

Access this article online
Quick Response Code:

Website: www.jehp.net
DOI: 10.4103/jehp.jehp_1552_20

# Diabetic foot infections: Profile and antibiotic susceptibility patterns of bacterial isolates in a tertiary care hospital of Oman

Mohan Bilikallahalli Sannathimmappa, Vinod Nambiar, Rajeev Aravindakshan<sup>1</sup>, Mohammad Saleem Jawad Al Khabori<sup>2</sup>, Asma Hamed Sulaiman Al-Flaiti<sup>2</sup>, Kadhiya Nasser Mohamed Al-Azri<sup>2</sup>, Ali Khamis Saif Al-Reesi<sup>3</sup>, Alya Rashid Mohammad Al Kiyumi<sup>4</sup>

Department of Microbiology, College of Medicine and Health Sciences, Sohar Campus, National University of Science and Technology, Oman, <sup>1</sup>Department of Community Medicine, All India Institute of Medical Sciences, Mangalagiri, Andhra Pradesh, India, <sup>2</sup>Oman Medical Specialty Board, Oman, <sup>3</sup>Department of Internal Medicine, Sohar Hospital, Oman, <sup>4</sup>Department of Podiatric, Sohar Hospital, Oman

## Address for correspondence:

Dr. Mohan Bilikallahalli Sannathimmappa, Department of Microbiology, College of Medicine and Health Sciences, National University of Science and Technology, PO Box: 391, PC: 321, Al Tareef, Sohar, Sultanate of Oman.  
E-mail: drmohan123@gmail.com

Received: 30-11-2020  
Accepted: 13-12-2020  
Published: 30-07-2021

## Abstract:

**BACKGROUND:** In diabetic foot infections (DFIs), the diversity of microbial profile and ever-changing antibiotic-resistance patterns emphasize accurate characterization of microbial profile and antibiotic susceptibility pattern. The aim of the study was to investigate the pathogens associated with DFI and their antibiotic susceptibility patterns.

**MATERIALS AND METHODS:** A cross-sectional retrospective study was conducted at a tertiary-care hospital, Oman. The socio-demographic and microbiological profile and antibiotic susceptibility patterns of pathogens isolated from patients with DFIs from January 2013 to December 2018 were reviewed. Quantitative and qualitative variables were expressed as mean  $\pm$  standard deviation and percentages, respectively. A Chi-square test was used for testing the association between multidrug-resistant (MDR) organisms and variables.

**RESULTS:** In total, 233 isolates recovered from 133 clinical specimens with an average of 1.8 organisms per specimen were included in the study. Fifty-six and forty-four percent of specimens showed monomicrobial and polymicrobial growth of two or more organisms, respectively. The frequency of isolation was predominant among males (65%). Aerobic Gram-negative rods were predominantly (75%) isolated compared to Gram-positive organisms (25%). *Staphylococcus aureus* and *Pseudomonas aeruginosa* were the most frequently isolated Gram-positive and Gram-negative bacteria, respectively. Thirty-eight percent of them were MDR strains. Gram-negative organisms showed fairly good susceptibility ranging from 75% to 100% to carbapenems, aminoglycosides, and piperacillin-tazobactam. While doxycycline and trimethoprim-sulfamethoxazole showed good susceptibility toward Gram-positive organisms.

**CONCLUSION:** DFIs are often polymicrobial with a predominance of Gram-negative pathogens. This study recommends the use of carbapenems and doxycycline for empirical therapy of Gram-negative and Gram-positive bacterial DFIs, respectively.

## Keywords:

Antibiogram, beta-lactamases, carbapenems, diabetic foot, polymicrobial infection

## Introduction

Diabetes is one of the oldest and major chronic noncommunicable endocrine disorders, which may result in severe health

consequences due to damage to various end organs.<sup>[1]</sup> It is of major global public health concern afflicting a large number of people of all socioeconomic statuses.<sup>[2]</sup> As per the report of the international diabetes

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow\_reprints@wolterskluwer.com

**How to cite this article:** Sannathimmappa MB, Nambiar V, Aravindakshan R, Al Khabori MS, Al-Flaiti AH, Al-Azri KN, *et al.* Diabetic foot infections: Profile and antibiotic susceptibility patterns of bacterial isolates in a tertiary care hospital of Oman. J Edu Health Promot 2021;10:254.

federation, the number of people living with diabetes in the world in 2017 was 435 million.<sup>[3]</sup> The number is alarmingly increasing and would rise to 728 million by the year 2045.<sup>[3]</sup> The prevalence of diabetes in Middle Eastern and North African (MENA) regions is also high. About 39 million people were diagnosed with diabetes in the MENA region in 2017.<sup>[4]</sup> In Oman, approximately 367 thousand people were found to be suffering from diabetes in 2017.<sup>[4]</sup> The prevalence of diabetes is projected to double in the MENA region by 2035.<sup>[4]</sup>

One of the serious consequences of diabetes is diabetic foot infections (DFIs) and its complications such as osteomyelitis.<sup>[1-5]</sup> These further may lead to repeated hospitalization, treatment failure, and increased health-care expenses.<sup>[1,6]</sup> A previous study reports that at least 20% of the DFIs are managed by lower limb amputation.<sup>[7]</sup> DFIs are common, especially in men and individuals older than 60 years.<sup>[1,5]</sup> The development of DFI is predisposed by multiple factors such as peripheral vascular disease (PVD), peripheral neuropathy, trauma, diabetic foot ulcer (DFU), and impaired host immunity.<sup>[2,8]</sup> However, the optimal management of DFIs and DFUs through a multi-disciplinary approach favors the better outcome in terms of reduced morbidity, mortality, and health-care costs.<sup>[9]</sup>

The microbiology of DFI is often polymicrobial comprising of both Gram-positive and Gram-negative aerobic bacteria and anaerobes.<sup>[4,8]</sup> Concerning the etiology of DFI, studies have shown diversity in pathogens and their susceptibility patterns. *Staphylococcus aureus* was reported as a predominant pathogen associated with DFI.<sup>[2]</sup> In contrast, the predominance of Gram-negative bacteria such as *Pseudomonas aeruginosa*, *Escherichia coli*, and *Klebsiella pneumoniae* was observed in some studies.<sup>[9,10]</sup> Other common Gram-negative rods isolated from DFI are *Proteus spp.* and *Acinetobacter baumannii*.<sup>[9,10]</sup>

Optimal management of DFI requires the appropriate selection of antibiotics based on the antibiotic susceptibility pattern of isolates.<sup>[7,9]</sup> The type of infecting microorganisms and their antibiotic susceptibility pattern differs from country to country and from one region to another within the country.<sup>[7,8]</sup> Globally, multidrug-resistant organisms (MDROs) such as methicillin-resistant *S. aureus* (MRSA), extended-spectrum beta-lactamase (ESBL) producers, carbapenem-resistant *Enterobacteriaceae* (CRE) have dramatically increased in the past two decades. These pose a serious challenge for physicians to treat DFIs and are often lead to treatment failure and increased mortality.<sup>[2,11,12]</sup> Indiscriminate use of antibiotics is a major factor driving antibiotic resistance.<sup>[7,11,12]</sup> Therefore, it is necessary to routinely assess microbes and their antibiotic resistance patterns. The precise knowledge among clinicians about the

pathogens and their antibiotic susceptibility pattern in a particular locality and judicious use of antibiotics is imperative for better management of DFIs and thereby to reduce the development of antimicrobial resistance and healthcare expenses.<sup>[11,12]</sup> On a thorough literature search, authors could not find any such studies related to DFI in Oman, particularly in the North-Batinah region of Oman. Hence, the aim of the current study was to determine the bacterial profile and antimicrobial susceptibility pattern of pathogens isolated from patients with DFI.

## Materials and Methods

### Study design

The current retrospective cross-sectional study was conducted at a 400-bed tertiary care hospital in the North Batinah region, Oman. The data of 233 bacterial isolates recovered from 74 patients diagnosed with a DFI from January 2013 to December 2018 were retrieved systematically from Al-Shifa Computerized System and microbiology laboratory records. The data included a socio-demography, clinical, and bacterial profile of DFIs and their antibiotic susceptibility patterns.

### Ethical consideration

The study was approved by the Research and Ethical Committee, Ministry of Health, Oman (MH/DHGS/NBG/9/2018).

### Data collection and sample processing procedure *Specimen collection and bacterial identification method*

The surface of the wound was vigorously cleaned with saline to avoid the possible isolation of normal skin commensals rather than the pathogen. After a thorough cleaning, the specimen was collected by scraping from the ulcer base, wound curettage, and aspiration of the pus, necrotic tissue, and bony fragments. Gram staining of these specimens was done to differentiate between colonization and infection using Q score. Specimens were cultured by plating on MacConkey agar and Blood agar and incubated at 37°C in ambient air. The isolates were identified up to the species level by the standard microbiological methods and the automated VITEK 2 system (Bio-Merieux, France) as recommended by the Clinical Laboratory Standards Institute (CLSI).<sup>[13]</sup> Antimicrobial susceptibility testing was performed using Kirby-Bauer's disc diffusion method on Mueller-Hinton agar using Oxoid antibiotic discs. The antibiotic panel used are gentamicin (10 µg), clindamycin (2 µg), linezolid (30 µg), erythromycin (15 µg), ampicillin (10 µg), trimethoprim-sulfamethoxazole (1.25/23.75 µg), ciprofloxacin (5 µg), amoxicillin-clavulanic acid (30 µg), piperacillin-tazobactam (100/10 µg), imipenem (10 µg), meropenem (10 µg), amikacin (10 µg), doxycycline (30 µg), vancomycin (30 µg), cefotaxime (30 µg), ceftriaxone (30 µg), cefuroxime (30 µg),

ceftazidime (30 µg), and colistin (10 µg) as recommended by the CLSI.<sup>[13]</sup> Vancomycin and oxacillin minimal inhibitory concentrations were determined by E-Test (Bio Mérieux) according to CLSI guidelines. Quality control was performed using *E. coli* ATCC 25922, *P. aeruginosa* ATCC 27853, and *S. aureus* ATCC 29213. The antibiotic susceptibility report of each isolate was interpreted as sensitive, intermediate, or resistance as per the CLSI guidelines.<sup>[13]</sup>

### Identification of multidrug-resistant organisms

The organisms that have acquired non-susceptibility to at least one antimicrobial agent in three or more classes of antimicrobial agents were termed as multidrug-resistant (MDR) pathogens. Further, MDROs were categorized as MRSA, ESBL producers, and CRE.

*Staphylococcus* species were tested for methicillin resistance using cefoxitin disc (30 µg). Inhibition zone  $\leq 21$  mm with cefoxitin disk was reported as methicillin-resistant and a zone diameter of  $\geq 22$  mm was considered sensitive according to the CLSI guidelines.<sup>[13]</sup> Gram-negative bacilli were further tested for the production of ESBL by a double-disc diffusion method using ceftazidime (30 µg) and ceftazidime/clavulanic acid (30/10 µg). An increase in diameter of  $\geq 5$  mm with ceftazidime plus clavulanic acid as compared to ceftazidime disk alone was considered positive for ESBL detection.<sup>[14]</sup> The resistance of Gram-negative *Enterobacteriaceae* organisms to carbapenems and colistin were referred to as CRE and colistin-resistant organisms, respectively.

### Data analysis

The data obtained were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 22, IBM, Chicago. Quantitative variables were expressed as mean  $\pm$  standard deviation, while qualitative variables were expressed as percentages. Chi-square test (with or without Yates correction) was used for testing the association between MDRO and variables. Odds Ratios were derived with 95% confidence intervals.

## Results

In the current study, a total of 233 isolates recovered from 133 clinical specimens with an average of 1.8 organisms per specimen were included in the study. Table 1 shows the socio-demography and clinical characteristics of patients with DFI. The frequency of isolation was predominant among males (65%) compared to females (35%). The mean age of the subjects was  $65 \pm 11$  and nearly three-fourth (76%) had a history of diabetes for more than 10 years. Among them, 24% and 46% had osteomyelitis and amputation, respectively. Concerning underlying comorbidity, the vast majority of

**Table 1: Sociodemographic characteristics of diabetic foot patients**

Characteristic (variables)	Values, n (%)
Age (mean $\pm$ SD)	65 $\pm$ 11
Gender	
Male	48 (65)
Female	26 (35)
Nature of the diabetic foot disease	
Diabetic foot ulcer	42 (57)
Diabetic foot gangrene	17 (23)
Diabetic foot abscess	17 (23)
Comorbidities and complications	
Peripheral vascular diseases	67 (91)
Cardiac complications	35 (47)
Peripheral neuropathy	33 (45)
Nephropathy	21 (28)
Retinopathy	7 (9)
Osteomyelitis	18 (24)
Amputation of the toes, foot or leg	34 (46)

SD=Standard deviation

the patients had PVDs (91%). Cardiac conditions including hypertension (47%), peripheral neuropathy (45%), nephropathy (28%), and retinopathy (9%) were the other comorbidities noticed in these patients.

Table 2 depicts the bacterial culture characteristics and the type of bacteria isolated from the clinical specimens obtained from the patients of DFI. Polymicrobial growth of two or more organisms was observed predominantly (56%) compared to monomicrobial growth (44%) in clinical samples. Gram-negative bacterial isolates were (75%) predominant compared to Gram-positive bacteria (25%). *S. aureus* (19%) was the most common Gram-positive isolate, followed by *Streptococcus spp.* (4%), *S. epidermidis* (1%), and *E. faecalis* (1%). Among the Gram-negative bacteria, *P. aeruginosa* was the predominant isolate (17%), followed by *Enterobacteriaceae* such as *E. coli* (16%), *K. pneumoniae* (15%), *Proteus spp.* (13%), *Enterobacter spp.* (5%), *Citrobacter spp.* (3%), and *M. morgagnii* (2%). *A. baumannii* (3%) was the other non-fermentative Gram-negative bacilli isolated apart from *P. aeruginosa*.

Antibiotic susceptibility pattern of the clinical isolates obtained by Kirby-Bauer disk diffusion technique are summarized in Table 3. All Gram-positive isolates were susceptible to doxycycline while all *Staphylococcus* strains were susceptible to trimethoprim-sulfamethoxazole (TMP-SMX). Fifty-nine percent (59%) of *S. aureus* strains were found to be methicillin-resistant *Staphylococcus aureus* (MRSA). All MRSA and *Enterococcus spp.* were susceptible to vancomycin and linezolid.

Gram-negative bacteria have shown a wide variation in their susceptibility pattern to the tested antibiotics [Table 3]. The

**Table 2: Characteristics of culture and bacteria isolated from diabetic foot lesions**

Culture characteristics	Value, n (%)
Total number of specimens cultured	133
Total number of isolates	233
Nature of the microbial growth	
Monomicrobial	74 (56)
Polymicrobial	59 (44)
Total number of Gram-positive bacteria isolated from the clinical specimen (n=59)	
<i>S. aureus</i>	44 (19)
CONS	03 (1)
<i>Streptococcus</i> spp.	09 (4)
<i>Enterococcus</i> spp.	03 (1)
Total number of gram negative bacteria isolated from the clinical specimen (n=174; 75%)	
<i>P. aeruginosa</i>	40 (17)
<i>E. coli</i>	37 (16)
<i>K. pneumoniae</i>	35 (15)
<i>Proteus</i> spp.	31 (13)
<i>Citrobacter</i> spp.	8 (3)
<i>Enterobacter</i> spp.	12 (5)
<i>A. baumannii</i>	7 (3)
<i>M. morgani</i>	4 (2)
MDR pathogens	
MRSA	26/54 (59)
MDR Gram negative pathogens	62/174 (36)
ESBL producers	32/52 (62)
CRE	7/62 (11)
Colistin resistant gram-negative pathogens	8/174 (5)
Other MDR pathogens	29/174 (17)

CONS=Coagulase negative staphylococci, MDR=Multidrug-resistant, *S. aureus*=*Staphylococcus aureus*, *P. aeruginosa*=*Pseudomonas aeruginosa*, *E. coli*=*Escherichia coli*, *K. pneumoniae*=*Klebsiella pneumoniae*, *A. baumannii*=*Acinetobacter baumannii*, *M. morgani*=*Morganella morgani*, ESBL=Extended-spectrum beta-lactamase, CRE=Carbapenem resistant *Enterobacteriaceae*, MRSA=Methicillin resistant *S. aureus*

susceptibility of Gram-negative organisms to carbapenems, piperacillin-tazobactam, and aminoglycosides ranged from 75% to 100%. While low to high-level resistance (0-75%) of Gram-negative organisms to cephalosporins, amoxicillin-clavulanic acid, ampicillin, and TMP-SMX was observed. Table 4 shows the association of study characteristics in patients infected with MDROs and non-MDROs. Thirty-six percent (36%) strains were found to be MDR Gram-negative pathogens. Among them, 52%, 11%, and 8% were ESBL producers, CRE, and colistin-resistant organisms, respectively. *K. pneumoniae* (38%), *E. coli* (36%), *P. aeruginosa* (10%), *Proteus* spp. (7%), *A. baumannii* (5%), *Citrobacter* spp. and *Enterobacter* spp. (2% each) were the commonly isolated MDR Gram-negative isolates. Colistin resistance was noticed in 3% and 2% of *K. pneumoniae* and *Proteus* spp. respectively.

## Discussion

DFIs are common devastating complications in diabetes mellitus (DM) patients.<sup>[1-5]</sup> Untreated DFIs may lead to

consequences such as osteomyelitis and amputation.<sup>[15]</sup> From time to time, the pattern of bacterial profile and their antibiotic susceptibility pattern changes from one region to another within the country and also between the countries. Lack of updated knowledge among physicians regarding the microbial profile and their antibiotic susceptibility pattern in a locality will hinder the selection of appropriate empirical antibiotic therapy of DFI for the best outcome.<sup>[15]</sup> In the current study, the majority (60%) of DFIs were seen predominantly in elderly people, aged >60 years and the odds ratio when age more than 60 years were compared with the rest was 1.851 (0.7041–4.917). Increased prevalence among the elderly is due to multiple reasons such as longer duration of DM, the presence of multiple comorbidities, and reduced immune status.<sup>[5]</sup> DFIs are more common among males due to the fact that they more frequently involved in outdoor activities and are prone to develop injuries and foot ulcers. These findings are consistent with previous studies.<sup>[1,12]</sup>

Among the co-morbidities, PVD was the most commonly associated comorbidity, followed by hypertension, neuropathy, nephropathy, and retinopathy. PVD increases the risk of microvascular and macrovascular complications. Common devastating problems of the DFIs are osteomyelitis and nontraumatic lower limb amputation.<sup>[16]</sup> A total of 1739 (47.3%) diabetes-related amputation was performed between 2002 and 2013 in Oman and about two-thirds of these patients were males.<sup>[17,18]</sup> Similar to these results, 46% of the patients in our study group had undergone amputation.

Microbiological evaluation revealed that DFIs are often polymicrobial (44%) similar to previous studies.<sup>[4,9,12,13]</sup> Regarding the predominance of the etiological agent in DFI, several studies have shown diversity in the pathogens associated with the infections.<sup>[9,10,19,20]</sup> Studies by Mohanty *et al.* and Sugandi *et al.* have shown the predominance of Gram-negative rods such as *P. aeruginosa* and *E. coli*.<sup>[9,10]</sup> In contrast, Mendes *et al.* and Ramakant *et al.*, in their studies observed the predominance of DFI by *S. aureus*.<sup>[19,20]</sup> In line with this, we observed the predominance of Gram-negative bacterial infection overall (75%) with *P. aeruginosa* being the most frequently isolated Gram-negative pathogen. However, overall *S. aureus* remains the most common isolate in our study subjects which is similar to studies mentioned elsewhere.<sup>[19,20]</sup>

Knowledge about the local antibiotic susceptibility pattern of the isolates is highly essential for the proper management of DFIs. In the present study, antibiotics such as vancomycin and linezolid showed 100% susceptibility toward Gram-positive isolates. These findings are congruent with the previous studies.<sup>[8,12,20]</sup>

**Table 3: Antibiotic susceptibility patterns of gram-negative and gram-positive isolates**

Antibiotics	Bacterial isolates and their antibiotic susceptibility rate (%)											
	<i>S. aureus</i> (n=18)	MRSA (n=26)	CONS (n=3)	<i>Streptococcus</i> spp. (n=9)	<i>Enterococcus</i> spp. (n=3)	<i>P. aeruginosa</i> (n=40)	<i>A. baumannii</i> (n=7)	<i>E. coli</i> (n=37)	<i>K. pneumoniae</i> (n=35)	<i>Proteus</i> spp. (n=31)	<i>Citrobacter</i> spp. (n=8)	<i>Enterobacter</i> spp. (n=12)
AUGM	100	0	100	100	67	-	51	40	65	50	17	0
CIPR	100	55	67	-	0	70	43	40	77	88	92	100
AMPI	44	0	67	100	33	-	24	25	58	13	8	100
TMP-SMX	100	100	100	67	50	-	59	57	71	88	83	-
ERYT	100	60	67	100	-	-	-	-	-	-	-	100
CLIN	100	83	67	100	-	-	-	-	-	-	-	-
AMIK	-	-	-	-	-	75	43	83	90	100	92	100
GENT	100	83	67	-	-	83	43	83	72	88	92	100
DOXY	100	100	100	100	100	-	-	-	72	-	-	-
VANC	100	100	100	-	100	-	-	-	-	-	-	-
LINZ	-	100	100	-	100	-	-	-	-	-	-	-
CFTX	-	-	-	100	67	55	-	62	87	75	100	100
CTAZ	-	-	-	-	-	65	43	37	42	-	-	100
CFXM	-	-	-	-	-	57	57	66	71	75	58	100
TAZP	-	-	-	-	-	88	86	57	100	100	100	100
IMIP	-	-	-	-	-	82	86	83	84	100	100	-
MERO	-	-	-	-	-	88	100	83	100	100	100	-
CL	-	-	-	-	-	100	100	92	90	-	-	-

AUGM=Amoxicillin-clavulanic acid, CIPR=Ciprofloxacin, AMPI=Ampicillin, ERYT=Erythromycin, CLIN=Clindamycin, GENT=Gentamicin, DOXY=Doxycycline, VANC=Vancomycin, LINZ=Linezolid, CFTX=Cefotaxime, CTAZ=Ceftazidime, TAZP=Piperacillin-tazobactam, IMIP=Imipenem, MERO=Meropenem, CL=Colistin, AMIK=Amikacin, CFXM=Cefturoxime, TMP-SMX=Trimethoprim-sulfamethoxazole, CONS=Coagulase negative staphylococci, *S. aureus*=Staphylococcus aureus, *P. aeruginosa*=Pseudomonas aeruginosa, *E. coli*=Escherichia coli, *K. pneumoniae*=Klebsiella pneumoniae, *A. baumannii*=Acinetobacter baumannii, *M. morganii*=Morganella morganii, MRSA=Methicillin resistant *S. aureus*

**Table 4: Association of study characteristics in patients infected with multidrug-resistant organisms and nonmultidrug-resistant organisms**

Characteristic	MDRO (n=45)	Non-MDRO (n=29)	P	OR (95%)
Age (years)				
<50	7	5	0.35887	1.000
51-60	8	9		0.635
> 60	30	15		1.429*
Patients with poor glycemic control (HBA1c >8%)*	27	5	0.04211	4.625 (1.031-23.25)
Patients with good/fairly good glycemic control (HBA1c <8%)*	9	8		
Number of patients with osteomyelitis (n=16)	12	6	0.5585	1.388 (0.4081-5.194)
Number of patients who underwent amputation (n=34)	27	7	0.002512	4.611 (1.511-15.62)

HBA1c=Hemoglobin A1c, OR=Odds ratio, MDRO=Multidrug-resistant organisms

However, several global reports have shown an increase in vancomycin-resistant strains of *S. aureus* and *E. faecalis*.<sup>[21,22]</sup> Therefore, the judicious use of this drug is highly warranted to prevent the future development of vancomycin-resistant strains in Oman. Apart from this, all Gram-positive isolates and *Staphylococcus* strains showed susceptibility to doxycycline and TMP-SMX, while all MRSA and 33% of *Enterococcus spp.* have shown resistance to amoxicillin-clavulanic acid. These findings are in line with a study by Al-Bshabshe *et al.*<sup>[23]</sup> Therefore, doxycycline and TMP-SMX are appropriate for empirical therapy of Gram-positive isolates. In the current study, coagulase-negative staphylococci showed only 67% susceptibility to ciprofloxacin, ampicillin, clindamycin, erythromycin, and gentamicin and most of the Gram-positive isolates showed low susceptibility to ampicillin and ciprofloxacin. This suggests the high-level acquisition of resistance to these drugs due to their extensive use in treating infections. Similar high-level resistance of Gram-positive isolates was reported by Joseph *et al.*<sup>[24]</sup>

In the present study, imipenem and meropenem showed good susceptibility against *P. aeruginosa*, *A. baumannii*, and *Enterobacteriaceae*. All *Enterobacteriaceae* showed good susceptibility ranging from 80% to 100% to aminoglycosides and piperacillin-tazobactam except for *K. pneumoniae* which showed low-level susceptibility to piperacillin-tazobactam (57%). Similar good susceptibility to these drugs reported by many studies.<sup>[12]</sup> The high rate of susceptibility is possibly due to the limited use of these drugs because of the high cost, more risk of side effects, and strict guidelines for their usage.<sup>[12]</sup> These findings suggest aminoglycosides/piperacillin-tazobactam/carbapenems are appropriate for empirical therapy of Gram-negative bacterial infections. Cephalosporins, amoxicillin-clavulanic acid, ampicillin, ciprofloxacin, and TMP-SMX have shown low susceptibility (<60%) against *P. aeruginosa*, *K. pneumoniae*, and *E. coli*, while *A. baumannii* showed low susceptibility to ciprofloxacin, aminoglycosides, TMP-SMX, and cephalosporins. Similar low to high-level resistance of *Enterobacteriaceae*

to amoxicillin-clavulanic acid, ampicillin, and cephalosporins was noticed by Kassam *et al.*<sup>[25]</sup> This is due to the fact of extensive use of these drugs both for the treatment and prophylaxis and the emergence of resistant strains.

Gram-negative organisms are known to develop resistance to multiple antibiotics rapidly compared to Gram-positive agents. In the last two decades, there is a rapid increase in the rate of infections caused by MDR Gram-negative pathogens as demonstrated by many studies.<sup>[2,11,12]</sup> These MDR strains including ESBL producers, colistin, and carbapenem-resistant (CRE) organisms are generally associated with severe infections in an increased number of patients. In the present study, we found 36% MDR Gram-negative pathogens and out of which 52%, 11%, and 8% were ESBL producers, a carbapenem (CRE), and colistin-resistant organisms, respectively. *K. pneumoniae* and *E. coli* were the predominant ESBL producers, while carbapenem and colistin-resistance was noticed predominantly in *K. pneumoniae*. Similar to our study, Akhi *et al.* reported ESBL production by various Gram-negative bacilli while Malchione *et al.* reported carbapenem and colistin resistance predominantly among *K. pneumoniae* and *E. coli*.<sup>[26,27]</sup> Treating the infections associated with these MDR pathogens has become a challenge to physicians and is associated with increased morbidity, mortality, and healthcare expenses. The widespread indiscriminate use of broad-spectrum antibiotics is the major factor that leads to selective pressure and the emergence of these deadly drug-resistant pathogens.<sup>[28]</sup> The increasing prevalence of these MDR pathogens is worrisome because they limit antibiotic choice and may lead to the worst outcome. In line with this, we observed a significantly increased association of MDR-pathogens with complications such as amputation and osteomyelitis compared to the patients infected with non-MDR pathogens [Table 4]. These findings are in accordance with the results of Banashankari *et al.*<sup>[29]</sup> This suggests a need for strict antibiotic policy and caution to careful use of antibiotics in infections caused by DFIs.<sup>[30]</sup>

### Limitation of the study

The present study report has some limitations. First of all, anaerobic organisms were excluded from the present study though they are important causes of DFI. Second, we did not collect data on a range of vital parameters such as length of hospital stay, history of prior antimicrobial use, and outcome of the infection such as recovery or death. Finally, it is a single centered study with small sample size. Hence, the generalization of the study results might be compromised. In spite of these limitations, the vital information reported in the study such as bacterial profile and their antibiotic susceptibility patterns in our hospital would help clinicians in selecting appropriate empirical therapy for treating DFIs for a better outcome.

### Conclusion

The findings of this study indicated that DFIs are often polymicrobial. Gram-negative organisms were predominantly isolated compared to Gram-positive organisms and in most cases, the infection was associated with *S. aureus*, *P. aeruginosa*, *K. pneumoniae*, and *E. coli*. The presence of MDR organisms was alarmingly high in the DFIs. Moreover, the increasing prevalence of MDROs is a serious concern because of limitations in the choice of antibiotic therapy and may lead to the worst outcome. Gram-negative organisms showed good *in-vitro* susceptibility to carbapenems, piperacillin, and aminoglycosides, while doxycycline and trimethoprim-sulfamethoxazole found to be effective against Gram-positive agents and hence they can be recommended for empirical therapy of Gram-negative and Gram-positive organisms respectively. The diversity of microbial profile and ever-changing antibiotic resistance patterns emphasize accurate microbial characterization from time to time and disseminating precise knowledge among physicians about usual pathogens and their antibiotic susceptibility pattern in a region will allow them to make the appropriate antibiotic of choice for better management of DFI. This further helps in controlling the emergence of drug-resistant pathogens, reduction in health-care costs and better outcomes.

### Acknowledgements

The authors express their sincere gratitude to all the staff of Microbiology laboratory as well as Information and technology department, Sohar hospital for their kind-hearted support. Authors also would like to thank Dr. Ali Al-Maqbali, Head of RERAC, North-Batinah region, Oman for his continued support and valuable feedback.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

### References

1. Busaidi I, Abdulhadi N, Coppel K. Care of patients with diabetic foot disease in Oman. Sultan Qaboos Univ Med J 2016; 16:e270-276. doi: 10.18295/squmj. 2016.16.03.002.
2. Son ST, Han SK, Lee TY, Namgoong S, Dhong ES. The microbiology of diabetic foot infections in Korea. J Wound Manage Res 2017;13(1):8-12. DOI: <https://doi.org/10.22467/jwmr.20170.00108>.
3. Cho NH, Shaw JE, Karuranga S, Huang Y, Fernandes JD, Ohlrogge AW, et al. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Research and Clinical Practice. 2018; 138: 271-281. DOI: <https://doi.org/10.1016/j.diabres.2018.02.023>.
4. International diabetes federation. Available from: <https://idf.org/our-network/regions-members/middle-east-and-north-africa/members/42-oman.html>. [Last accessed on 2020 February 25].
5. Mairghani M, Elmusharaf K, Patton D, Burns J, Eltahir O, Jassim G, et al. The prevalence and incidence of diabetic foot ulcers among five countries in the Arab world: A systematic review. J Wound Care 2017; 26:S27-34. doi: 10.12968/jowc.2017.26.Sup9.S27.
6. Miyan Z, Fawwad A, Sabir R, Basit A. Microbiological pattern of diabetic foot infections at a tertiary care center in a developing country. J Pak Med Assoc 2017; 67:665-9. PMID: 28507348.
7. Spichler A, Hurwitz BL, Armstrong DG, Lipsky BA. Microbiology of diabetic foot infections: From Louis Pasteur to 'crime scene investigation'. BMC Med 2015; 13:2. <https://doi.org/10.1186/s12916-014-0232-0>.
8. Sasedharan S, Sahu M, Chaddha R, Pathrose E, Bal A, Bhalekar P, et al. Epidemiology of diabetic foot infections in a reference tertiary hospital in India. Braz J Microbiol 2018; 49:401-6. doi: 10.1016/j.bjm.2017.09.003. Epub 2017 Nov 1.
9. Mohanty DP, Mulki SS, Mishra DN. Clinico-microbiological profile of diabetic foot ulcer: The common anatomical site. J Med Sci Clin R 2017; 5:26585-93. DOI: <https://dx.doi.org/10.18535/jmscr/v5i8.100>.
10. Sugandhi P, Prasanth DA. Microbiological profile of bacterial pathogens from diabetic foot infections in tertiary care hospitals, Salem. Diabetes Metab Syndr 2014; 8:129-32. DOI: 10.1016/j.dsx.2014.07.004.
11. Sannathimmappa MB, Nambiar V, Aravindakshan R, Al-Kasaby NM. Profile and antibiotic-resistance pattern of bacteria isolated from endotracheal secretions of mechanically ventilated patients at a tertiary care hospital. J Edu Health Promot. 2021; 10:195. DOI: 10.4103/jehp.jehp\_1517\_20.
12. Sekhar S, Vyas N, Unnikrishnan M, Rodrigues G, Mukhopadhyay C. Antimicrobial susceptibility pattern in diabetic foot ulcer: A pilot study. Ann Med Health Sci Res 2014; 4:742-5. doi: 10.4103/2141-9248.141541.
13. CLSI. Performance Standards for Antimicrobial Susceptibility Testing. CLSI Supplement M100. 27<sup>th</sup> ed. Wayne, PA: Clinical and Laboratory Standards Institute; 2017.
14. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing. 29<sup>th</sup> 251 ed. CLSI Supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2019.
15. Shareef J, Sunny S, Bhagavan KR. Study on bacteriological profile and antibiotic susceptibility pattern in patients with diabetic foot ulcers in a tertiary care teaching hospital. J Soc Health Diabetes 2018; 6:40-7. DOI: 10.4103/JSHD.JSHD\_30\_17.
16. Lee JH, Yoon JS, Lee HW, Won KC, Moon JS, Chung SM, et al. Risk factors affecting amputation in diabetic foot. Yeungnam Univ J

- Med 2020; 37:314-20. doi: 10.12701/yujm. 2020.00129.
17. Oman Ministry of Health. Annual Health Report; 2002. Available from: [www.moh.gov.om/en/web/statistics/annual-reports](http://www.moh.gov.om/en/web/statistics/annual-reports). [Last accessed on 2020, Aug 25].
  18. Oman Ministry of Health. Annual Health Report 2013. Available from: [www.moh.gov.om/en/web/statistics/annual-reports](http://www.moh.gov.om/en/web/statistics/annual-reports). [Last accessed on 2020, Aug 25].
  19. 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; 95:153-61. doi: 10.1016/j.diabres. 2011.10.001.
  20. Ramakant P, Verma AK, Misra R, Prasad KN, Chand G, Mishra A, et al. Changing microbiological profile of pathogenic bacteria in diabetic foot infections: Time for a rethink on which empirical therapy to choose? *Diabetologia* 2011; 54:58-64. DOI: 10.1007/s00125-010-1893-7.
  21. McGuinness WA, Malachowa N, DeLeo FR. Vancomycin resistance in *Staphylococcus aureus*. *Yale J Biol Med* 2017; 90:269-81. PMID: 28656013; PMCID: PMC5482303.
  22. Mac S, Fitzpatrick T, Johnstone J, Sander B. Vancomycin-resistant enterococci (VRE) screening and isolation in the general medicine ward: A cost-effectiveness analysis. *Antimicrob Resist Infect Control* 2019; 8:168. DOI: <https://doi.org/10.1186/s13756-019-0628-x>
  23. Al-Bshabshe A, Joseph MR, El-Gied AA, Fadul AN, Chandramoorthy HC, Hamid ME. Clinical relevance and antimicrobial profiling of methicillin-resistant *staphylococcus aureus* (MRSA) on routine antibiotics and ethanol extract of mango kernel (*Mangifera indica* L.). *Biomed Res Int* 2020 2020:4150678. <https://doi.org/10.1155/2020/4150678>.
  24. Joseph K, George AT, Divya MB, Ameena KK. Diabetic foot infections: Characterization and antibiotic resistance pattern of aerobic bacterial isolates in a tertiary care hospital of North Kerala. *Int J Curr Microbiol App Sci* 2017; 6:3493-9. <https://doi.org/10.20546/ijcmas0.2017.609.429>.
  25. Kassam NA, Damian DJ, Kajeguka D, Nyombi B, Kibiki GS. Spectrum and antibiogram of bacteria isolated from patients presenting with infected wounds in a tertiary hospital, Northern Tanzania. *BMC Res Notes* 2017; 10:757. DOI <https://doi.org/10.1186/s13104-017-3092-9>.
  26. Akhi MT, Ghotaslou R, Asgharzadeh M, Varschochi M, Pirzadeh T, Memar MY, et al. Bacterial etiology and antibiotic susceptibility pattern of diabetic foot infections in Tabriz, Iran. *GMS Hyg Infect Control* 2015; 10: Doc 02. doi: 10.3205/dgkh000245.
  27. Malchione MD, Torres LM, Hartley DM, Koch M, Goodman JL. Carbapenem and colistin resistance in *Enterobacteriaceae* in Southeast Asia: Review and mapping of emerging and overlapping challenges. *Int J Antimicrob Agents* 2019; 54:381-99. doi: 10.1016/j.ijantimicag. 2019.070.019.
  28. Sannathimmappa MB, Nambiar V, Aravindakshan R. A cross-sectional study to evaluate the knowledge and attitude of medical students concerning antibiotic usage and antimicrobial resistance. *Int J Acad Med* 2021;7:113-9. DOI: 10.4103/IJAM.IJAM\_57\_20.
  29. Banashakari GS, Rudresh HK, Harsha AH. Prevalence of Gram-negative bacteria in diabetic foot – A clinic-microbiological study. *Al Ameen J Med Sci* 2012; 5:224-32.
  30. Algã A, Wong S, Shoaib M, Lundgren K, Giske CG, von Schreeb J, et al. Infection with high proportion of multidrug-resistant bacteria in conflict-related injuries is associated with poor outcomes and excess resource consumption: A cohort study of Syrian patients treated in Jordan. *BMC Infect Dis* 2018; 18:233. DOI: <https://doi.org/10.1186/s12879-018-3149-y>.