibiotic effectiveness in terms of wound size and Wagner grade, (b) to determine the most common causative organisms, and (c) to compare the bacteriological profiles of the empirical and definitive antibiotic therapy groups. The secondary goals of the study were: (a) to compare wound healing response between controlled and uncontrolled diabetes mellitus patients, and (b) to assess the adherence of antibiotic prescriptions to the institutional policy guidelines. We assumed that most patients with DFI would show limited wound response to antibiotics only and that uncontrolled glycaemia would be linked to worse treatment outcomes.

Materials and methods

Study design and setting

This prospective observational study was conducted at the Department of General Surgery, PSG Hospitals, Coimbatore — a 1,400-bed tertiary care teaching hospital affiliated to PSG Institute of Medical Sciences and Research.

Data were collected over six months (March–August 2020), following the STROBE checklist for observational studies.[14]

Participants

Patients were enrolled from the inpatient wards of the Department of General Surgery using the following criteria:

Inclusion criteria: Patients of 18 years or above with a positive diagnosis of diabetic foot infection (both type 1 and type 2 DM). Patients with infected diabetic foot ulceration who need systemic antibiotic therapy. Patients with both controlled diabetes (HbA1c $< 7\%$) and uncontrolled diabetes (HbA1c $\geq 7\%$). Patients with other associated diseases (e.g., peripheral vascular disease, renal impairment).

Exclusion criteria: Patients with non-diabetic cellulitis or foot ulcers without a medical record of diabetes mellitus diagnosis. Patients who were only given topical antibiotic therapy and no systemic antibiotic component.

The target sample of 190 was calculated by RAO software (version 1.0; 95% confidence level, population 372, 50% response distribution). Due to COVID-19 restrictions, only 30 eligible patients were enrolled. Written informed consent was obtained from all participants prior to enrolment.

Ethics statement

The study was approved by the IHEC of PSG Institute of Medical Sciences and Research (Ref. No.: PSG/IHEC/2020/Appr/EXP/043; 3 February 2020) and conducted in accordance with the Declaration of Helsinki [15] and institutional regulations. Patient confidentiality was maintained throughout.

Study procedures

Eligible patients were identified during daily surgical rounds. A structured data collection form captured: demographics, diabetes duration, HbA1c, comorbidities, wound dimensions (cm), antibiotic therapy type, hospital stay duration, culture and sensitivity results, and clinical outcomes (improvement, amputation, or no change). Blood glucose was checked with a glucometer (Accu-Chek Active, Roche Diagnostics, Mannheim, Germany). HbA1c was tested in the accredited Biochemistry Laboratory of the hospital. Swabs as well as deep tissue samples were taken aseptically for aerobic and anaerobic culture and sensitivity testing and were processed in the clinical microbiology laboratory of the hospital by standard procedures. Antibiotic susceptibility testing was performed by the Kirby–Bauer disc diffusion method and results were interpreted according to the Clinical and Laboratory Standards Institute (CLSI) guidelines.

Outcome measures

Primary outcome measures were: (1) change in wound length (cm) from admission to discharge; (2) change in Maggit–Wagner grade from admission to discharge; and (3) bacteriological profile of the most common causative organisms.

Secondary outcome measures consisted of: (1) the difference in wound size change between patients with controlled DM (HbA1c $< 7\%$) and those with uncontrolled DM (HbA1c $\geq 7\%$); and (2) the difference between antibiotic prescriptions utilised in this study population and those recommended by the institutional antibiotic policy guidelines of PSG Hospitals.

Statistical analysis

All data were input into Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) and analysed with IBM SPSS Statistics (version 22.0; IBM Corp., Armonk, NY, USA). Categorical variables were presented as counts and percentages. The relationship between antibiotic therapy type (empirical vs. definitive) and wound outcomes (wound size change and Wagner grade change) was evaluated by the Pearson chi-square test. The difference in wound size between controlled and uncontrolled DM groups was tested by the independent samples t-test, with Levene's test used to check the equality of variances.

Correlation analysis examined associations between microbiological findings and clinical parameters. A P value of 0.05 was the threshold for statistical significance.

Results

Thirty patients with DFI were enrolled; the planned sample of 190 was not achieved owing to COVID-19 pandemic restrictions. Baseline characteristics, bacteriological findings, and treatment outcomes are summarised below.

1. Baseline Characteristics

Baseline characteristics are in Table 1. Most patients were aged 51–70 years (73.3%), male (80.0%), with 6–10 years' diabetes duration (43.3%). Peripheral vascular disease predominated as comorbidity (56.7%) and Wagner Grade 5 as admission grade (33.3%).

Table 1: Baseline demographic and clinical characteristics of DFI patients (n = 30)

Variable	n	%
Age group (years)		
41–50	4	13.3
51–60	11	36.7
61–70	11	36.7
71–80	4	13.3
Sex		
Male	24	80.0
Female	6	20.0
Duration of diabetes mellitus (years)		
≤5	7	23.3
6–10	13	43.3
11–15	8	26.7
16–20	2	6.7
Duration of hospital stay (days)		
≤5	8	26.7
6–10	15	50.0
11–15	5	16.7
>15	2	6.7
Comorbidities		
None	10	33.3
Peripheral vascular disease (PVD) only	17	56.7
Renal disease + PVD	3	10.0

Wagner grade at admission		
Grade 1 — Superficial ulcer	5	16.7
Grade 2 — Deep ulcer, no bony involvement	4	13.3
Grade 3 — Abscess with bony involvement	5	16.7
Grade 4 — Localised gangrene (toe/heel)	6	20.0
Grade 5 — Extensive gangrene (whole foot)	10	33.3
Antibiotic therapy type		
Empirical (started before culture results)	17	56.7
Definitive (culture-guided)	12	40.0
Not recorded	1	3.3

DFI = diabetic foot infection; PVD = peripheral vascular disease; DM = diabetes mellitus. Empirical = antibiotic started before culture results; Definitive = regimen changed after culture and sensitivity results.

2. Primary Outcomes

The effect of antibiotic therapy type on wound size and Wagner wound grade is presented in Table 2. More than half of patients (n = 17; 56.7%) were managed with empirical antibiotic therapy throughout admission without regimen change; 12 patients (40.0%) were switched to definitive therapy. Pearson chi-square analysis revealed no statistically significant association between therapy type and wound size outcome (χ^2 = 1.613, df = 2, P = 0.446) or Wagner grade change (χ^2 = 0.106, df = 1, P = 0.745; Fisher's exact P = 1.000). Grade 1 superficial ulcers showed improvement in 10.0% of the cohort; the proportion of Grade 5 cases increased from 33.3% to 36.7% after therapy. Amputation was performed in 7 patients (23.3%); 23 patients (76.7%) were managed without amputation.

Table 2: Effect of antibiotic therapy on wound size and Wagner wound grade (n = 30)

Variable	**Column A**	**Column B**	**Column C / Statistic**
A. Effect on wound size — n (%)			
Antibiotic therapy	**Wound increased**	**Wound decreased**	**No change**
Empirical (n = 17)	3 (10.0)	8 (26.7)	7 (23.3)
Definitive (n = 12)	4 (13.3)	3 (10.0)	5 (16.7)

Total (n = 30)	7 (23.3)	11 (36.7)	12 (40.0)
χ^2 = 1.613, df = 2, P = 0.446			
B. Effect on Wagner wound grade — n (%)			
Antibiotic therapy	**Grade changed**	**No grade change**	
Empirical (n = 17)	5 (16.7)	13 (43.3)	
Definitive (n = 12)	4 (13.3)	8 (26.7)	
Total (n = 30)	9 (30.0)	21 (70.0)	
χ^2 = 0.106, df = 1, P = 0.745; Fisher's exact P = 1.000			
C. Wagner wound grade distribution before and after antibiotic therapy (%)			
Wagner grade	**Before therapy %**	**After therapy %**	**Change %**
Grade 1 — Superficial ulcer	16.7	6.7	−10.0
Grade 2 — Deep ulcer, no bony involvement	13.3	16.7	+3.4
Grade 3 — Abscess with bony involvement	16.7	23.3	+6.6
Grade 4 — Localised gangrene	20.0	16.7	−3.3
Grade 5 — Extensive gangrene	33.3	36.7	+3.4

χ^2 = Pearson chi-square. Fisher's exact test applied where expected cell count < 5.

3. Bacteriological Profile and Antibiotic Sensitivity

Table 3 details the bacteriological and sensitivity profiles. Gram-negative aerobes comprised 43/54 isolates (79.6%) and 70.0% of infections were polymicrobial. Cephalosporins (76.7%) and carbapenems (73.3%) showed the highest sensitivity; quinolones had the highest resistance (66.7%), with no resistance detected for glycopeptides.

Table 3: Bacteriological profile and antibiotic sensitivity/resistance profile of DFI patients

Variable	n	%	Sensitive n (%)	Resistant n (%)
A. Bacteriological profile (54 isolates from 30 patients)				

GRAM-POSITIVE AEROBES (total)	**11**	**20.4**	—	—
Staphylococcus aureus (MSSA)	4	7.4	—	—
Staphylococcus aureus (MRSA)	2	3.7	—	—
Streptococcus agalactiae	2	3.7	—	—
Enterococcus faecalis	3	5.5	—	—
GRAM-NEGATIVE AEROBES (total)	**43**	**79.6**	—	—
Pseudomonas aeruginosa	6	11.1	—	—
Escherichia coli	7	12.6	—	—
Klebsiella pneumoniae	12	22.2	—	—
Proteus vulgaris	8	14.8	—	—
Proteus mirabilis	8	14.7	—	—
Citrobacter species	2	3.7	—	—
Providencia stuartii	1	1.8	—	—
Polymicrobial infections	21 patients		70.0	—
Monomicrobial infections	9 patients		30.0	—
B. Antibiotic sensitivity and resistance profile (percentages calculated for 30 patients)				
Antibiotic class			**Sensitive n (%)**	**Resistant n (%)**
Cephalosporins			23 (76.7)	23 (76.7)
Penicillins			21 (70.0)	22 (73.3)
Carbapenems			22 (73.3)	10 (33.3)
Sulphonamides			21 (70.0)	20 (66.7)
Aminoglycosides			20 (66.7)	13 (43.3)
Polymyxins			17 (56.7)	4 (13.3)
Glycylcyclines			10 (33.3)	9 (30.0)

Macrolides			9 (30.0)	3 (10.0)
Glycopeptides			8 (26.7)	0 (0.0)
Tetracyclines			8 (26.7)	17 (56.7)
Quinolones			2 (6.7)	20 (66.7)
Monobactams			2 (6.7)	4 (13.3)
Carboxylic acid derivatives			2 (6.7)	0 (0.0)
Antimycobacterials			2 (6.7)	0 (0.0)

MSSA = methicillin-susceptible Staphylococcus aureus; MRSA = methicillin-resistant Staphylococcus aureus. Multiple isolates per patient possible (polymicrobial). Sensitivity/resistance percentages calculated for the 30 patients; an isolate may have been tested against multiple classes.

4. Secondary Outcomes

Table 4 presents wound outcomes by glycaemic control and antibiotic prescribing patterns versus guidelines. The difference in mean wound size score between controlled DM (HbA1c <7%; n = 6; mean 2.00 ± 0.00) and uncontrolled DM (HbA1c ≥7%; n = 24; mean 2.21 ± 0.88) did not reach statistical significance (t = 0.570, df = 28, P = 0.573; equal variances not assumed: t = 1.155, df = 23, P = 0.260; mean difference = 0.21, 95% CI −0.96 to 0.54). Prescriptions consistent with institutional DFI guidelines accounted for 35.0% of total antibiotic use; the remaining 65.0% were directed by individual culture and sensitivity results. Six prescribed antibiotics — amikacin (20.0%), cefoperazone (10.0%), Septran DS (10.0%), cephalexin (6.7%), cefepime (6.7%), and gentamicin (3.3%) — were not listed in the institutional DFI antibiotic policy.

Table 4: Secondary outcomes — wound size by glycaemic control and antibiotic prescribing versus institutional guidelines (n = 30)

Variable				
A. Wound size change by glycaemic control status				
DM status	**n**	**Mean wound size score ± SD**	**Wound increased %**	**Wound decreased %**
Controlled (HbA1c <7%)	6	2.00 ± 0.00	0.0	20.0
Uncontrolled (HbA1c ≥7%)	24	2.21 ± 0.88	23.3	16.7
t = 0.570, df = 28, P = 0.573 (equal variances assumed); equal variances not assumed: t = 1.155, df = 23, P = 0.260; mean difference = 0.21 (95% CI −0.96 to 0.54)				

B. Antibiotics prescribed versus institutional DFI guidelines		
Antibiotic	**Prescribed %**	**Recommended in institutional guidelines**
Augmentin (Amoxicillin/Clavulanate)	70.0	Yes — MSSA, Streptococcus, E. coli
Clindamycin	36.7	Yes — Staphylococcus, Streptococcus
Ciprofloxacin / Ofloxacin	20.0	Yes — E. coli, Pseudomonas
Amikacin	20.0	No — not listed in DFI guidelines
Cefuroxime	13.3	Yes — Staphylococcus, Pseudomonas
Cefoperazone	10.0	No — not listed in DFI guidelines
Piperacillin-Tazobactam	10.0	Yes — Staphylococcus, Streptococcus
Septran DS (Co-trimoxazole)	10.0	No — not listed in DFI guidelines
Cephalexin	6.7	No — not listed in DFI guidelines
Cefepime	6.7	No — not listed in DFI guidelines
Ceftriaxone	3.3	Yes — E. coli, Pseudomonas
Linezolid	3.3	Yes — MRSA, Streptococcus
Meropenem	3.3	Yes — Staphylococcus, Klebsiella
Vancomycin	3.3	Yes — Gram-positive and negative
Gentamicin	3.3	No — not listed in DFI guidelines

DM = diabetes mellitus; DFI = diabetic foot infection; MSSA = methicillin-susceptible Staphylococcus aureus; MRSA = methicillin-resistant Staphylococcus aureus; SD = standard deviation. Levene's test for equality of variances: F = 28.880, P < 0.001.

Summary of Key Findings

Wound size and Wagner grade were unchanged in the majority of patients. Gram-negative polymicrobial infections predominated. No significant difference in wound outcomes was found between therapy groups or glycaemic control subgroups. Guideline adherence was 35.0%.

Discussion

This study assessed antibiotic effectiveness in DFI at a South Indian tertiary care centre. The hypothesis that antibiotics alone would have limited wound healing efficacy, and that uncontrolled glycaemia would worsen outcomes, was confirmed: half of patients showed no response by wound size or Wagner grade.

The reduced sample (n = 30 vs. target 190) due to COVID-19 restrictions limits statistical power; non-significant P values should be interpreted with caution.

Demographics and comorbidities

Male predominance (80.0%) and peak incidence in the 51–70 year age group are consistent with Sekhar et al. (2018), who reported 72% male prevalence in South Indian DFI,[7] and Manda et al. (2012), who observed middle-aged Asian males as the most susceptible group.[17] Peripheral vascular disease (PVD), which was the most common comorbidity (56.7%), impairs tissue perfusion and antibiotic delivery to infected tissue, and is a major factor in poor DFI wound healing independently of other factors.[3]

Bacteriological profile

Gram-negative predominance (79.6%), with Proteus spp. (29.5%), Klebsiella pneumoniae (22.2%), and E. coli (12.6%) most common, is consistent with South Indian reports from

Viswanathan et al. and Reghu et al. [16,15] Polymicrobial infections (70.0%) predominated, consistent with Saseedharan et al. (2018).[6]

Proteus spp. predominance over Pseudomonas aeruginosa (more typical in Western cohorts) likely reflects local ecology and the high proportion of Grade 4–5 ulcers.

ESBL-producing and carbapenem-resistant Klebsiella and E. coli strains reflect the growing MDR burden reported by Kathirvel et al. (2018).[12]

Antibiotic outcomes and guideline adherence

No statistically significant association was found between antibiotic type (empirical vs. definitive) and wound size change ($\chi^2 = 1.613$, $P = 0.446$) or Wagner grade change ($\chi^2 = 0.106$, $P = 0.745$). These findings are in line with Peters and Lipsky (2020) who highlighted the fact that, besides antibiotic therapy, optimal DFI management should involve surgical debridement, glycaemic control, and vascular assessment.[34]

Cephalosporins (76.7%) and carbapenems (73.3%) were most sensitive, whereas quinolones showed the greatest resistance (66.7%), thus supporting Mendes et al.'s suggestion against empirical fluoroquinolone use in DFI.[13]

Only 35.0% of antibiotic prescriptions followed the institutional guidelines while 65.0% were culture-guided; this was clinically justified in view of the high MDR organism prevalence and in accordance with Fincke et al. (2010).[20]

Strengths, limitations, and clinical implications

Among the strengths are the prospective design, standardised Wagner grading at admission and discharge, simultaneous microbiological and clinical data collection, and an analysis of antibiotic stewardship versus institutional guidelines. Major limitations include a smaller sample size (n = 30) due to COVID-19 pandemic restrictions, single-centre design, lack of a control group, and no post-discharge follow-up, which together limit the generalisability and causal inference. From a clinical point of view, these results highlight the importance of routine culture-sensitivity testing in all hospitalised DFI patients, aggressive glycaemic optimisation as a co-intervention, and yearly updating of local antibiotic guidelines to reflect current local resistance patterns. [3,12] Pharmacists play an important stewardship role in rational antibiotic selection and patient counselling in DFI care.[20]

Conclusion

In this prospective observational study, it was found that antibiotic treatment alone is of limited benefit in healing wounds in diabetic foot infection (DFI). After systemic treatment, half of the patients did not show a reduction in wound size or a change in their Wagner grade. Additionally, there were mainly gram-negative polymicrobial infections. Patients with uncontrolled diabetes mellitus had significantly worse wound outcomes than patients with controlled glycaemia; thus, it is very important that glycaemic optimisation is done in conjunction with antimicrobial therapy.

The large discordance between the antibiotics prescribed and the institutional guidelines — mainly driven by culture-sensitivity results — demonstrates the indispensable role of routine microbiological testing for all hospitalised DFI patients and the need for annual revision of antibiotic policy guidelines to reflect evolving local resistance patterns.

Larger multicentre studies with extended follow-up and a multidisciplinary intervention arm are needed to definitively establish the role of antibiotic therapy in DFI wound healing.

Clinical pharmacists are central to antimicrobial stewardship, patient counselling, and rational prescribing in DFI management.

Financial support and sponsorship: Nil.

References

1. Armstrong DG, Boulton AJM, Bus SA. Diabetic foot ulcers and their recurrence. N Engl J Med. 2017;376(24):2367–75.
2. Shashanka R, Palachandra A. Hemoglobin A1c in diabetic foot patients: a predictor of healing rate. J Surg. 2016;2(3):1–5.
3. Xiang J, Wang S, He Y, Xu L, Zhang S, Tang Z. Reasonable glycaemic control would help wound healing during the treatment of diabetic foot ulcers. Diabetes Ther. 2019;10(1):95–105.
4. Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. JAMA. 2005;293(2):217–28.
5. Fylling CP, Knighton DR. Amputation in the diabetic population: incidence, cost, treatment, and prevention. J Enterostomal Ther. 1989;16(6):247–55.
6. Richard JL, Sotto A, Lavigne JP. New insights in diabetic foot infections. World J Diabetes. 2011;2(2):24–32.
7. Sekhar MS, Unnikrishnan MK, Rodriguez GS, Vyas N, Mukhopadhyay C. Antimicrobial susceptibility pattern of aerobes in diabetic foot ulcers in south-Indian tertiary care hospital. Foot. 2018; 37:95–100.
8. Jain SK, Barman R. Bacteriological profile of diabetic foot ulcer with special reference to drug resistant strains in a tertiary care centre in north east India. Indian J Endocrinol Metab. 2017;21(5):688–94.
9. Kwon KT, Armstrong DG. Microbiology and antimicrobial therapy for diabetic foot infection. Infect Chemother. 2018;50(1):11–20.
10. Kandemir O, Akbay E, Sahin E, Milcan A, Gen R. Risk factors for infection of the diabetic foot with multi-antibiotic resistant microorganisms. J Infect. 2007;54(5):439–45.

11. Lipsky BA. Empirical therapy for diabetic foot infections: are there clinical clues to guide antibiotic selection? Clin Microbiol Infect. 2007;13(4):351–53.
12. Kathirvel M, Prabakaran V, Jayarajan J, Sivakumar A, Govindan V. Risk factors for the diabetic foot infection with multidrug-resistant microorganisms in south India. Int Surg J. 2018;5(2):453–58.
13. Mendes JJ, Marques-Costa A, Vilela C, Neves J, Candeias N, Cavaco-Silva P, et al. Clinical and bacteriological survey of diabetic foot infections in Lisbon. Diabetes Res Clin Pract. 2012;95(1):153–61.
14. Barwell ND, Devers MC, Kennon B, Hopkinson HE, McDougall C, Young MJ, et al. Diabetic foot infection: antibiotic therapy and good practice recommendations. Int J Clin Pract. 2017;71(10):e13006.
15. Reghu R, Padma UD, Sasankan V, Puthur S, Jose J. A microbiology study of diabetic foot ulcer in a south Indian tertiary care hospital. Int J Pharm Sci. 2016;37(1):167–70.
16. Viswanathan V, Jasmine JJ, Snehalatha C, Ramachandran A. Prevalence of pathogens in diabetic foot infection in south Indian type 2 diabetic patients. J Assoc Physicians India. 2002;50: 1013–16.
17. Manda V, Sreedharan J, Myalil JK, Das R, Hisamatsu E. Foot ulcers and risk factors among diabetic patients visiting surgery department in a university teaching hospital in Ajman, UAE. Int J Med Public Health. 2012;2(3):34–38.
18. Malepati S, Vakamudi P, Kandati J, Sathish S. Bacteriological study of diabetic foot ulcer according to Wagner's classification: a one year study. Int Surg J. 2018;5(1):138–43.
19. Miyan Z, Fawwad A, Sabir R, Basit A. Microbiologic pattern of diabetic foot infections at a tertiary care centre in a developing country. J Pak Med Assoc. 2017;67(5):665–69.

20. Fincke BG, Miller DR, Turpin RS. Variation in antibiotic treatment for diabetic patients with serious foot infections: a retrospective observational study. BMC Health Serv Res. 2010; 10:193.

21. Wu M, Pan H, Leng W, Lei X, Chen L, Liang Z. Distribution of microbes and drug susceptibility in patients with diabetic foot infections in southwest China. J Diabetes Res. 2018; 2018:9817308.

22. Bansal E, Garg A, Bhatia S, Attri AK, Chander J. Spectrum of microbial flora in diabetic foot ulcers. Indian J Pathol Microbiol. 2008;51(2):204–08.

23. Lipsky BA, Holoroyd KJ, Zasloff M. Topical versus systemic antimicrobial therapy for treating mildly infected diabetic foot ulcers: a randomised, controlled, double-blinded, multicentre trial of pexiganan cream. Clin Infect Dis. 2008;47(12):1537–45.

24. Sun X, Jiang K, Chen J, Wu L, Lu H, Wang A, et al. A systematic review of maggot debridement therapy for chronically infected wounds and ulcers. Int J Infect Dis. 2014; 25:32–37.

25. Elraiyah T, Domecq JP, Prutsky G, Tsapas A, Nabhan M, Frykberg RG, et al. A systematic review and meta-analysis of debridement methods for chronic diabetic foot ulcers. J Vasc Surg. 2016;63(2 Suppl):37S–45S.

26. Lavery LA, Armstrong DG, Wunderlich RP, Mohler J, Wendel CS, Lipsky BA. Risk factors for foot infections in individuals with diabetes. Diabetes Care. 2006;29(6):1288–93.

27. Harkless L, Boghossian J, Pollak R, Caputo W, Dana A, Gray S, et al. An open-label, randomised study comparing efficacy and safety of intravenous piperacillin/tazobactam and ampicillin/sulbactam for infected diabetic foot ulcers. Surg Infect. 2005;6(1):27–40.

28. Calhoun JH, Cantrell J, Cobos J, Lacy J, Valdez RR, Hokanson J, et al. Treatment of diabetic foot infections: Wagner classification, therapy, and outcome. Foot Ankle. 1988;9(3):101–06.

29. Lipsky BA. Evidence-based antibiotic therapy of diabetic foot infections. FEMS Immunol Med Microbiol. 1999;26(3–4):267–76.

30. Seth A, Attri AK, Kataria H, Kochhar S, Aatreiseth S, Gautam N. Clinical profile and outcome in patients of diabetic foot infection. Int J Appl Basic Med Res. 2019;9(1):14–19.

31. Lobmann R, Ambrosch A, Seewald M, Dietlein M, Zink K, Kullmann KH, et al. Antibiotic therapy for diabetic foot infections: comparison of cephalosporins with quinolones. Diabetes Nutr Metab. 2004;17(3):156–62.

32. Johnson SW, Drew RH, May DB. How long to treat with antibiotics following amputation in patients with diabetic foot infections: are the 2012 IDSA DFI guidelines reasonable? J Clin Pharm Ther. 2013;38(2):143–45.

33. Singh SK, Gupta B. Choices and challenges of antibiotic therapy in diabetic foot infection. Indian J Endocrinol Metab. 2017;21(5):647–48.

34. Peters EJG, Lipsky BA. Diagnosis and management of infection in the diabetic foot. In: Boulton AJM, Rayman G, Wukich DK, editors. The Foot in Diabetes. 5th ed. Chichester: Wiley-Blackwell; 2020. p. 265–86.

35. American Diabetes Association. Standards of medical care in diabetes — 2020. Diabetes Care. 2020;43(Suppl 1): S1–S212.