World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(RESEARCH ARTICLE)

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A study on bacteriological profile and prescription pattern of antibiotics in the management of diabetic foot ulcers in a tertiary healthcare teaching hospital

Taeyyeb Mahboub Moghaddam *

Karavali College of Pharmcy, Mangloor, Karnataka, India.

World Journal of Biology Pharmacy and Health Sciences, 2023, 13(02), 238–248

Publication history: Received on 01 January 2023; revised on 13 February 2023; accepted on 16 February 2023

Article DOI: https://doi.org/10.30574/wjbphs.2023.13.2.0087

Abstract

Infection of diabetic foot ulcers is the most common cause of hospitalization among diabetic patients. If not treated properly in time, the infection will eventually lead to septicemia,amputation and even death. It is found that more than 40 percent of amputations can be prevented by the appropriate treatment of diabetic foot ulcers. Irrational antibiotic use leads totreatment failure adverse drug reactions, superinfections, prolongation of treatment, increasedcost and development of antibiotic resistance. Study of the bacteriological profile, antimicrobial susceptibility and prescription pattern aids in evaluating the rationality of antibiotic therapy and promote rational drug use and quality of life of patients.

Aims and objectives: To study the prevalence and antibiogram of causative organisms, and the prescriptionpattern of antibiotics used in the treatment of diabetic foot infection.

Methodology: The retrospective study is conducted for a period of 6 months. Case records of 210 patients were selected based on the study criteria. A suitably designed data collection form wasused to collect the required data. Statistical analysis was done using Microsoft Excel.

Results: Males (77.6%) were more prone to diabetic foot infections. Hypertension (42%) was the most common comorbidity. *Staphylococcus aureus* (16%) was the most frequently isolatedbacteria and most of the infections were monomicrobial (63.8%). Cephalosporin class of antibiotics (34.6%) were most commonly prescribed. Clindamycin (26.6%) was the commonest empirical antibiotic. Out of 273 bacterial isolates, 229 isolates showed resistance to one or more antibiotics.

Conclusion: Since there is no antibiotic except for Tigecycline which is 100% sensitive in both Gram-negative and Gram-positive bacteria, it is recommended to prescribe a combination of highly effective antibiotics for empirical therapy.

Keywords: Bacteriological profile; Prescription pattern; Antibiotics; Diabetic foot ulcers Tertiary healthcare teaching hospital

1. Introduction

Diabetes mellitus is considered as one of the main public health issues worldwide. It is estimated that about 150-170 million of the world's population is suffering from this condition. Macrovascular and microvascular complications arise due to long-term poor control of blood glucose level. Neuropathy, retinopathy and foot ulcers are the most common complications [1]. Approximately 15% of diabetic patients are found to develop foot ulcers that can lead to osteomyelitis [2]. An ulcer is a result of actions of multiple contributing factors. The pathophysiology of ulcer is complicated and it

* Corresponding author: Taeyyeb Mahboub Moghaddam

includes neuropathy, vascular and immune system components. Neuropathy is a disease that affects nerves causing impaired sensations, movement and other aspects based on the affected nerve. It is found that elevated levels of intracellular advanced glycated end products, activation of protein kinase C, increased hexosamine pathway flux and polyol pathway. Damage to motor neurons cause anatomical deformities eventually leading to skin ulcerations. Sensory neuropathy results in recurrent foot injuries causing disruption in skin integrity. [3] Infection worsens the wound conditions by interfering with the healing mechanism, which if not treated in time, eventually lead to septicemia, amputation or death. In addition to optimum glycemic control, wound care, surgical debridement, pressure offloading and maintaining adequate blood supply, evaluation of microbiological profile is essential [4]. non-ischemic clean wound. (B) indicates non-ischemic infected wounds. (C) indicates ischemic wounds and (D) represents infected ischemic wounds. Clinical and laboratory data serve as criteria for each of the stages [5]. A relationship between the types of infections and the number and types of organisms recovered from wound infections has been investigated and it was found that mild infections are monomicrobial and are caused by aerobic gram-positive cocci such as *Staphylococcus aureus* and *Streptococcus* spp. Polymicrobial infections are severe and caused by aerobic gram-positive cocci, gram-negative bacilli (e.g: *Pseudomonas* spp, *Escherichia coli*, *Klebsiella* spp and *Proteus* spp) and anaerobes [6]. Recent studies have indicated the dominance of gram- negative pathogens in monomicrobial infections [7]. Development of complex colonizing flora is found in chronic wounds & they include*Enterococci*, various *Enterobacteriaceae*, obligate anaerobes, *Pseudomonas aeruginosa* and sometimes, other non-fermentation gram-negative rods. Patients are predisposed to antibiotic- resistant organisms [e.g., methicillin-resistant *Staphylococcus aureus* (MRSA) or vancomycin- resistant *Enterococci* (VRE)] due to hospitalization, surgical procedures and particularlyprolonged or broad-spectrum antibiotic treatment. Community cases associated with MRSA strains are now becoming common and are associated with worse therapeutic outcomes in patients with diabetic foot infections [8]. Many studies have been conducted on the bacteriology of DFIs but the results have been varied. These could be due to geographical variations, changes in pathogens over time, type and severity of infection [9].

2. Material and methods

2.1. Study design

Non-experimental, prospective, observational study.

2.1.1. Study site

The study was conducted at the surgical wards and general medicine wards of Father MullerMedical College “tertiary care teaching hospital”, Kankanady, Mangalore.

2.1.2. Sample size

n= 210

2.1.3. Duration of the study

The study was conducted over a period of 6 months.

2.1.4. Sources of data

The data sources required for the study were collected from the patient’s medical records(case sheets, laboratory investigations, medication charts).

2.2. Method of collection

2.2.1. Steps

- The records of patients admitted with the diagnosis of Diabetic Foot Ulcer weredocumented using data collection form.
- The treatment strategy subjected to the patient was documented and analysed.
- The obtained results were subjected to a suitable statistical method.

2.3. Operational modality

- Identification of the patient- Patients with Diabetic Foot Ulcer along with or without complications were identified from male medical wards, female medical wards, semi private and private wards.
- Collection of data- Patient demographic details, past medical history, past medication history, social history,

personal history, general examination, antibiogram reports were collected and recorded in the pre-designed data entry form.

2.4. Data collection

- IP number
- Bed number
- OP number
- Gender
- Age
- Date of admission and date of discharge
- Time since onset of diabetes
- Random blood sugar at admission
- Hba1c
- Fasting blood sugar
- Treatment chart
- Microbial culture report
- Antibiotic sensitivity report
- Details of complications (if present)
- All drugs used by patients prior to admissions

2.5. Study parameters

- Name, category and combination of antibiotics prescribed.
- Dose of the drug.
- Route of administration.
- Culture report
- Antimicrobial susceptibility data.

2.6. Statistical analysis

Descriptive statistical tools such as frequency, percentage, mean, standard deviation wasused to assess the pertinent data.

2.7. The outcome of analysis

The outcome of the analysis was to determine the prevalence of various pathogens responsiblefor DFIs and their antibiotic sensitivity pattern.

3. Results and discussion

The study was undertaken in Father Muller Multi-Specialty Hospital, Mangalore, Indiaand was approved by IEC. This retrospective study was conducted for a period of 6 months. Patient case records were reviewed and a total of 210 subjects were selected based on the studycriteria and a total of 284 microbiological investigations were done.

3.1. Age-wise distribution of patients

Table 1 Age wise distribution of the patients N=210

Age distribution (Years)	Frequency (%) (n=210)
31-40	7 (3.3%)
41-50	40 (19.05%)
51-60	77 (36.7%)
61-70	65 (31%)
71-80	19 (9.05%)
81-90	2 (0.9%)

The age of patients ranged from 31 to 87 with an average of 58.4(±10.2). The most prevalent age group was between 51 and 60 years (36.7%). The distribution in other age groupsis summarized in Table 1.

3.2. Gender-wise distribution of the patients

Gender wise distributions of the patients were analyzed and a majority of patients weremales (77.6%) with a male to female ratio of 3.46:1. The details are summarized in Table 2.

Table 2 Gender wise distribution of the patients N=210

Gender	Frequency (%) (n=210)
Male	163 (77.6%)
Female	47 (22.4%)

3.3. The duration of diabetes mellitus

The duration of diabetes mellitus ranged from 1 month to 40 years. A detailed summaryof results is given in Table 3.

Table 3 The duration of diabetes mellitus N=210

Duration of Diabetes mellitus (Years)	Frequency (%) n=210
<1	11 (5.2%)
1-10	99 (47%)
11-20	72 (34.2%)
21-30	26 (12.3%)
31-40	2 (0.9%)

3.4. Duration of diabetic foot ulcer

The duration of diabetic foot ulcers ranged from 1 day to one year. The details are summarized in Table 4.

Table 4 Duration of diabetic foot ulcer N=210

Duration of diabetic foot ulcer (months)	Frequency (%)
<1	128 (61%)
1-3	67 (32%)
4-6	8 (3.8%)
7-9	4 (1.9%)
10-12	3 (1.4%)

3.5. Duration of hospital stay

Out of 210 patients, it was found that most of the patients were hospitalized for 2- 10 days (46%), followed by 11-20 days (30.9%). A detailed summary of results is given in Table5.

Table 5 Duration of Hospital stay N=210

Duration of hospital stay (days)	Frequency (%) (n=210)
1-10	97 (46%)
11-20	65 (31%)
21-30	31 (14.8%)
>30	17 (8%)

3.6. Frequency distribution of Co-morbidities

87 (41.4%) patients out of 210 had no comorbidity and a total of 203 comorbidities were identified from 123 patients. 86 patients had hypertension (41%) which makes it the mostcommon comorbidity identified during the study. 39 patients had Ischemic Heart Disease (18.6%), followed by 24 patients with Chronic Kidney Disease (11.4%) and 17 patients with Peripheral Arterial Occlusive Disease (8%). The details are summarized in Table 6(Chart 1).

Table 6 Co-morbidities of the patients N=210

Co-morbidity	Frequency (%)
Hypertension	86 (41%)
Ischemic Heart disease	39 (18.6%)
Chronic Kidney Disease	24 (11.4%)
Peripheral Arterial Occlusive Disease	17 (8%)
Anemia	7 (3.3%)
Thyroid disease	2 (0.9%)

3.7. Microbiology of Diabetic Foot Ulcer

In the present study, 134 out of 210 cultures were monomicrobial (63.8%), 67 cultures revealed polymicrobial growth (32%) and 9 were culture-negative (4.2%). The details are summarized in Table 7 (Chart 2). A total of 275 microbial isolates were identified from 201 specimens with an average of 1.3 pathogens per lesion. 155 out of 275 were Gram-negative bacteria (56.4%), 118 were Gram-positive bacteria (42.9%) and 2 were Candida species (0.7%). The details are summarized in Table 8. *Staphylococcus aureus* was the most frequent bacteria isolated from 44 microbial cultures (16%) followed by *Escherichia coli* isolated from 37 cultures (13.4%), *Pseudomonas aeruginosa* isolated from 34 cultures (12.3%) and *Klebsiella pneumonia* isolated from 30 cultures (10.3%). Out of 155 Gram-negative bacteria isolated, the five most common were *Escherichia coli* (37; 23.8%), *Pseudomonas aeruginosa* (34; 22%), *Klebsiella pneumonia* (30;19.3%), Citrobacter species (17; 11%) and Proteus species (12; 7.7%). The five most frequently isolated Gram-positive bacteria (118) were *Staphylococcus aureus* (44; 37.2%), *Enterococcus species* (26; 22%), *Streptococcus agalactiae* (16;13.5), Methicillin-Resistant *Staphylococcus aureus* (14;11.8%) and Coagulase-negative Staphylococci (13; 11%). The most predominant bacteria involved in monomicrobial infection was *Staphylococcus aureus* (29; 22%), followed by *Escherichia coli* (20; 15%), *Pseudomonas aeruginosa* (17; 12.6%) and *Streptococcus agalactiae* (11; 8.2%). *Klebsiella pneumonia* (11; 64.4%) was the most prevalent bacteria in polymicrobial infections followed by *Staphylococcus aureus* (10; 15%), *Pseudomonas aeruginosa* (10; 15%) and *Escherichia coli* (8; 12%).

Table 7 Type of infection N=210

Type of infection	Number of specimen (%)
Culture negative	9 (4.2%)
Monomicrobial infection	134 (63.8%)
Polymicrobial infection	67 (32%)

Table 8 Microorganisms isolated from the diabetic foot wound culture N=210

Isolated pathogens	No. of isolates	Frequency
Gram- positive bacteria		
Coagulase negative *Staphylococci*	13	4.70%
Enterococcus species	26	9.45%
Methicillin-resistant *Staphylococcus aureus*	14	5.09%
Staphylococcus aureus	44	16%
Streptococcus agalactiae	16	5.80%
Streptococcus pyogenes	5	1.80%
Gram-negative bacteria		
Acinetobacter species	9	3.20%
Citrobacter species	17	6.20%
Enterobacter species	6	2.10%
Escherichia coli	37	13.50%
Klebsiella oxytoca	3	1.09%
Klebsiella pneumoniae	30	10.90%
Morganella species	3	1.09%
Proteus species	12	4.36%
Pseudomonas aeruginosa	34	12.36%
Pseudomonas species	4	1.40%
Fungal species:		
Candida species	2	0.70%

3.8. Prescription pattern of antibiotics

Table 9 Most commonly used empirical antibiotics N=210

Antibiotics	Frequency
Clindamycin	95 (45.2%)
Amoxicillin- Clavulanic acid	74 (35.2%)
Cefuroxime-Sulbactam	32 (15.2%)
Piperacillin- Tazobactam	31 (14.8%)
Metronidazole	23 (10.9%)
Ceftriaxone	19 (9%)
Cefuroxime	19 (9%)
Cefoperazone	11 (5.2%)
Ceftriaxone+Sulbactum	11 (5.2%)

A total of 566 antibiotics were prescribed and with respect to the class of antibiotics, Cephalosporins (34.6%) were majorly prescribed, followed by Penicillins(20.6%). 356 empirical antibiotics were prescribed in 210 patients.

Clindamycin (45.2%), Amoxicillin- Clavulanic acid (35.2%), Cefuroxime-Sulbactam (15.2%) and Piperacillin-Tazobactam (14.8%) were the most commonly prescribed empirical antibiotics. The detailed summary is given in Table 9. The empirical antibiotics were prescribed as dual therapy in 122 patients (58%) followed by monotherapy in 76 patients (36%) and triple therapy in 12 patients (5%). 45(22%) out of 200 specimens with positive bacterial culture indicated resistance to the prescribed empirical antibiotics. 210 definitive antibiotics were prescribed and Linezolid constituted for 16% of the prescribed definitive antibiotics.

3.9. Antibiogram of gram-positive and gram-negative bacteria

Table 10 Antibiotic resistance in Gram positive bacteria N=210

Antibiotics	Coagulase negative *Staphylococci*	*Enterococcus* species	Methicillin Resistant *Staphylococcus aureus*	*Staphylococcus aureus*	*Streptococcus agalactiae*	*Streptococcus pyogenes*
AMC	40%	14%	100%	31%	0%	0%
AMP	54%	35%	100%	47%	0%	0%
PPT	—	100%	—	—	—	—
CFZ	42%	100%	100%	38%	0%	0%
CFR	42%	100%	100%	24%	0%	0%
CFT	42%	100%	100%	24%	0%	0%
CFD	—	—	—	0%	0%	—
CFN	100%	—	100%	0%	0%	—
CFS	—	100%	—	—	—	—
CFO	100%	—	—	0%	—	—
GTN	36%	75%	50%	16%	20%	50%
AMK	13%	75%	25%	0%	13%	100%
CPF	50%	38%	75%	50%	8%	0%
LVF	45%	35%	75%	53%	10%	0%
IMP	0%	18%	0%	—	0%	0%
MRP	—	42%	—	—	0%	0%
TGC	—	0%	—	—	—	—
AZT	82%	81%	71%	51%	31%	0%
VNC	9%	5%	0%	0%	0%	0%
TCP	9%	0%	0%	0%	0%	20%
ATN	—	—	—	—	0%	—
LZD	0%	0%	0%	0%	0%	0%
CLN	82%	73%	36%	13%	17%	0%
CTZ	36%	57%	10%	13%	38%	0%
PMB	0%	—	—	—	—	—

AMC: Amoxicillin- Clavulanic acid; AMP: Ampicillin; PPT: Piperacillin-Tazobactam; CFZ: Cefazolin; CFR: Cefuroxime; CFT: Cefotaxime; CFD: Ceftazidime; CFN: Ceftriaxone; CFS: Cefoperazone-Sulbactam; CFO: Cefoxitin; GTN: Gentamicin; AMK: Amikacin; CPF: Ciprofloxacin; LVF: Levofloxacin; IMP: Imipenem; MRP: Meropenem; TGC: Tigecycline; AZT: Azithromycin; VNC: Vancomycin; TCP: Teicoplanin; ATN: Aztreonam; LZD:

44 bacterial isolates had no antibiotic resistance, out of which 20 were Gram-positive and 24 were Gram-negative. Cefazolin, Cefotaxime, Azithromycin and Clindamycin were found to be highly resistant in Gram-positive bacteria. Vancomycin, Teicoplanin, Linezolid and Tigecycline were the antibiotics to which gram-positive bacteria had maximum susceptibility. Table.10 and Table.12 present the antibiotic resistance pattern and sensitivity pattern of Gram-positive bacteria respectively. Gram-negative bacteria had high resistance to antibiotics like Amoxicillin-Clavulanic acid, Ampicillin, Cefazolin, Cefuroxime and Cefotaxime. They were highly sensitive to Piperacillin-Tazobactam, Gentamicin, Amikacin, Ciprofloxacin, Levofloxacin, Imipenem, Meropenem, Tigecycline, Aztreonam and Polymyxin B. Table.11 and table.13 illustrate the antibiotic resistance and sensitivity pattern of gram- negative bacteria respectively.

Table 11 Antibiotic resistance in Gram negative bacteria N=210

←Antibiotics	*Acinetobacter* species	*Citrobacter* species	*Enterobacter* species	*Escherichia coli*	*Klebsiella oxytoca*	*Klebsiella pneumoniae*	*Morganella* species	*Proteus* species	*Pseudomonas aeruginosa*	*Pseudomonas* species
AMC	50%	75%	0%	82%	100%	75%	—	67%	—	—
AMP	67%	93%	100%	87%	100%	96%	—	73%	—	—
PPT	22%	0%	0%	14%	0%	13%	0%	0%	16%	25%
CFZ	63%	63%	60%	68%	100%	48%	50%	50%	—	—
CFR	71%	63%	60%	70%	67%	50%	50%	50%	—	—
CFT	75%	47%	60%	58%	100%	45%	0%	17%	0%	—
CFD	—	—	100%	—	—	100%	—	—	20%	25%
CFN	—	—	100%	33%	—	33%	0%	25%	—	—
CFS	13%	0%	0%	12%	0%	17%	0%	0%	21%	75%
GTN	38%	25%	25%	22%	0%	21%	0%	9%	26%	20%
AMK	44%	6%	0%	12%	0%	17%	0%	9%	21%	0%
CPF	44%	33%	50%	63%	33%	19%	0%	10%	36%	0%
LVF	44%	23%	50%	66%	33%	15%	0%	11%	36%	0%
IMP	22%	0%	17%	3%	0%	10%	0%	0%	9%	0%
MRP	22%	0%	17%	3%	0%	11%	0%	0%	16%	0%
TGC	0%	0%	0%	0%	0%	0%	—	0%	0%	0%
AZT	—	100%	100%	—	—	—	—	—	0%	—
VNC	—	100%	0%	0%	—	—	—	—	—	—
TCP	—	100%	0%	0%	—	—	—	—	—	—
ATN	0%	0%	100%	0%	—	0%	—	—	8%	—
LZD	—	100%	0%	—	—	—	—	—	—	—
CLN	—	—	100%	—	—	0%	—	—	—	—
CTZ	50%	14%	50%	53%	0%	38%	100%	33%	69%	0%
PMB	0%	0%	—	0%	0%	0%	100%	—	13%	0%

Table 12 Antibiotic sensitivity in Gram positive bacteria N=210

←Antibiotics	Coagulase negative *Staphylococci*	*Enterococcus* species	Methicillin Resistant *Staphylococcus aureus*	*Staphylococcus aureus*	*Streptococcus agalactiae*	*Streptococcus pyogenes*
AMC	60%	86%	0%	69%	100%	100%
AMP	46%	65%	0%	53%	100%	100%
PPT	—	0%	—	—	—	—
CFZ	58%	0%	0%	62%	100%	100%
CFR	58%	0%	0%	76%	100%	100%
CFT	58%	0%	0%	76%	100%	100%
CFD	—	—	—	100%	100%	—
CFN	0%	—	0%	100%	100%	—
CFS	—	0%	—	—	—	—
CFO	0%	—	—	100%	—	—
GTN	64%	25%	50%	84%	80%	50%
AMK	88%	25%	75%	100%	88%	0%
CPF	50%	62%	25%	50%	92%	100%
LVF	55%	65%	25%	47%	90%	100%
IMP	100%	82%	100%	—	100%	100%
MRP	—	58%	—	—	100%	100%
TGC	—	100%	—	—	—	—
AZT	18%	19%	29%	49%	69%	100%
VNC	91%	95%	100%	100%	100%	100%
TCP	91%	100%	100%	100%	100%	80%
ATN	—	—	—	—	100%	—
LZD	100%	100%	100%	100%	100%	100%
CLN	18%	27%	64%	88%	83%	100%
CTZ	64%	43%	90%	87%	62%	100%
PMB	100%	—	—	—	—	—

Table 13 Antibiotic sensitivity in Gram negative bacteria N=210

←Antibiotics	*Acinetobacter species*	*Citrobacter species*	*Enterobacter spe*	*Escherichia coli*	*Klebsiella oxytoca*	*Klebsiella pneumoniae*	*Morganella species*	*Proteus species*	*Pseudomonas aeruginosa*	*Pseudomonas species*
AMC	50%	25%	100%	18%	0%	25%	—	33%	—	—
AMP	33%	7%	0%	13%	0%	4%	—	27%	—	—
PPT	78%	100%	100%	86%	100%	87%	100%	100%	84%	75%
CFZ	38%	38%	40%	32%	0%	52%	50%	50%	—	—
CFR	29%	38%	40%	30%	33%	50%	50%	50%	—	—
CFT	25%	53%	40%	42%	0%	55%	100%	83%	100%	—
CFD	—	—	0%	—	—	0%	—	—	80%	75%
CFN	—	—	0%	67%	—	67%	100%	75%	—	—
CFS	88%	100%	100%	88%	100%	83%	100%	100%	79%	25%
CFO	—	—	—	—	—	—	—	—	—	—
GTN	63%	75%	75%	78%	100%	79%	100%	91%	74%	80%
AMK	56%	94%	100%	88%	100%	83%	100%	91%	79%	100%
CPF	56%	67%	50%	37%	67%	81%	100%	90%	64%	100%
LVF	56%	77%	50%	34%	67%	85%	100%	89%	64%	100%
IMP	78%	100%	83%	97%	100%	90%	100%	100%	91%	100%
MRP	78%	100%	83%	97%	100%	89%	100%	100%	84%	100%
TGC	100%	100%	100%	100%	100%	100%	—	100%	100%	100%
AZT	—	0%	0%	—	—	—	—	—	100%	—
VNC	—	0%	100%	100%	—	—	—	—	—	—
TCP	—	0%	100%	100%	—	—	—	—	—	—
ATN	100%	100%	0%	100%	—	100%	—	—	92%	—
LZD	—	0%	100%	—	—	—	—	—	—	—
CLN	—	—	0%	—	—	100%	—	—	—	—
CTZ	50%	86%	50%	47%	100%	63%	0%	67%	31%	100%
PMB	100%	100%	—	100%	100%	100%	0%	—	87%	100%

4. Conclusion

In our study, the most prevalent age group was between 51 and 60 years and majority of patients were males. Hypertension was the most common comorbidity. Gram-negative bacteria were the most commonly isolated pathogens. The majority of diabetic foot infectionswere monomicrobial in nature. *Staphylococcus aureus* is the most frequently isolated bacteria.Cephalosporins were a majorly prescribed class of antibiotics followed by Penicillins. Clindamycin was the most commonly prescribed empirical antibiotic. The empirical antibioticswere prescribed as dual therapy in most of the patients. Gram-positive bacteria were highly susceptible to Vancomycin, Teicoplanin, Linezolid and Tigecycline. Most of the Gram- negative bacteria were highly sensitive to Piperacillin- Tazobactam, Cefoperazone- Sulbactam, Imipenem, Meropenem and Tigecycline. Except for Tigecycline, no other antibiotic has 100%sensitivity in both Gram-positive and Gram-negative bacteria. Hence a combination of antibiotics is preferred for empirical therapy which can

then be modified based on culture- sensitivity results and patient's response. It can be concluded that our study may help in the rational prescription of antibiotics in the treatment of diabetic foot infections.

Compliance with ethical standards

Acknowledgments

We are very much delighted to connote our vehement indebtedness to our beloved teacher and guide Dr. K. Ravi Kumar, M.Pharm, Ph.D, Principal, Karavali College of Pharmacy, Vamanjoor, Mangalore who is extending timely guidance at each and every step of this work, enthusiastic encouragement and excellent support which helped us to complete this work successfully. We sincerely thank our co-guide Dr. Prasanna M Bhat, MBBS, MD, Department of Microbiology, FMMCH whose help guided us throughout our work. We owe our heartfelt thankfulness to our teacher Mr. Sandeep Kumar B, M.Pharm, Assistant Professor & Head, Department of Pharmacy Practice, for providing all the necessary guidance and facilities to carry out this project work. It is our privilege and wonderful experience to be part of this esteemed institution and we owe our sincere thanks to Sri S. Ganesh Rao, founder, and chairman of Karavali group of institutions.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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