

ROLE OF ANTIBIOTICS IN INFECTED DIABETIC FOOT ULCER IN AL-JUMHOORI TEACHING HOSPITAL

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ABSTRACT

Introduction: The most common complication of Diabetes Mellitus is infection, it's the most prevalent cause of non-traumatic amputation among all diabetes, 15% have foot infection and 28% of them require amputation.

Aim: To determine the most sensitive antibiotic. **Materials and Methods:** This prospective observational study conducted for a period of 2 years from June 2022 to June 2024 a total of 200 swab were collected from infected diabetic foot ulcer patients in surgery department in government of Nineveh Al-Jumhoori teaching hospital in Mosul. Collected swabs were cultured and isolates we identified by microbiological techniques. **Results:** Total of 220 isolates were obtained from 200 swab samples. Among them 200 were Gram-negative bacilli, 12 were Gram-positive cocci and 8 were negative cocci-bacilli. Two organisms were obtained in 10 swabs culture (polyorganism). The most common isolates was Pseudomonas species 66 (30%) followed by Klebsiella species 55 (25%), Proteus species 44 (20%), Escherichia coli 33 (15%), Staphylococcus aureus 10 (4.5%) and Acinetobacter species 6 (2.7%). Majority of Gram-negative isolates (208) were sensitive to cefaperazone-sulbactam (71%), Meropenem (40%). All Gram-positive isolates (12) were sensitive to Linezolid, Amoxyclav. **Conclusion:** Present study confirmed the presence of multidrug resistant pathogens in diabetic foot ulcers. This knowledge of antibiotic susceptibility, patterns of isolates from wound helps in guiding clinicians for better planning of treatment with appropriate antibiotics, reducing the resistance patterns and minimizing healthcare costs.

KEYWORDS: Antimicrobial Sensitivity, Diabetic foot, Multidrug Resistance.

1. INTRODUCTION

Diabetes mellitus is a persistent metabolic condition characterized by hyperglycemia due to defects in insulin secretions and insulin action or combination of both.^[1] Globally diabetes incidence is increasing from last few decades, presently 500 million people are living with diabetes worldwide and further increase to 30% in 2045.^[2] Diabetes is a heavy burden disease. In 2017, the mortality rate due to diabetes reached 10.7% in adult patients (20- 79years). In Middle East and North Africa (MENA) Region, diabetes accounts for 373557 deaths (21 countries and territories including Iraq) and an estimate of 51.8% of deaths are due to diabetes in patients aged below 60; this puts the region in the highest second level among International Diabetes Federation (IDF) regions.^[3] Diabetes has several adverse complications including foot ulcers, neuropathy, and atherosclerosis.^[4] Nearly 12–25% of individuals with diabetes are at risk of developing diabetic foot ulcers (DFUs). DFU is a complex cellulitis or osteomyelitis situation caused by

interaction between the host immune system and colonizing bacteria.^[5] Once DFUs are infected with external agents, mainly bacteria, the situation gets worse, and finally, patients are advised to get hospitalized. It is estimated that approximately 44–68% of patients admitted to hospitals develop osteomyelitis, which eventually leads to amputation. The major obstacles in treating DFU is bacterial colonization and antibiotic resistance.^[6] DFUs can progress rapidly to infection, contributes to morbidity and mortality among diabetic patients. DFUs can be infected by different Gram-positive and Gram-negative bacteria. Polymicrobial DFUs infections can occur in chronic DFUs which can be colonized by different types of aerobic bacteria, such as Staphylococcus, Streptococcus, Enterococcus, Pseudomonas species, and anaerobic pathogens.^[7] The frequency of typical microorganisms isolated from DFUs differs across studies carried out in various locations throughout the world. The bacterial distribution in DFUs can be influenced by different factors such as

geographical features and antibiotic use. Initially antimicrobials are selected empirically for treatment of DFU infections. Due to the improper use of available antibiotics, antibiotic resistance has become a universal issue in healthcare institutions. Incidence of multi drug resistant infections in DFU has increased and which is challenging for clinicians in treating these patients.^[8] This study was aimed to determine the bacterial profile of infected diabetic foot ulcers and antibiotic sensitivity and resistant patterns of isolates. As there are less studies from this region which have formulated an empiric therapy for diabetic foot infections, knowledge of antibiotic sensitivity pattern would help make empiric antibiotic treatment protocol for this region and help primary care physicians as well as specialists in initiating more effective empiric antibiotic therapy which in turn may reduce antibiotic resistance and cost of treatment to patients.

2. PATIENTS AND METHODS

Present study was a prospective, observational study conducted in the Department of Surgery in government of Nineveh, Al-Jumhoori teaching hospital in Mosul city, Iraq. The study was conducted from June 2022 to June 2024 for a period of 2 years. The research was approved by Institutional Ethical committee.

Inclusion Criteria: Inclusion Criteria was all diabetic patients with diabetic foot infection were randomly selected from outpatient departments (OPDs) and wards of Surgery and Medicine department (forwarded from other hospitals), with Wagner grade 2-4 ulcers and irrespective of anti-diabetic treatment and diabetic foot injury treatment, willing to participate in the study.

Exclusion Criteria: Exclusion criteria were those patients who were seriously ill, patients with neuropathy

other than diabetic neuropathy, patients with acute limb ischemia, patients not willing to participate and inadequately collected samples. Wagner's grade 0 and grade 5 are excluded from the study. Only Wagner's grade 2 to 4 were included in the study.

Study was explained to patients and a written informed consent was taken from patients. The clinical details of the patients such as age, sex, type of diabetes, duration of diabetes, size of ulcer and duration of ulcer were recorded. The ulcers were graded according to Wagner's grade classification. A total of 200 Samples (pus, debrided ulcer material or aspirate of material from infected wound) from the infected foot lesions were collected aseptically by using sterile cotton swab. Sterile cotton swab sticks were moistened with sterile normal saline before collecting the specimens. The swab sticks were extended deeply into the depth of the lesion avoiding touching of surrounding skin area around the wound. The collected samples were immediately transported to the microbiology department. Samples were processed & bacterial isolates were identified by standard microbiological procedures (Macroscopic evaluation, microscopic examination, culture, motility and biochemical tests) and antibiotic susceptibility testing was performed through the Kirby Bauer's disc diffusion method. Results of the culture and antimicrobial sensitivity testing were documented. Collected data was entered in Microsoft excel sheet & analyzed. Statistical analysis was done using descriptive statistics.

3. RESULTS

A total of 200 patients who met the exclusion criteria were included in the study. The Sociodemographic details of the participants are given in the table below (Table 1).

Table 1: Demographic and Risk Factors of Diabetic Foot Patients.

No.	Characteristics	No. of Patients	Percentage
1.	Age Group		
	21-30	3	1.5
	31-40	12	6
	41-50	40	20
	51-60	70	35
	61-70	70	35
	71 and above	5	2.5
2.	Sex		
	Male	122	61
	Female	78	39
3.	Risk Factors		
	History of Trauma	55	27.5
	Family History of Diabetes	49	24.5
	Hypertension	40	20
	Smoking	46	23
	Alcohol	10	5
4.	Duration of Diabetes		
	< 5 Years	25	12.5
	5-10 Years	75	37.5

	> 10 Years	100	50
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The mean age of the participants is 55.8 ± 9.3 years. Around 32% (64) of the participants have more than one risk factor. More than half 56% of the participants are diabetics for more than 10 years. Around 68% (136) of the participants reported the duration of ulcer to be more than 1 month. Around 43% (86) of the patients have ulcer

<5mm in size, 36% (72) have a size of 5-20 mm and 21% (42) have ulcer size more than 20mm. Around 74% of the participants have developed ulcers for the first time whereas 26% have recurrent ulcers over the foot. The ulcers are classified according to Keith Wagner's classification (Table 2).

Table 2: Classification of Ulcers According to Keith Wagner's Classification.

Grade	Clinical Signs	Frequency	Percentage
1	Superficial ulcer of skin/subcutaneous tissue	44	22
2	Ulcer extending up to tendon/bone/capsule	39	19.5
3	Deep ulcer with osteomyelitis/abscess	20	10
4	Gangrene of foot/toes/localized gangrene	97	48.5

Distribution of bacteria isolated from diabetic foot ulcers: In this study, organisms were isolated from 200 swabs. monomicrobial growth was seen predominantly in

180 (90%) while 20 (10%) subjects developed polymicrobial growth. The nature of microbial growth in diabetic foot ulcers is shown in Figure 1.

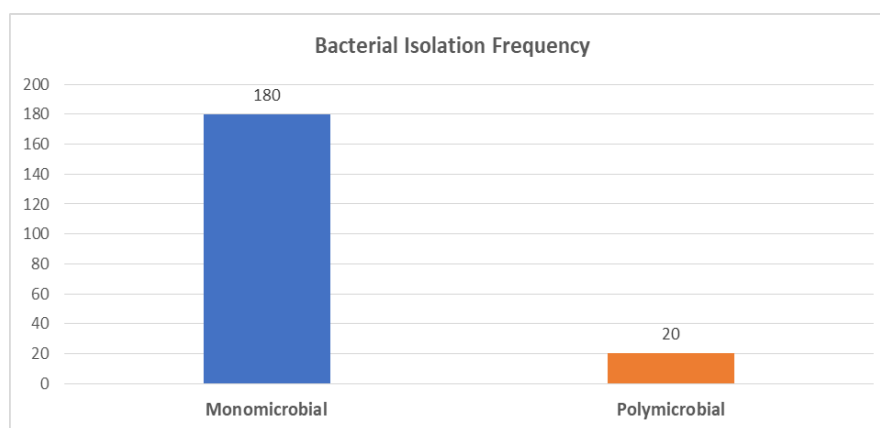


Figure 1: Nature of microbial growth in patients with diabetic foot ulcer.

Bacteria isolated from DFUs of the study subjects: Cultures from the swabs of the foot ulcers showed that the prevalence of gram-negative organisms 208 (94.55%), 12 are Gram-positive organisms (5.45%). A total of 220 organisms were isolated from 200 subjects. The most common organism isolated from the diabetic foot ulcers

is *Pseudomonas aeruginosa*, isolated from 66 (33%) subjects followed by *Klebsiella pneumoniae* isolated from 54 (27%) subjects. The different types of Grams-negative and Gram-positive bacteria isolated from diabetic foot ulcers are summarized in Figure 2.

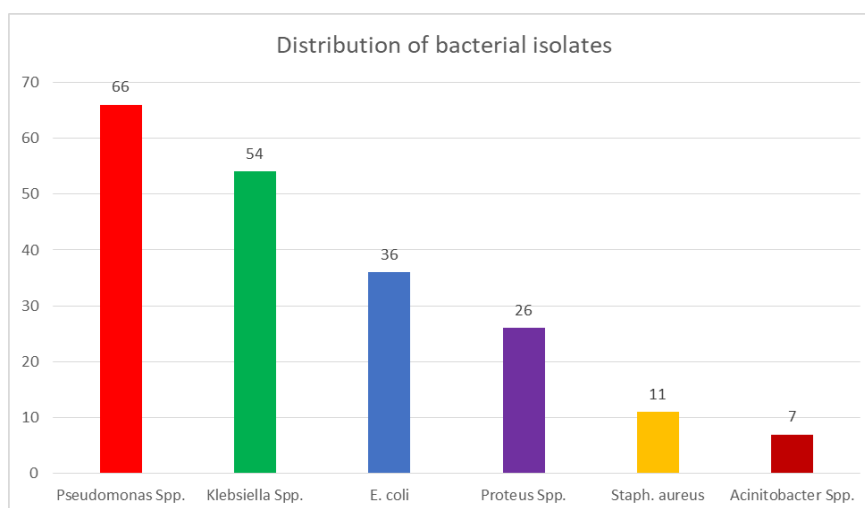


Figure 2: Distribution of various bacterial isolates.

Antibiotic susceptibility pattern of Gram positive and Gram-negative organisms: The common antibiotics are tested to determine the sensitivity pattern of the organism isolated. *Pseudomonas* species are most sensitive to meropenem (75%), followed by amikacin (69.4%) and not sensitive to ampicillin and amoxiclav. *E. coli* species

are susceptible to Meropenem (95%), Amikacin (95%) and gentamycin (90%). *Klebsiella* species are most sensitive to Amikacin (83.3%), Meropenem (76.6%) followed by Cefoperazone-Sulbactam (56.66%). The following table shows the sensitivity pattern of various antibiotics to a particular group of organisms (Table 3).

Table 3: Antibiotic susceptibility pattern of Gram-Positive and Gram-Negative organisms.

Antibiotics	Ps. aeruginosa (n=72)	Klebsiella (n=60)	E. coli (n=40)	Proteus (n=28)	Staph. aureus (n=12)	Acinetobacter (n=8)
Amikacin	50 (69.4%)	50 (83.3%)	38 (95%)	18 (64.3%)	0	6 (75%)
Amoxiclav	0	32 (53.3%)	0	0	0	0
Ampicillin	0	0	0	14 (50%)	8 (66.6%)	0
Cefoperazone/Sulbactam	40 (55.5%)	34 (56.6%)	34 (85%)	24 (85.7%)	0	6 (75%)
Ceftriaxone	0	18 (30%)	10 (25%)	16 (57.1%)	0	0
Ciprofloxacin	36 (50%)	26 (43.3%)	10 (25%)	10 (35.7%)	2 (16.6%)	6 (75%)
Gentamicin	30 (41.6%)	24 (40%)	36 (90%)	14 (50%)	10 (83.3%)	4 (50%)
Levofloxacin	32 (44.4%)	0	2 (5%)	0	6 (50%)	4 (50%)
Linezolid	-	-	-	-	10 (83.3%)	-
Meropenem	54 (75%)	46 (76.7%)	38 (95%)	26 (92.8%)	0	4 (50%)
Piperacillin Tazobactam	22 (30.5%)	32 (53.3%)	14 (35%)	28 (100%)	0	6 (75%)

In Gram-positive organisms, Gentamicin (83%), Linezolid (83%) and Ampicillin (75%) are the most effective among the antibiotics used in the study. The present study shows that ceftriaxone is completely ineffective against *Pseudomonas* and *Acinetobacter* species, Penicillins are ineffective against *Pseudomonas*, *E. coli* and *Acinetobacter*. Piperacillin-tazobactam, Meropenem, Amikacin and Ceftriaxone are completely ineffective against *S. aureus* whereas Linezolid and Gentamicin showed promising results against *S. aureus*. Therefore, it can be summarized that the Gram-positive organisms isolated were most commonly sensitive to antibiotics Gentamicin and Linezolid while the Gram-negative organisms isolated were found to be sensitive to antibiotics like Amikacin, Meropenem, and Cefoperazone/Sulbactam combination.

4. DISCUSSION

Diabetic foot ulcer is one of the major complications in diabetes patients. If left untreated or poorly managed, they lead to disastrous complications like gangrene, infections, cellulitis leading to sepsis, severe renal dysfunction, pre renal acute kidney injury and may also rarely cause multiple organ dysfunction syndrome. In the present study, slight male predominance was noted over females. Previous studies have shown that the susceptibility to foot infections is significantly greater in male patients than in female patients.^[9,10,11] The mean age of the participants is 55.8±9.3 years which is similar to other studies from different parts of the world.^[11,12,13] The major risk factors like alcohol and duration of diabetes are also similar to the Jammu study.^[14] Most of the ulcers fall into Wagner's class 4 (38%) which is high compared to Jammu study^[14], Ethiopia study.^[15] The present study shows that the major organisms to be isolated from the

swabs are *Pseudomonas* spp. (32.7%) and *Klebsiella* spp. (27.2%).

The present study shows *Pseudomonas* spp. as the most common species to be isolated from the swabs which is similar to other studies like Singh et al.^[13], Ozer et al.^[14] The present study shows a poly microbial growth in 10% of the study subjects which is very less compared to Shareef et al.^[11] (46.47%), Singh et al.^[13] (43.8%) and Aleem et al.^[16] (39.80%). The present study shows that Gram negative organisms are most susceptible to Amikacin, Meropenem, Cefoperazone-Sulbactam. Most of the studies show that gram negative organisms are most susceptible to Meropenem and Amikacin, which is similar to the present study. In the present study, Gram-positive organisms are more susceptible to Gentamicin (83%), Linezolid (83%) and Ampicillin (75%). The present study shows that penicillins are not effective against Gram-negative organisms like *E. coli*, *Acinetobacter*, *Klebsiella* and *Pseudomonas* which is similar to Shareef et al.^[11] and Mehta VJ et al.^[10]

5. CONCLUSION

This study shows predominant Gram-negative organisms over Gram-positive organisms in the bacterial isolates of diabetic foot ulcers with the majority being monomicrobial in nature (90%). *Pseudomonas* spp. are the most commonly isolated species in diabetic foot ulcers (32.7%). Amikacin and Meropenem are most effective against Gram-negative organisms and Linezolid is most effective against *S. aureus*. Evaluation of microbial spectrum is necessary as it not only highlights the major organisms, but can be used to compare the spectrum across various timelines and geographic locations to identify evolving and changing patterns. It is necessary to evaluate the culture sensitivity pattern from

the infected wound and the knowledge on the antibiotic sensitivity and resistance to start appropriate antibiotics at early time and to initiate appropriate treatment. This in turn reduces the antimicrobial resistance.

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