

EVALUATION OF ANTIBIOTIC PRESCRIPTION PATTERNS BASED ON ANTIMICROBIAL SENSITIVITY PROFILES IN DIABETIC FOOT ULCERS: A RETROSPECTIVE STUDY

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ABSTRACT

Background: Diabetic foot ulcer is the most prevalent and severe complication of type 2 diabetes. It is a multifaceted process involving neuropathy, atherosclerosis, poor blood circulation, and infection, all of which predispose to tissue death referred to as diabetic gangrene leading to discharge from a wound with ulceration. Antibiotic therapy is very crucial in eradicating infections related to diabetic foot. **Aim:** Our study aims at determining clinical improvement in patients receiving culture-guided antibiotic therapy that results in improved management, minimized recurrence, and shortened hospital stays. **Materials and Methods:** This retrospective cohort study was conducted in the inpatient departments of general medicine and general surgery in a tertiary care hospital for a period of six months. The data was collected from patient's medical records and documented in a designed data collection form. 116 patients who met the inclusion and exclusion criteria were included in the study. **Results:** In our study, out of 116 diabetic foot ulcer patients, a total of 94 bacterial isolates were identified, gram-negative being more prevalent than gram-positive organisms. On evaluating the culture results, 15.95% were found to be *Pseudomonas aeruginosa*. The most recurring isolated organisms were *Pseudomonas aeruginosa* and *Escherichia coli*. Moreover, the antibiotic susceptibility pattern showed that piperacillin + tazobactam, amikacin, and gentamicin have the highest activity against the isolated bacteria. Among patients treated with empirical antibiotics, 51.7% showed recurrence compared to 33.9% in the culture-based therapy group. Conversely, 48.3% of the empirical group and 66.1% of the culture-based group did not experience recurrence. **Conclusion:** Among the study samples, the findings indicate a lower recurrence rate with culture-based therapy, suggesting that tailored antibiotic selection based on culture sensitivity may contribute to better long-term outcomes and reduced treatment failure.

INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by elevated blood glucose levels. According to a 2021 study by the International Diabetes Federation, diabetes affects 537 million individuals aged 20–79 years. This number is expected to increase to approximately 783 million by

2045.^[1] The likelihood of developing a foot ulcer over a lifetime varies between 19% and 34%. The complications associated with a new ulcer are significant, with recurrence rates of 65% occurring within three–five years, a lifetime risk of lower-extremity amputation of 20%, and a five-year mortality rate ranging from 50% to 70%.^[2] Diabetic foot ulcers (DFUs) are common and severe complications of inadequately controlled type 2

diabetes. This condition is characterized by a combination of nerve damage (neuropathy), decreased blood circulation (ischemia), and infection, which can ultimately result in tissue death, referred to as diabetic gangrene.^[3] The pathophysiology of diabetes involves several factors; however, its key feature is persistent hyperglycemia, which triggers a series of complications that impact various organs, particularly the microvasculature.^[4] The emergence of diabetic foot ulcers (DFUs) is strongly associated with both microvascular and macrovascular issues, such as diabetic neuropathy and peripheral artery disease (PAD), which are notably more common among individuals with diabetes than in the general population.^[5] Hyperglycemia-induced oxidative stress, along with endothelial dysfunction and inflammatory responses, plays a role in the development of these vascular complications, thereby accelerating the progression of ulcers and hindering wound healing.^[6] Foot ulcers among individuals with diabetes can result in severe consequences, including decreased mobility, infections, extended hospitalizations, lower limb amputations, and even mortality.^[7]

Diabetic foot ulcers are frequently categorized using the Wagner classification. This classification evaluates the depth of the ulcer and the presence of osteomyelitis or gangrene. The Wagner classification comprises grade 0, which indicates a foot at risk; grade 1, referring to a localized, superficial ulcer; grade 2, denoting a deep ulcer affecting the muscle, ligament, or tendon; grade 3, indicating a deep abscess or osteomyelitis; grade 4, associated with gangrene of the toes or forefoot; and grade 5, characterized by gangrene of the entire foot.^[8] Tissue samples and wound swabs for antibiotic culture and sensitivity help evaluate the seriousness of the infection and determine the sensitivity or resistance of organisms in an infected ulcer to antibiotic therapy, thus reducing the need for amputation in diabetic patients with an infected foot ulcer.^[9] For mild diabetic foot infections without any complicating factors, the typical pathogens are gram-positive cocci, and appropriate empirical treatment includes semi-synthetic penicillin or first-generation cephalosporins. In patients with β -lactam allergy, alternatives such as clindamycin, fluoroquinolones, macrolides, or doxycycline may be considered. For moderate to severe infections without complicating factors, empirical treatment usually focuses on gram-positive cocci and potentially gram-negative rods, utilizing β -lactamase inhibitors or second or third-generation cephalosporins.^[10]

This retrospective study aimed to assess the microbial profile (frequent pathogens) obtained from cultures of diabetic foot ulcers, examine the patterns of antibiotic use in patients with diabetic foot ulcers, and determine local antimicrobial resistance trends in DFU. This study analyzed the suitability of empirical antibiotic treatment in comparison to culture and sensitivity results and evaluated the clinical outcomes

(such as amputation, mortality, and infection recurrence) concerning antibiotic choices.

MATERIALS AND METHODS

Study design

This retrospective observational study was conducted in the general surgery and general medicine departments of Apollo Institute of Medical Sciences and Research Hospital, Jubilee Hills, Hyderabad, Telangana, India, for six months.

Inclusion and Exclusion Criteria

A total of 116 patients diagnosed with diabetic foot ulcers were screened for eligibility. This study included patients older than 18 years of age, individuals of both sexes, and patients diagnosed with type two diabetes mellitus presenting with diabetic foot infections. Patients with type one diabetes mellitus, pregnant women, psychiatric patients, individuals with non-diabetic foot infections, and immunocompromised patients were excluded from the study.

Sample size

Cochran's formula, $(n) = z^2pq/d^2$, where n = desired sample size, with a 7% margin of error ($d = 0.07$) and a 95% confidence interval ($z = 1.96$), where $q = 1 - p$.^[11] Based on previous studies, the prevalence of diabetic foot ulcers (p) was 18%.^[12] The required sample size of patients with DFUs was determined to be 116.

Methods and data collection

A data collection form was designed for this study. It comprises information regarding the study subject's data, such as demographics, medical and medication history, social and family history, laboratory investigations, diagnosis, current medications prescribed, and a progress chart. Relevant data were collected and recorded in the data collection form from the patient's medical records. The collected data was entered into a spreadsheet (Excel).

Statistical tools: The data collected were analyzed using SPSS software (version 27.0), and a chi-square test was applied to assess the appropriateness of empirical antibiotics and evaluate the clinical outcomes in patients with diabetic foot ulcers. The probability value obtained [$p < 0.05$] was considered significant.

RESULTS

During the study, 116 patients were included as per inclusion criteria (Table 1). The population predominantly comprised individuals aged 50-59 years (42.20%), followed by those aged 40-49 years (22.40%). Most participants were male (78.40 %). Individuals with diabetic foot ulcers often present with comorbidities. Hypertension was the most common comorbidity, affecting 50% of patients, and coronary artery disease was present in 12.90% of cases. Chronic obstructive pulmonary disease was the least common occurring in 1.72% of patients.

Additionally, 44.80% of patients had been diagnosed with type 2 diabetes mellitus for 10-19 years. 76.70% of participants had an HbA1c level exceeding 7%, with the left extremity most affected in 51.70% of cases. When comparing locations, 71.60% of participants had ulcers on their feet, while 28.40% had ulcers on their toes. Only 35.30% of participants underwent amputation, whereas 64.70% did not. A

proportion of patients (71.60%) experienced hospital stays lasting 10 days. Ulcer recurrence was observed in 43.10% of participants. The mortality rate was 0.90%, but this was attributed to other comorbidities. The largest percentage of participants exhibited Wagner grade 2, accounting for approximately 30.20% of the sample, followed by grade 4 (20.70%, grade 1 (19%), and grade 3 (18.10%).

Table 1: Socio-Demographics and Clinical Characteristics of Participants (n = 116)

Variables	Number (frequency%)
Age	
30-39	4 (3.40%)
40-49	26 (22.40%)
50-59	49 (42.20%)
60-69	23 (19.80%)
>=70	14 (12.10%)
Gender	
Female	25 (21.60%)
Male	91 (78.40%)
Comorbidities	
Hypertension	58 (50%)
Coronary artery disease	15 (12.90%)
Hypothyroidism	12 (10.30%)
Chronic kidney disease	11 (9.48%)
Epilepsy	6 (5.17%)
HFmrEF	6 (5.17%)
Anaemia	5 (4.31%)
Tuberculosis	4 (3.44%)
Asthma	3 (2.58%)
Diabetic neuropathy	2 (1.72%)
Diabetic retinopathy	2 (1.72%)
COPD	2 (1.72%)
Others	9 (7.75%)
Duration of diabetes	
<10	46 (39.70%)
10-19	52 (44.80%)
>=20	18 (15.50%)
HbA1C	
<7	27 (23.30%)
>=7	89 (76.70%)
Affected extremity	
Left	60 (51.70%)
Right	54 (46.60%)
Right/Left	2 (1.70%)
Location of ulcer	
Foot	83 (71.60%)
Toe	33 (28.40%)
Amputation	
No	75 (64.70%)
Yes	41 (35.30%)
Length of stay	
1-10	83 (71.60%)
11-20	23 (19.80%)
21-30	9 (7.80%)
>=31	1 (0.90%)
Recurrence	
No	66 (56.90%)
Yes	50 (43.10%)
Mortality	
No	115 (99.10%)
Yes	1 (0.90%)

Based on the distribution of pathogenic bacteria identified from diabetic foot ulcers (DFU), 94 samples (81.03%) exhibited positive bacterial growth, whereas 22 samples (18.96%) were culture negative. Among the isolated bacteria, gram-negative strains were the most prevalent, with 78 isolates

(82.9%), where *Pseudomonas aeruginosa* was the most frequently identified pathogen, followed by *Escherichia coli* and *Proteus mirabilis*. Gram-positive bacteria accounted for 16 isolates (17%), with *Enterococcus* species and *Staphylococcus aureus* being the most common, as shown in Table 2.

Table 2: Distribution of the Pathogenic Bacteria Isolated from Diabetic Foot Ulcers

Variables	Number (frequency %)
Bacterial growth (116)	
Positive	94 (81.03%)
Negative	22 (18.96%)
Microorganisms type (94)	
Gram positive	16 (17%)
Gram negative	78 (82.9%)
Isolated microorganisms	
Gram positive bacteria	
Enterococcus species	6 (6.38%)
S.aureus	5 (5.31%)
Streptococcus species	2 (2.12%)
Enterococcus faecalis	2 (2.12%)
Others	1 (1.06%)
Gram negative bacteria	
Pseudomonas aeruginosa	15 (15.95%)
E. coli	14 (14.89%)
Proteus mirabilis	14 (14.89%)
Klebsiella pneumoniae	7 (7.44%)
Enterobacter aerogenes	6 (6.38%)
Proteus vulgaris	5 (5.31%)
Klebsiella species	4 (4.25%)
Others	13 (13.79%)

Table 3 shows the antimicrobial resistance profiles of the primary gram-negative isolates. *Pseudomonas aeruginosa* showed a notably higher sensitivity to piperacillin+tazobactam (88.8%), aminoglycosides such as amikacin (64.3%) and gentamicin (61.5%), and carbapenems such as meropenem (63.6%) and imipenem (60%). Conversely, significant resistance was noted against cephalosporins such as ceftriaxone (100%) and ceftazidime (54.5%), in addition to co-trimoxazole (80%). Colistin exhibited predominantly intermediate susceptibility (75%). *Escherichia coli* isolates displayed strong sensitivity to amikacin (92.30%) and gentamicin (83.33%), whereas significant resistance was observed against third-generation cephalosporins, such as ceftazidime (100%), ceftriaxone (91.7%), and cefuroxime (90%). There was also a high level of resistance to fluoroquinolones, especially ciprofloxacin (76.92%). Carbapenems showed moderate effectiveness, with a sensitivity rate of 55.5% for both meropenem and imipenem, respectively. All *E. coli* isolates displayed an intermediate susceptibility to colistin. *Proteus mirabilis* exhibited consistently high sensitivity to aminoglycosides (100%), piperacillin+tazobactam (100%), and carbapenems (100%). Additionally, good sensitivity was observed for fluoroquinolones and third-generation cephalosporins. However, resistance was detected against co-trimoxazole (58.33%) and cefazolin (75%), with complete resistance observed to colistin. *Klebsiella pneumoniae* displayed a comparatively resistant pattern, showing high resistance to gentamicin

(66.7%), ciprofloxacin (71.4%), cefuroxime (100%), ceftriaxone (80%), and imipenem (66.7%). Moderate sensitivity was observed with piperacillin+tazobactam (66.7%), meropenem (50%), and amikacin (42.85%). All isolates displayed intermediate susceptibility to colistin, whereas tigecycline and teicoplanin exhibited 100% sensitivity in the tested isolates. *Proteus vulgaris* (n = 5) displayed full sensitivity to piperacillin+tazobactam, meropenem, faropenem, and cefoperazone+sulbactam. Significant resistance was observed against co-trimoxazole (80%), ciprofloxacin (60%), ofloxacin (60%), and cefazolin (100%). *Klebsiella species* (n = 4) showed 100% sensitivity to aminoglycosides, carbapenems, amoxicillin+clavulanate, and cefoperazone+sulbactam, whereas resistance was noted against cefuroxime (75%) and ceftazidime (66.7%). *Citrobacter freundii* (n = 2) showed 100% sensitivity to all the antibiotics tested. *Burkholderia cepacia* (n = 2) exhibited complete resistance to aminoglycosides, piperacillin+tazobactam, ceftriaxone, cefepime, and imipenem but showed 100% sensitivity to ciprofloxacin, co-trimoxazole, and meropenem. Both *Acinetobacter species* (n = 1) and *Acinetobacter baumannii* (n = 1) displayed multidrug resistance, with sensitivity only evident to carbapenems in isolated cases. Rare isolates, such as *Raoultella ornithinolytica* (n = 1) and *Enterobacter species* (n = 1), exhibited full sensitivity to most antibiotics tested.

Table 3: Sensitivity, Resistance and Intermediate Pattern of Gram-Negative Microorganisms

Microorganism	Antibiotics (number of tested isolate)	Sensitive N (%)	Resistant N (%)	Intermediate N (%)
<i>Pseudomonas aeruginosa</i>	Gentamicin (13)	8 (61.53%)	5 (38.46%)	0 (0%)
	Amikacin (14)	9 (64.28%)	5 (35.71%)	0 (0%)
	Ceftazidime (11)	4 (36.36%)	6 (54.54%)	1 (9.09%)
	Ciprofloxacin (12)	7 (58.33%)	5 (41.66%)	0 (0%)
	Ofloxacin (4)	3 (75%)	1 (25%)	0 (0%)

	Co-trimoxazole (5)	1 (20%)	4 (80%)	0 (0%)	
	Piperacillin+tazobactam (9)	8 (88.8%)	1 (11.11%)	0 (0%)	
	Ceftriaxone (2)	0 (0%)	2 (100%)	0 (0%)	
	Tobramycin (2)	2 (100%)	0 (0%)	0 (0%)	
	Vancomycin (1)	1 (100%)	0 (0%)	0 (0%)	
	Teicoplanin (1)	1 (100%)	0 (0%)	0 (0%)	
	Clindamycin (4)	4 (100%)	0 (0%)	0 (0%)	
	Linezolid (2)	2 (100%)	0 (0%)	0 (0%)	
	Tigecycline (1)	1 (100%)	0 (0%)	0 (0%)	
	Amoxicillin+clavulanate (1)	1 (100%)	0 (0%)	0 (0%)	
	Meropenem (11)	7 (63.63%)	4 (36.36%)	0 (0%)	
	Imipenem (10)	6 (60%)	4 (40%)	0 (0%)	
	Faropenem (1)	1 (100%)	0 (0%)	0 (0%)	
	Cefoperazone+sulbactam (12)	7 (58.33%)	5 (41.66%)	0 (0%)	
	Cefipime (8)	3 (37.5%)	4 (50%)	1 (12.5%)	
	Levofloxacin (7)	3 (42.85%)	4 (57.14%)	0 (0%)	
	Minocycline (3)	1 (33.33%)	2 (66.66%)	0 (0%)	
	Colistin (4)	0 (0%)	1 (25%)	3 (75%)	
	Doxycycline (1)	0 (0%)	1 (100%)	0 (0%)	
	Cefazolin (1)	0 (0%)	1 (100%)	0 (0%)	
	Metronidazole (2)	2 (100%)	0 (0%)	0 (0%)	
E. coli	Gentamicin (12)	10 (83.33%)	2 (16.66%)	0 (0%)	
	Amikacin (13)	12 (92.30%)	1 (7.69%)	0 (0%)	
	Ceftazidime (6)	0 (0%)	6 (100%)	0 (0%)	
	Cefotaxime (2)	2 (100%)	0 (0%)	0 (0%)	
	Cefuroxime (10)	0 (0%)	9 (90%)	1 (10%)	
	Ciprofloxacin (13)	3 (23.07%)	10 (76.92%)	0 (0%)	
	Ofloxacin (6)	3 (50%)	3 (50%)	0 (0%)	
	Co-trimoxazole (13)	4 (30.76%)	9 (69.23%)	0 (0%)	
	Piperacillin+tazobactam (13)	2 (15.38%)	11 (84.61%)	0 (0%)	
	Ceftriaxone (12)	1 (8.33%)	11 (91.66%)	0 (0%)	
	Metronidazole (1)	1 (100%)	0 (0%)	0 (0%)	
	Clindamycin (2)	2 (100%)	0 (0%)	0 (0%)	
	Linezolid (2)	2 (100%)	0 (0%)	0 (0%)	
	Tigecycline (4)	3 (75%)	0 (0%)	1 (25%)	
	Amoxicillin+clavulonate (8)	4 (50%)	4 (50%)	0 (0%)	
	Meropenem (9)	5 (55.55%)	4 (44.44%)	0 (0%)	
	Imipenem (9)	5 (55.55%)	3 (33.33%)	1 (11.11%)	
	Faropenem (2)	2 (100%)	0 (0%)	0 (0%)	
	Cefoperazone+sulbactam (13)	3 (23.07%)	9 (69.23%)	1 (7.69%)	
	Cefipime (9)	2 (22.22%)	6 (66.66%)	1 (11.11%)	
	Erythromycin (1)	0 (0%)	1 (100%)	0 (0%)	
	Levofloxacin (2)	1 (50%)	1 (50%)	0 (0%)	
	Colistin (5)	0 (0%)	0 (0%)	5 (100%)	
	Tetracycline (3)	2 (66.66%)	1 (33.33%)	0 (0%)	
	Cefazolin (3)	0 (0%)	3 (100%)	0 (0%)	
	Proteus mirabilis	Gentamicin (14)	14 (100%)	0 (0%)	0 (0%)
		Amikacin (14)	14 (100%)	0 (0%)	0 (0%)
Ceftazidime (9)		7 (77.77%)	2 (22.22%)	0 (0%)	
Cefuroxime (6)		4 (66.66%)	2 (33.33%)	0 (0%)	
Ciprofloxacin (10)		8 (80%)	2 (20%)	0 (0%)	
Ofloxacin (9)		5 (55.55%)	4 (44.44%)	0 (0%)	
Co-trimoxazole (12)		5 (41.66%)	7 (58.33%)	0 (0%)	
Piperacillin+tazobactam (13)		13 (100%)	0 (0%)	0 (0%)	
Ceftriaxone (9)		6 (66.66%)	3 (33.33%)	0 (0%)	
Tobramycin (2)		2 (100%)	0 (0%)	0 (0%)	
Clindamycin (5)		5 (100%)	0 (0%)	0 (0%)	
Amoxicillin+clavulonate (6)		3 (50%)	2 (33.33%)	1 (16.66%)	
Meropenem (2)		2 (100%)	0 (0%)	0 (0%)	
Imipenem (2)		2 (100%)	0 (0%)	0 (0%)	
Cefoperazone+sulbactam (9)		7 (77.77%)	2 (22.22%)	0 (0%)	
Cefipime (8)		6 (75%)	0 (0%)	2 (25%)	
Levofloxacin (2)		2 (100%)	0 (0%)	0 (0%)	
Colistin (2)		0 (0%)	2 (100%)	0 (0%)	
Cefazolin (4)		1 (25%)	3 (75%)	0 (0%)	
Cefixime (1)		1 (100%)	0 (0%)	0 (0%)	
Klebsiella pneumoniae		Gentamicin (6)	2 (33.33%)	4 (66.66%)	0 (0%)
	Amikacin (7)	3 (42.85%)	4 (57.14%)	0 (0%)	
	Ceftazidime (2)	2 (100%)	0 (0%)	0 (0%)	
	Cefuroxime (4)	0 (0%)	4 (100%)	0 (0%)	
	Ciprofloxacin (7)	2 (28.57%)	5 (71.42%)	0 (0%)	
	Ofloxacin (1)	0 (0%)	1 (100%)	0 (0%)	
	Co-triamoxazole (7)	3 (42.85%)	4 (57.14%)	0 (0%)	

Piperacillin+tazobactam (6)	4 (66.66%)	2 (33.33%)	0 (0%)
Ceftriaxone (5)	1 (20%)	4 (80%)	0 (0%)
Teicoplanin (3)	3 (100%)	0 (0%)	0 (0%)
Tigecycline (3)	3 (100%)	0 (0%)	0 (0%)
Amoxicillin+clavulonate (4)	2 (50%)	2 (50%)	0 (0%)
Meropenem (6)	3 (50%)	3 (50%)	0 (0%)
Imipenem (6)	2 (33.33%)	4 (66.66%)	0 (0%)
Faropenem (6)	3 (50%)	3 (50%)	0 (0%)
Cefoperazone+sulbactam (7)	3 (42.85%)	4 (57.14%)	0 (0%)
Cefipime (6)	2 (33.33%)	4 (66.66%)	0 (0%)
Minocycline (1)	0 (0%)	1 (100%)	0 (0%)
Colistin (3)	0 (0%)	0 (0%)	3 (100%)
Metronidazole (1)	1 (100%)	0 (0%)	0 (0%)
Clindamycin (3)	3 (100%)	0 (0%)	0 (0%)
Cefotaxime (4)	2 (50%)	2 (50%)	0 (0%)

The patterns of antimicrobial susceptibility for gram-positive microorganisms are shown in Table 4. Enterococcus species showed total resistance (100%) to cefotaxime, ofloxacin, and co-trimoxazole. High sensitivity was noted for vancomycin, linezolid, levofloxacin, ciprofloxacin, and piperacillin+tazobactam (100% for each). The Staphylococcus aureus isolates display 100% sensitivity to gentamicin, amikacin, cefuroxime, piperacillin+tazobactam, vancomycin/teicoplanin, clindamycin, linezolid, tigecycline, amoxicillin+clavulanate, erythromycin, tetracycline, and daptomycin. Complete resistance was observed against ciprofloxacin, ofloxacin, penicillin, and levofloxacin. Co-trimoxazole showed lower sensitivity (33.3%) with predominant resistance (66.6%). Streptococcus species showed 100% sensitivity to ciprofloxacin, co-trimoxazole, ceftriaxone, clindamycin, amoxicillin+clavulanate, and erythromycin. Penicillin demonstrated equal rates of sensitivity and resistance (50% each), whereas total resistance was observed against ampicillin. Enterococcus faecalis was completely sensitive to ciprofloxacin, vancomycin, teicoplanin,

linezolid, amoxicillin+clavulanate, levofloxacin, tetracycline, and daptomycin. Resistance was observed for ampicillin (100%). Erythromycin exhibited variable susceptibility, with 50% of the isolates showing resistance and 50% showing intermediate susceptibility. Enterobacter aerogenes (n = 6) displayed high susceptibility to piperacillin+tazobactam, gentamicin, ciprofloxacin, co-trimoxazole, cefoperazone+sulbactam, and cefepime ($\geq 83\%$). Significant resistance was detected against amoxicillin+clavulanate (83.3%) and ertapenem (100%), whereas colistin showed intermediate susceptibility (100%) in one isolate. Enterobacter cloacae (n = 3) showed complete susceptibility to piperacillin+tazobactam, and total resistance was observed against cefuroxime, ciprofloxacin, co-trimoxazole, ceftriaxone, and all tested carbapenems. A single isolate of Enterococcus faecium (n = 1) demonstrated 100% sensitivity to vancomycin, linezolid, cefoperazone+sulbactam, penicillin, and metronidazole but exhibited complete resistance to fluoroquinolones, erythromycin, and tetracycline.

Table 4: Sensitivity, Resistance and Intermediate Pattern of Gram-Positive Microorganisms

Microorganism	Antibiotics (number of tested isolate)	Sensitive N (%)	Resistant N (%)	Intermediate N (%)	
Enterococcus species	Cefotaxim (3)	0 (0%)	3 (100%)	0 (0%)	
	Ciprofloxacin (2)	2 (100%)	0 (0%)	0 (0%)	
	Ofloxacin (3)	0 (0%)	3 (100%)	0 (0%)	
	Co-trimoxazole (3)	0 (0%)	3 (100%)	0 (0%)	
	Piperacillin+tazobactam (2)	2 (100%)	0 (0%)	0 (0%)	
	Vancomycin (4)	4 (100%)	0 (0%)	0 (0%)	
	Teicoplanin (4)	1 (25%)	3 (75%)	0 (0%)	
	Linezolid (4)	4 (100%)	0 (0%)	0 (0%)	
	Erythromycin (6)	2 (33.33%)	4 (66.66%)	0 (0%)	
	Penicillin (6)	3 (50%)	3 (50%)	0 (0%)	
	Levofloxacin (2)	2 (100%)	0	0 (0%)	
	Ampicillin (6)	3 (50%)	3 (50%)	0 (0%)	
	S.aureus	Gentamicin (2)	2 (100%)	0 (0%)	0 (0%)
		Amikacin (1)	1 (100%)	0 (0%)	0 (0%)
Cefuroxime (2)		2 (100%)	0 (0%)	0 (0%)	
Ciprofloxacin (5)		0 (0%)	5 (100%)	0 (0%)	
Ofloxacin (3)		0 (0%)	3 (100%)	0 (0%)	
Co-trimoxazole (3)		1 (33.33%)	2 (66.66%)	0 (0%)	
Piperacillin+tazobactam (1)		1 (100%)	0 (0%)	0 (0%)	
Vancomycin (2)		2 (100%)	0 (0%)	0 (0%)	
Teicoplanin (2)		2 (100%)	0 (0%)	0 (0%)	
Clindamycin (3)		3 (100%)	0 (0%)	0 (0%)	
Linezolid (3)		3 (100%)	0 (0%)	0 (0%)	
Tigecycline (1)		1 (100%)	0 (0%)	0 (0%)	

	Amoxicillin+clavulonate (1)	1 (100%)	0 (0%)	0 (0%)
	Erythromycin (2)	2 (100%)	0 (0%)	0 (0%)
	Penicillin (2)	0 (0%)	2 (100%)	0 (0%)
	Levofloxacin (1)	0 (0%)	1 (100%)	0 (0%)
	Tetracycline (1)	1 (100%)	0 (0%)	0 (0%)
	Daptomycin (1)	1 (100%)	0 (0%)	0 (0%)
Streptococcus species	Ciprofloxacin (1)	1 (100%)	0 (0%)	0 (0%)
	Co-trimoxazole (1)	1 (100%)	0 (0%)	0 (0%)
	Ceftriaxone (2)	2 (100%)	0 (0%)	0 (0%)
	Clindamycin (1)	1 (100%)	0 (0%)	0 (0%)
	Amoxicillin+clavulonate (1)	1 (100%)	0 (0%)	0 (0%)
	Erythromycin (1)	1 (100%)	0 (0%)	0 (0%)
	Penicillin (2)	1 (50%)	1 (50%)	0 (0%)
Enterococcus faecalis	Ampicillin (1)	0 (0%)	1 (100%)	0 (0%)
	Ciprofloxacin (2)	2 (100%)	0 (0%)	0 (0%)
	Vancomycin (1)	1 (100%)	0 (0%)	0 (0%)
	Teicoplanin (1)	1 (100%)	0 (0%)	0 (0%)
	Linezolid (2)	2 (100%)	0 (0%)	0 (0%)
	Amoxicillin+clavulonate (1)	1 (100%)	0 (0%)	0 (0%)
	Erythromycin (2)	0 (0%)	1 (50%)	1 (50%)
	Penicillin (2)	1 (50%)	1 (50%)	0 (0%)
	Levofloxacin (2)	2 (100%)	0 (0%)	0 (0%)
	Tetracycline (1)	1 (100%)	0 (0%)	0 (0%)
	Daptomycin (1)	1 (100%)	0 (0%)	0 (0%)
Ampicillin (1)	0 (0%)	1 (100%)	0 (0%)	

The pattern of antibiotic prescription revealed that empirical antibiotics were slightly more commonly used than culture-based antibiotics, accounting for 51.7% and 48.2% respectively. This reflects moderate reliance on empirical therapy while also highlighting the importance of culture-guided treatment in clinical practice. In a study involving 114 patients undergoing empirical therapy, clindamycin was the most prescribed antibiotic, accounting for 61.4% of cases, followed by amoxicillin+clavulanate (44.73%) and cefoperazone+sulbactam (25.43%). Piperacillin+tazobactam was used in 10.5% of the cases. Metronidazole (7.01%) and meropenem (6.14%) were less frequently prescribed, whereas linezolid was administered to 5.3% of patients. Other antibiotics, such as cefotaxime, ciprofloxacin, cefixime, tigecycline, faropenem, cefuroxime,

meropenem+sulbactam, and ceftriaxone, were used in fewer than 3% of the cases.

In a group of 94 patients receiving therapy guided by culture results, ciprofloxacin was the most prescribed antibiotic (18.1%). This was followed closely by piperacillin+tazobactam (17.02%) and cefoperazone+sulbactam (16.0%). Clindamycin was used in 13.82% of the cases, while comparable prescription rates were observed for amikacin (11.7%), linezolid (10.63%), and meropenem (10.63%). Amoxicillin+clavulanate was prescribed less frequently (9.6%), and faropenem was used in 5.31% of cases. Metronidazole was administered to 5.31% of patients, whereas other medications, such as cefuroxime, tigecycline, cefotaxime, ceftriaxone, cefixime, ceftazidime, and co-trimoxazole, were prescribed in less than 4% of the cases each, as shown in Table 5.

Table 5: Prescription Pattern of Empirical and Culture Based Antibiotics

Antibiotics	Empirical Antibiotic Therapy (N=114)	Culture-Based Antibiotic Therapy (N=94)
Amikacin	0 (0%)	11 (11.7%)
Amoxicillin+clavulanate	51 (44.73%)	9 (9.57%)
cefixime	2 (1.75%)	1 (1.06%)
cefoperazone+sulbactam	29 (25.43%)	15 (15.95%)
cefotaxime	3 (2.63%)	2 (2.12%)
ceftazidime	0 (0%)	1 (1.06%)
ceftriaxone	1 (0.87%)	2 (2.12%)
cefuroxime	1 (0.87%)	3 (3.19%)
ciprofloxacin	3 (2.63%)	17 (18.08%)
clindamycin	70 (61.4%)	13 (13.82%)
co-trimoxazole	0 (0%)	1 (1.06%)
faropenem	2 (1.75%)	5 (5.31%)
linezolid	6 (5.26%)	10 (10.63%)
meropenem	7 (6.14%)	10 (10.63%)
meropenem+sulbactam	1 (0.87%)	0 (0%)
Metronidazole	8 (7.01%)	5 (5.31%)
piperacillin+tazobactam	12 (10.52%)	16 (17.02%)
tigecycline	2 (1.75%)	3 (3.19%)

Amputation was necessary in 41 patients (35.30%). The amputation rate was similar between those

receiving empirical treatment (33.30%) and those receiving culture-guided therapy (37.50%). A total of

50 patients (43.1%) experienced recurrence, with a notably higher rate in the empirical antibiotic group (51.7%) than in the culture-guided group (33.9%). Among those who received empirical antibiotic therapy, one patient (1.7%) succumbed; however, the

death was due to acute decompensated heart failure secondary to HFrEF (30%), while no deaths were reported among patients treated with culture-based antibiotics, as shown in Table 6.

Table 6: Comparison of Amputation, Recurrence, Mortality Rates in Empiric v/s Culture Based Antibiotic Therapy

variables	Yes	No	Chi-square value (x ²)	Pearson chi-square P-value	Fisher's Exact Test value
Amputation					
Empirical based (60)	20(33.30%)	40(66.70%)	0.220	0.639	0.700
Culture based (56)	21(37.50%)	35(62.50%)			
Recurrence					
Empirical based (60)	31(51.7%)	29(48.3%)	3.716	0.054	0.063
Culture based (56)	19(33.9%)	37(66.1%)			
Mortality					
Empirical based (60)	1(1.7%)	59(98.3%)	0.941	0.332	1.000
Culture based (56)	0(0%)	56(100%)			

DISCUSSION

Diabetic foot ulcers (DFU) are common, highly morbid consequences of longstanding and poorly managed diabetes. The most frequently prescribed empirical antibiotics include lincomycin, beta-lactam antibiotics, and cephalosporins. This observational study was conducted at a tertiary care hospital and involved 116 participants, of whom 91 were male and 25 were female. The analysis of sex distribution showed a higher number of male patients (78.40%) than female patients (21.60%), suggesting that males are more susceptible to diabetic foot ulcers. This pattern is consistent with earlier findings by Anand Shanmugaiah et al., who noted that 71.3% of those affected were male, as well as the observations by Maram Hamid et al., who also identified male gender as a significant risk factor for the onset of diabetic foot ulcers.^[11,12] The current analysis showed that gram-negative bacteria predominated in diabetic foot ulcer (DFU) infections, which is consistent with previous research. According to Maram Hamid et al., 41.2% of isolates were Gram-positive and 58.8% of isolates were Gram-negative. Similarly, a greater percentage of gram-negative organisms (82.90%) than gram-positive organisms (17%) were found in the current data.^[12] Singh et al. analyzed 105 patients with DFU and identified 110 bacterial isolates from 97 samples, of which 73.7% were gram-negative and 27.3% were gram-positive, further supporting this pattern. Microbiological findings from Singh et al. indicated that *Pseudomonas* (27.3%) and *Staphylococcus aureus* (19.05%) were the most frequently isolated bacteria.^[13] Similarly, *Pseudomonas aeruginosa* (15.95%) and *E. coli* (14.89%) were the most common pathogens in this evaluation. The antibiotic prescribing patterns observed in the present study partially align with previous findings, although some significant differences are evident. Aviatin et al. found that penicillins and meropenems were the most prescribed antibiotics. In this analysis, amoxicillin+clavulanate (44.73%) still ranked among the most frequently prescribed drugs, but clindamycin (61.4%) emerged

as the most dominant antibiotic, suggesting a change in preference for its use.^[14] Furthermore, Gilang Rizki Al Farizi et al. identified meropenem (31.71%) and levofloxacin (17.07%) as the leading antibiotics prescribed.^[15] In contrast, this study showed that clindamycin (61.4%) and amoxicillin+clavulanate (44.73%) were the most frequently used agents, highlighting local prescribing habits and potentially varying microbial resistance patterns. In accordance with earlier studies, this study highlights the dominance of gram-negative bacteria in infections related to diabetic foot ulcers (DFUs). Similarly, the current study found *Pseudomonas aeruginosa* (15.95%) and *Escherichia coli* (14.89%) to be the primary isolates, indicating an even greater proportion of gram-negative organisms (82.90%). Interestingly, both studies observed consistent antibiotic susceptibility among gram-negative bacteria to amikacin, piperacillin+tazobactam, gentamicin, and cefotaxime. Clinical observations made by Maram Hamid et al. indicated that 87.2% of patients with HbA1c levels exceeding 7% were at a higher risk for diabetic foot ulcers.^[12] In agreement with this, 76.70% of the individuals evaluated in this study also had HbA1c levels > 7%. Most cases (71.60%) had ulcers located on the foot, while 28.40% had ulcers specifically on the toe. 41 out of 116 patients (35.30%) of the overall patient population required amputation, highlighting the severity and advanced stage of diabetic foot ulcers in many cases. Amputation was necessary for 33.30% (20 out of 60) of patients undergoing empirical antibiotic therapy and 37.50% (21 out of 56) of patients receiving culture-based therapy. In contrast, 66.7% of the empirical group and 62.5% of the culture-based group underwent limb preservation, indicating similar clinical outcomes between the two therapy modalities in terms of amputation risk. The occurrence of diabetic foot ulcers recurred in 43.1% of patients (50 out of 116) after antibiotic treatment, while 56.9% remained ulcer-free throughout the follow-up duration. Notably, recurrence rates were higher in patients receiving empirical treatment, with 51.7% (31 out of 60) facing a recurrence, as opposed

to 33.9% (19 out of 56) in the culture-based therapy group. In contrast, 48.3% of patients in the empirical group and 66.1% in the culture-guided group did not experience recurrence, suggesting that culture-directed antibiotic treatment may lead to improved long-term results in avoiding ulcer recurrence. Mortality rates were low, with only 0.9% of patients not surviving the condition. In culture-directed therapy, fluoroquinolones were administered in 18.08% of cases, whereas penicillins accounted for 17.02%, reflecting their importance in targeted treatment. The overall trend in antibiotic prescriptions indicated that empirical antibiotics were slightly more frequently utilized than culture-based antibiotics, with 51.7% and 48.2% of patients receiving these treatments, respectively. Survival rates were promising in both groups, achieving survival rates of 98.3% and 100% in the empirical and culture-based therapy groups, respectively. A chi-square test was used to assess the efficacy of empirical antibiotic therapy and its correlation with the clinical outcomes. The results highlight the importance of choosing the right antibiotics based on culture and sensitivity data to enhance treatment outcomes for individuals with diabetic foot ulcers.

CONCLUSION

This observational study highlights the significant clinical impact of diabetic foot ulcers (DFUs), particularly in males aged 50-59 with prevalent type 2 diabetes. Most cases involved advanced-stage ulcers, often requiring amputation, with comorbidities such as hypertension and poor glycemic control playing a role. Microbiological analysis indicated the dominance of gram-negative bacteria, particularly *Pseudomonas aeruginosa* and *Escherichia coli*, which showed higher sensitivity to Piperacillin+Tazobactam, Amikacin, and Meropenem, while resistance was noted to Ceftriaxone and Ofloxacin. Clindamycin and amoxicillin+clavulanate are commonly prescribed, although empirical treatments are often misaligned with culture results. Culture-guided therapy yielded lower recurrence rates than empirical methods, emphasizing the need for evidence-based, personalized treatment. Integrating microbial surveillance, culture-guided antibiotic selection, glycemic control, and patient education is essential for improving the management of DFUs and preventing amputation.

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