Section: Pharmacology

Original Research Article

ANTIBIOTIC PRESCRIBING TRENDS IN DIABETIC FOOT INFECTIONS: A STUDY FROM A TERTIARY CARE HOSPITAL IN KERALA

Received : 01/10/2024
Received in revised form : 12/11/2024
Accepted : 28/11/2024

Keywords:
Antibiotic prescribing patterns, diabetic foot infection, optimal antibiotic therapy.

Corresponding Author:
Dr. Dona Dominic,
Email: donagarent@gmail.com

DOI: 10.47009/jamp.2024.6.6.100

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (6); 522-527

Dona Dominic[1], Ramani P T[2], Sajan M G[3]

[1]Assistant Professor, Department of Pharmacology, Pushpagiri Institute of Medical Sciences & Research Centre, Tiruvalla, Kerala, India
[2]Professor & Head, Department of Pharmacology, Sree Gokulam Medical College & Research Foundation, Venjaramodu, Thiruvananthapuram, Kerala, India
[3]Senior Consultant, Department of Neurosurgery, St. Thomas Hospital, Chethipuzha, Kerala, India

Abstract

Background: Diabetic foot Infections are a major complication of Diabetes Mellitus, significantly contributing to morbidity and mortality. Assessing the prescription pattern of antibiotics is essential for optimizing treatment protocols and improving patient outcomes. The study aimed to analyze the prescribing pattern of antibiotics in diabetic foot infections. **Materials and Methods:** A twelve-month prospective observational study was conducted in patients admitted with Diabetic foot infections in Surgery inpatient wards. Information regarding the patient demographics, comorbid conditions, ulcer characteristics, antibiotic usage, and microbiological culture findings were collected. Data were analyzed using descriptive statistics and relevant statistical methods. **Result:** The study included 162 patients with diabetic foot infections, with a slight male predominance (51.9%). The majority of patients were in the age group of 61-70 years (27.2%), and hypertension was the most common comorbidity (50.6%). Gram-negative organisms were predominant (67.9%), with Pseudomonas aeruginosa (19.4%) and Klebsiella species (14.9%) being the most frequent isolates. Beta-lactam antibiotics accounted for 58.4% of prescriptions, with Cefotaxime (n=76; 17%), Piperacillin-tazobactam (n=67; 15.8%) and Cefoperazone-Sulbactam (n=48; 10.7%) being the most frequently used and 85.8% of patients received antibiotics via the parenteral route. **Conclusion:** The study highlights the predominance of gram-negative organisms, with Pseudomonas aeruginosa being the most frequent isolate, in diabetic foot infections. Beta-lactam antibiotics were the most commonly prescribed, with a preference for parenteral administration due to the severity of infections. These findings emphasize the importance of optimal antibiotic therapy tailored to local microbial patterns to improve outcomes and address antimicrobial resistance in diabetic foot infections.

INTRODUCTION

Diabetes Mellitus is a chronic metabolic disorder that leads to substantial physical, psychological, and economic challenges for individuals and society as a whole. As per the International Diabetes Federation (IDF), approximately 537 million people are living with Diabetes worldwide with increased prevalence in low and middle-income countries like India.[1] Diabetic foot infections (DFI) are one of the major complications of Diabetes causing significant morbidity and mortality.[2] It is a leading issue accounting for majority of the diabetes-related hospital admissions and lower limb amputations.[3] The management of DFI relies on the appropriate antibiotic therapy targeting the possible causative microorganisms. Understanding the prescribing patterns is crucial for several reasons: it can inform clinicians about the most effective empirical therapies based on local microbial resistance profiles, guide the development of targeted antimicrobial stewardship programs, and ultimately improve patient outcomes.[4] In light of the rising concerns surrounding antimicrobial resistance, our study explores the relationship between antibiotic prescribing practices and microbial susceptibility, aiming to provide insights that can enhance clinical decision-making. By analyzing data from patients diagnosed with DFIs, this study seeks to contribute valuable information to the existing body of knowledge regarding antibiotic use in diabetic foot care. As such, it underscores the necessity for continuous monitoring and evaluation of antibiotic prescribing trends to combat the growing threat of resistance while ensuring effective management of diabetic foot infections.

MATERIALS AND METHODS

After obtaining clearance from the Institutional Ethics Committee, this 12-month prospective observational study was conducted on the patients admitted with Diabetic foot infections in the surgery ward of a tertiary care hospital in Kerala. Inclusion criteria were as follows: Age: > 20 years of either gender, diagnosed with diabetic foot infections, and prescribed at least one antibiotic. Pregnant and lactating women, those with ulcers in sites other than the foot, Diabetic patients with HIV and tuberculosis Diabetic patients on cancer chemotherapy, long-term steroid use, and other immunosuppressant drugs were excluded from the study.

Sample size was calculated as per the formula: N = (Zα)2 P Q / D2. With Zα= 1.96 P – 12[5]: the proportion of least commonly prescribed antibiotic. Q = 1 – P. Sample size was calculated to be 162.

Confidentiality and anonymity of the patient's information were maintained during and after the study The relevant data were collected from records of inpatients with a diabetic foot infection admitted during the study period. To evaluate the drug prescribing pattern, a proforma containing relevant details such as demographics (age, sex), inpatient number, admission and discharge dates, duration of hospital stay, clinical data (Clinical diagnosis and associated co-morbid conditions), surgical data (debridement, amputation, skin grafting), laboratory parameters (hemoglobin %, total WBC count, FBS, PPBS, RBS, blood urea, serum creatinine, serum electrolytes) were recorded. Antibiotics prescribed (generic/brand name) with respect to criteria for selection of antibiotics (empirical or definitive based on laboratory investigations, and also to assess the pattern of antimicrobial therapy), the class of AMAs, dosage, route, frequency and duration of administration, before and after culture sensitivity were recorded as per proforma. Drugs prescribed apart from antibiotics were also recorded in the same proforma. The patients were followed up throughout the hospital stay, to assess the course and outcome of antibiotic therapy, to evaluate laboratory data and their implications on antibiotic therapy, any further changes in the antibiotic regimen, and the safety and tolerability of antibiotics. The data collected were analyzed at the end of the study using Microsoft Office Excel and SPSS version 23. Descriptive statistics were employed to summarize the demographic details presenting categorical variables as frequencies(n) and percentages (%).

RESULTS

The study included 162 patients diagnosed with Diabetic foot infections. 84 patients (51.9%) were males and 78 (48.1%) were females. Maximum number of the patients were in the age group 61-70 (27.2%).

The most common co-morbid condition in the study population was hypertension (50.6%). Peripheral arterial disease was identified in 60 patients, renal dysfunction in 45 patients, and coronary artery disease in 17 patients. 16 patients had a history of previous amputations.

Wound Culture characteristics

Microbiology Pattern

The following table shows the pattern of wound cultures obtained. Out of the 97 cultures obtained 68 (70.1%) cultures were monomicrobial and 29 cultures (29.9%) were polymicrobial. Out of the 134 organisms isolated, gram-negative organisms (67.9%) were more predominant than gram-positive ones. Of these Pseudomonas aeruginosa was the most frequent organism (n = 26, 19.4%), Second being Klebsiella species (n=20; 14.9%). Escherichia Coli and Acinetobacter species were isolated in 18 cultures (13.5%). Out of 18, three Acinetobacter were multidrug resistant. Among the gram-positive organisms isolated Staphylococcus aureus was the predominant one. MRSA was isolated in six (4.6%) cultures.

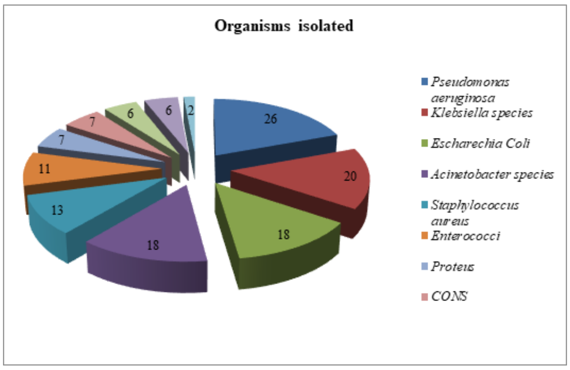

Figure 1: Organisms isolated

Antibiotics used

Beta-lactam antibiotics (n= 261, 58.4%) were the most commonly used group of antibiotics. Among beta-lactam antibiotics, commonly used agents were Cefotaxime (n=76; 17%), Piperacillin-tazobactam (n=67; 15.8%) and Cefoperazone-Sulbactam (n=48; 10.7%).

ISSN (O): 2687-5365; ISSN (P): 2753-6556

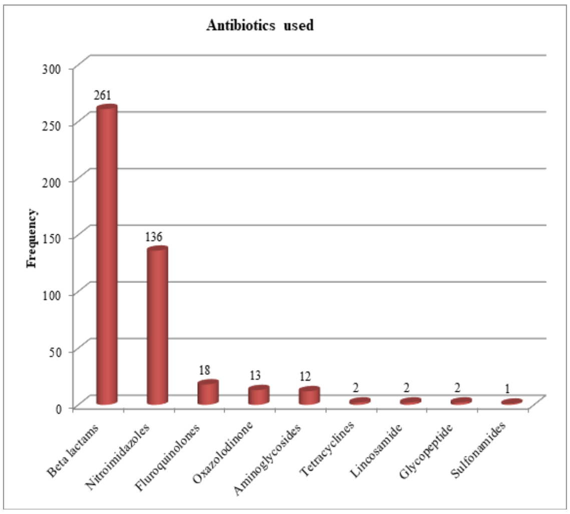

Figure 2: Antibiotics used – group wise

Criteria for Initial Antibiotic Selection

Antibiotics were started empirically in 153 patients (94.4%). In 9 patients (5.6%) initial selection of antibiotics was according to the culture report.

96 patients (59.3%) had either a change or addition of a new antibiotic to the ongoing treatment. 66 patients (40.7%) had no change/addition to the existing treatment. Most of the antibiotics were changed to Piperacillin–Tazobactam alone or in combination with other antibiotics. Cefoperazone–sulbactam and Ciprofloxacin were the next commonly changed / newly added antibiotics. The reason for the change of antibiotics was based on culture and sensitivity reports in 71 patients (73.9%).

Empirical antibiotics

Piperacillin – Tazobactam (n=45, 29.2%) was the most commonly used empirical antibiotic followed by Cefotaxime + Metronidazole (n=40, 26.1%). Crystalline penicillin + Cefotaxime + Metronidazole was used in 25 patients (16.3%) and Cefoperazone – sulbactam + Metronidazole was used in 21 patients (13.7%).

Route of administration

Among the 139 patients (85.8%), antibiotics were administered exclusively through the parenteral route. 22 patients (13.6%) received both parenteral and oral antibiotics. One patient required only an oral route. A total of 23 patients (14.2%) received oral antibiotics.

The pattern of antibiotic therapy

In this study, 155 combinations were used and 99 drugs were given as monotherapy.

Outcome of treatment

Clinical cure was achieved in 78(48%) patients and minor amputations were performed for 45(27.8%) patients and major amputations (above knee and below knee) were done for 36 (22.2%) patients and 3 patients (1.9%) died other co-morbid conditions or complications.

Empirical Antibiotics and clinical cure

Among 25 patients who received Crystalline penicillin + Cefotaxime + Metronidazole as the empirical antibiotic clinical cure was achieved in 4 patients (16%). Only 2 patients received Crystalline penicillin + Cefoperazone – sulbactam + Metronidazole combination as an empirical antibiotic and both of them were cured. In those who received Piperacillin–tazobactam as an empirical antibiotic 6 patients (13.3%) achieved a clinical cure. However, the difference in amputation prevention rates across the antibiotic groups is not statistically significant.

Table 1: Age distribution of the study population.

Age group (in years)	Frequency(n)	Percentage (%)
18-40	13	8
41-50	29	17.9
51-60	40	24.7
61-70	44	27.2
71-80	24	14.8
>80	12	7.4

Table 2: Comorbid conditions of the study population

Condition	Frequency (n)	Percentage (%)
Hypertension	82	50.6
Peripheral arterial disease	60	37.1
Renal dysfunction	45	27.7
Dyslipidemia	40	24.6
CAD	17	10.4
Previous amputations	16	9.8
CVA	7	5.5
Psychiatric illness	5	3.1
Liver dysfunction	4	2.4
Previous Carcinoma	3	1.8
Hypothyroidism	3	1.8
Previous TB	3	1.8
Seizure disorder	1	0.6

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 3: List of Empirical antibiotics

Antibiotic	Frequency (n)	Percentage (%)
Piperacillin – tazobactam	45	29.2
Cefotaxime + Metronidazole	40	26.1
Crystalline penicillin + Cefotaxime + Metronidazole	25	16.3
Cefoperazone – sulbactam + Metronidazole	21	13.7
Cefoperazone – sulbactam	6	3.9
Co-Amoxiclav + Metronidazole	4	2.6
Cefotaxime	4	2.6
Amoxiclav	3	2
Crystalline penicillin + Cefoperazone–sulbactam + Metronidazole	2	1.3
Ampicillin + Gentamicin + Metronidazole	1	0.7
Ceftriaxone + Metronidazole	1	0.7
Co-Amoxiclav + Cefotaxime + Metronidazole	1	0.7
Total	153	100

Table 4: Antibiotics given as monotherapy

Antibiotic	Frequency (n)	Percentage (%)
Piperacillin – tazobactam	61	44.9
Cefoperazone – sulbactam	21	15.4
Ciprofloxacin	11	8.1
Amoxiclav	9	6.6
Linezolid	8	5.9
Cefotaxime	7	5.1
Cloxacillin	6	4.4
Amikacin	4	2.9
Meropenem	3	2.2
Imipenem	2	1.5
Cefuroxime	1	0.7
Levofloxacin	1	0.7
Tetracycline	1	0.7
Vancomycin	1	0.7
Total	136	100

Table 5: Antibiotics given as combination therapy

Antibiotic combination	Frequency	Percentage
Cefotaxime + Metronidazole	40	34.2
Crystalline penicillin + Cefotaxime + Metronidazole	27	23.1
Cefoperazone – sulbactam + Metronidazole	21	17.9
Co- Amoxiclav + Metronidazole	4	3.4
Piperacillin – tazobactam + Linezolid	2	1.7
Meropenem + Gentamicin	2	1.7
Crystalline penicillin + Cefoperazone + Metronidazole	2	1.7
Cefoperazone – sulbactam + Amikacin	2	1.7
Ceftriaxone – sulbactam + Metronidazole	1	0.9
Crystalline penicillin + Cephalexin + Linezolid	1	0.9
Co-Amoxiclav +Cotrimoxazole	1	0.9
Co-Amoxiclav + Cefotaxime	1	0.9
Amoxiclav + Linezolid	1	0.9
Piperacillin –tazobactam + Vancomycin	1	0.9
Piperacillin – tazobactam + Amikacin	1	0.9
Piperacillin – tazobactam + ciprofloxacin	1	0.9
Piperacillin – tazobactam + Norfloxacin	1	0.9
Cefoperazone– sulbactam + Cefotaxime + Metronidazole	1	0.9
Cefoperazone– sulbactam + Tetracycline	1	0.9
Ciprofloxacin – Tinidazole	1	0.9
Ciprofloxacin + Clindamycin	1	0.9
Ciprofloxacin + Cloxacillin	1	0.9
Ofloxacin + Metronidazole	1	0.9
Amikacin+ Clindamycin	1	0.9
Amikacin + Linezolid	1	0.9

DISCUSSION

Infections of the ulcerated foot are the foremost cause of both diabetes-associated hospitalization and lower extremity losses. The management of this infection requires appropriate antibiotic therapy according to the local sensitivity pattern and appropriate surgical intervention.6 Analysis of the current study revealed the age distribution of the study population to be between 30 to 90 years. The maximum number of patients were in the age group 61-70 (27.2%) followed by the age group 51-60(24.7%). This result was similar to previous studies in that diabetic foot infections often occur in patients older than 50 years.[7] The gender-wise distribution of the study population showed that diabetic foot infection affected males slightly more frequently (51.9%) as

ISSN (O): 2687-5365; ISSN (P): 2753-6556

compared to females (48.1%); results were similar to a study by Radji et al.[7] Higher prevalence in males has also been observed in other research studies.[8] The most common co-morbid condition in the study population was hypertension (50.6%), which is also a lifestyle disease like Diabetes in line with the findings of Nagaya et al,[8] Dasaraju et al,[9] and Jyothilekshmy et al.[10]

Out of the 97 wound cultures obtained 68 (70.1%) cultures were monomicrobial and 29 cultures (29.9%) were polymicrobial. The findings of the study are similar to the one reported by Rastogi et al,[11] and Sultana et al.[12] However, in some studies, polymicrobial cultures were most common.[9,10] Gram-negative organisms (67.9%) were more predominant than gram-positive ones (32.1%) similar to studies by Mehta et al,[13] Nagaya et al.[8] In some studies, gram-positive bacteria were most common i.e 55% of the samples, with Staphylococcus aureus (33%) in the first position.[9] This kind of discrepancy could be because of geographical variations, or the types and severity of infection included in the studies. Pseudomonas aeruginosa was the most frequent organism (n = 26, 19.4%) isolated followed by Klebsiella species (n=20; 14.9%) similar to study by Singh et al, Mehta et al.[13,14]

Beta-lactam antibiotics (n= 261, 58.4%) were the most commonly used group of antibiotics; similar to that seen in studies by Farooqui et al,[15] and Dasaraju et al.[9] Among beta-lactam antibiotics, commonly used agents were Cefotaxime (n=76; 17%), Piperacillin-Tazobactam (n=67; 15.8%) and Cefoperazone-Sulbactam (n=48; 10.7%). Other beta-lactams prescribed were Crystalline penicillin, Coamoxiclav, Cloxacillin, Meropenem, Imipenem, Ampicillin, Cephalexin, Ceftriaxone-sulbactam, and Cefuroxime. Fluoroquinolones (Ciprofloxacin, Ofloxacin, Levofloxacin, and Norfloxacin), Linezolid, Aminoglycosides (Amikacin and Gentamicin), Tetracycline, Clindamycin, Vancomycin and Cotrimoxazole were the other agents prescribed in our study. The findings are similar to that of the existing literature.[8,16]

Among the 139 patients (85.8%), antibiotics were administered exclusively through the parenteral route. 22 patients (13.6%) received both parenteral and oral antibiotics. One patient required only oral route. A total of 23 patients (14.2%) received oral antibiotics. Since most of the infections were serious, parenteral routes were preferred to ensure antibiotic concentrations in the plasma and the infected sites. The results were similar to a study by Finke et al,[17] which showed that 79.8% of patients received antibiotics parenterally, 15.6% both parenterally and orally. In the present study, 155 antibiotic combinations were used and 99 drugs were given as monotherapy. Clinical outcomes demonstrated that 48% of patients achieved clinical cure through antibiotic therapy and wound debridement, while a significant proportion required amputations due to severe infections or comorbid conditions such as peripheral arterial disease (PAD) and renal dysfunction. These findings are consistent with previous studies, indicating that severe infections and comorbidities significantly increase the risk of amputation.[18]

This study reinforces existing knowledge regarding the age distribution and microbiological profile of DFIs while highlighting important trends in antibiotic usage and treatment outcomes. The findings suggest that tailored empirical therapy based on local microbiological data may improve patient outcomes, particularly in populations at high risk for severe infections and complications. Further research is warranted to explore the impact of geographical variations on microbial patterns and antibiotic resistance trends in diabetic foot infections.

Limitations of the study

The duration of the study was only one year and the sample size was small. The study population represented patients belonging to a small area and the results could not be extrapolated to the rest of the population of the country satisfactorily.

CONCLUSION

This study provides valuable insights into the antibiotic prescribing patterns and clinical outcomes associated with diabetic foot infections in a tertiary care setting. The findings emphasize the predominance of gram-negative organisms, particularly Pseudomonas aeruginosa and Klebsiella species, in these infections. The extensive use of beta-lactam antibiotics as both empirical and definitive therapy reflects current treatment trends, while the reliance on parenteral administration highlights the severity of infections in the studied population.

Despite achieving clinical cure in nearly half of the patients, the high rates of amputation underline the need for early intervention and effective management strategies, particularly in patients with comorbidities such as peripheral arterial disease. This study also reinforces the importance of tailoring empirical antibiotic therapy to local microbiological and resistance profiles to optimize outcomes and mitigate antimicrobial resistance.

Further research with larger sample sizes and diverse populations is necessary to validate these findings and explore geographical variations in microbial patterns and resistance trends. Continuous monitoring and the development of robust antimicrobial stewardship programs are essential for improving the care of diabetic foot infections and reducing associated morbidity and mortality.

REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas. 10th ed. Brussels: International Diabetes Federation; 2021. Available from: https://www.diabetesatlas.org.
2. Maity S, Leton N, Nayak N, Jha A, Anand N, Thompson K. et al. (2024) A systematic review of diabetic foot infections: pathogenesis, diagnosis, and management strategies. Front.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Clin. Diabetes Healthc. 5:1393309. doi: 10.3389/fcdhc.2024.1393309
3. Tabur S, Eren MA, Dag OF, Sabuncu T, Sayiner ZA, Savas E. The major predictors of amputation and length of stay in diabetic patients with acute foot ulceration. Wien Klin Wochenschr. 2015;127(1-2):45-50. doi:10.1007/s00508-014-0630-5.
4. Ilker U, Martin B, Parham S, Benjamin AL. Principles and practice of antibiotic stewardship in the management of diabetic foot infections. Current Opinion in Infectious Diseases.32(2):p 95-101, April 2019.
5. Wong ML, Coppini DV. Diabetic foot infections: an audit of antibiotic prescribing in a diabetic foot clinic. Practical Diabetes Int.2006;23(9):401–405.
6. Armstrong DG, Lipsky BA. Diabetic foot infections: stepwise medical and surgical management. Int Wound J. 2004 Jun;1(2):123-32. doi:10.1111/j.1742-4801.
7. Radji M, Putri CS, Fauziyah S. Antibiotic therapy for diabetic foot infections in a tertiary care hospital in Jakarta, Indonesia. Diabetes Metab Syndr. 2014 Oct-Dec;8(4):221-4. doi:10.1016/j.dsx.2014.09.006.
8. Nagaya R, RP, Deva R, et al. Optimizing antibiotic treatment for diabetic foot infections: a study from a tertiary public healthcare center in Puducherry, South India. Cureus.2024;16(5):e60139. doi:10.7759/cureus.60139.
9. Dasaraju R, Advaitha MV, Holla R. Prescription pattern and usage of antimicrobial agents for treating diabetic foot infections at a tertiary care centre. Int J Pharm Pharm Sci. 2020;12(8):136-141.
10. Jyothylekshmy V, Menon AS, Abraham S. Epidemiology of diabetic foot complications in a podiatry clinic of a tertiary hospital in South India. Indian J Health Sci Biomed Res (KLEU). 2015 Jan-Jun;8(1):48-51. doi:10.4103/2349-5006.158231.
11. Rastogi A, Sukumar S, Hajela A, Mukherjee S, Dutta P, Bhadada SK, et al. The microbiology of diabetic foot infections in patients recently treated with antibiotic therapy: a prospective study from India. J Diabetes Complications. 2017;31(2):407-412. doi:10.1016/j.jdiacomp.2016.11.001
12. Sultana R, Ahmed I, Saima S, Salam MT, Sultana S. Diabetic foot ulcer—a systematic review on relevant microbial etiology and antibiotic resistance in Asian countries. Diabetes Metab Syndr Clin Res Rev. 2023;17(6):102783. doi:10.1016/j.dsx.2023.102783.
13. Mehta VJ, Kikani KM, Mehta SJ. Microbiological profile of diabetic foot ulcers and its antibiotic susceptibility pattern in a teaching hospital, Gujarat. Int J Basic Clin Pharmacol. 2017;3(1):92-5.
14. Singh AK, Yeola M, Singh N, Damke S. A study on diabetic foot ulcers in Central rural India to formulate empiric antimicrobial therapy. J Family Med Prim Care.2020;9:4216-22.
15. Farooqui HH, Mehta A, Selvaraj S. Outpatient antibiotic prescription rate and pattern in the private sector in India: Evidence from medical audit data. PLoS One 2019;14:e0224848.
16. Paramasivamsasanger K, Mariappan P, Govindasamy D, Karunakaran P, Ramesh R. A prospective observational study of drug prescription pattern of antibiotics in diabetic foot ulcer in tertiary care teaching hospital. Int J Basic Clin Pharmacol. 2020;9:1020-7.
17. Fincke BG, Miller DR, Christiansen CL, Turpin RS. Variation in antibiotic treatment for diabetic patients with serious foot infections: a retrospective observational study. BMC Health Serv Res. 2010;10:193.
18. Quilici MT, Del Fiol Fde S, Vieira AE, Toledo MI. Risk factors for foot amputation in patients hospitalized for diabetic foot infection. J Diabetes Res. 2016;2016:8931508. doi:10.1155/2016/8931508.