ANTIBIOTIC SENSITIVITY AND MICROBIOLOGICAL PATTERNS OF DIABETIC FOOT ULCERS

Dipak Chaulagain[1], Sanaullah Hafiz[2]
[1]Jalal-Abad International University, Jalal-Abad, Kyrgyzstan
[2]Jalalabad State Medical University named after B. Osmonov, Jalal-Abad, Kyrgyzstan

Abstract
Introduction: Diabetes mellitus, characterized by chronic hyperglycemia due to defects in insulin secretion, action, or both, is a prevalent metabolic disorder with severe long-term complications, including nephropathy, retinopathy, peripheral neuropathy, and vasculopathy. These conditions predispose patients to diabetic foot ulcers (DFUs), chronic non-healing wounds associated with high risks of infection, amputation, and Charcot joint deformities. DFUs represent a significant cause of hospitalization among diabetic individuals.

Methods
A cross-sectional descriptive study was conducted involving 138 DFU patients across multiple hospitals in the Malakand Division, Pakistan. Data were collected from patient interviews, clinical observations, and hospital records. Of the 138 patients, 13 underwent amputation, and 3 required re-amputation.

Results
The mean age of participants was 45.7 ± 10 years, with a mean diabetes duration of 8.7 ± 3 years and ulceration duration of 4 ± 2 years. The study population comprised 65% males and 45% females. From 150 specimens, 455 aerobic bacteria were isolated (average of 3.03 isolates per specimen), with notable prevalence of multidrug-resistant (MDR) organisms and methicillin-resistant Staphylococcus aureus (MRSA). Among gram-positive aerobes, S. aureus (25.4%) was predominant, while Escherichia coli (16%) led among gram-negative isolates. Gram-positive isolates exhibited resistance to ciprofloxacin (54.5%), erythromycin (53.2%), and clarithromycin (52.56%), but were universally sensitive to vancomycin. Gram-negative isolates showed resistance to ciprofloxacin (75%), cefuroxime (85%), and cefotaxime (54.43%), with imipenem and sulbactam-cefoperazone demonstrating high sensitivity.

Conclusion
DFUs predominantly affect individuals around 50 years of age, with ulceration linked to diabetes duration, treatment adherence, and wound care. Males are more affected than females. Vancomycin exhibited 100% efficacy against gram-positive isolates, while linezolid was effective in 92% of cases, aiding recovery in many patients. The presence of MDR isolates underscores the need for tailored antibiotic therapy.

Keywords: Antibiotic sensitivity, diabetic foot ulcer, multidrug resistance, microbiological profile

ЧУВСТВИТЕЛЬНОСТЬ К АНТИБИОТИКАМ И МИКРОБИОЛОГИЧЕСКИЕ ЗАКОНОМЕРНОСТИ ДИАБЕТИЧЕСКИХ ЯЗВ СТОПЫ

Дипак Чаулагаин[1], Санауллах Хафиз[2]
[1]Джалал-Абадский международный университет, Джалал-Абад, Кыргызстан
[2]Джалал-Абадский государственный медицинский университет им. Б. Осмонова, Джалал-Абад, Кыргызстан

Аннотация
Введение: Сахарный диабет, характеризующийся хронической гипергликемией из-за дефектов секреции инсулина, действия или обоих факторов, является распространенным метаболическим расстройством с тяжелыми долгосрочными осложнениями, включая нефропатию, ретинопатию, периферическую нейропатию и васкулопатию. Эти состояния предрасполагают пациентов к диабетическим язвам стопы (ДЯС), хроническим незаживающим ранам, связанным с высоким риском инфекции, ампутации и деформациями суставов Шарко. ДЯС являются важной причиной госпитализации среди больных диабетом.

Методы
было проведено поперечное описательное исследование с участием 138 пациентов с DFU в нескольких больницах в округе Малаканд, Пакистан. Данные были собраны из интервью с пациентами, клинических наблюдений и больничных записей. Из 138 пациентов 13 перенесли ампутацию, а 3 потребовалась повторная ампутация.

Результаты
средний возраст участников составил 45,7 ± 10 лет, средняя продолжительность диабета составила 8,7 ± 3 года, а продолжительность язвы — 4 ± 2 года. Исследуемая популяция состояла из 65% мужчин и 45% женщин. Из 150 образцов было выделено 455 аэробных бактерий (в среднем 3,03 изолята на образец) с заметным преобладанием организмов с множественной лекарственной устойчивостью (МЛУ) и метициллин-резистентного золотистого стафилококка (MRSA). Среди грамположительных аэробов преобладал S. aureus (25,4%), в то время как среди грамотрицательных изолятов лидировала Escherichia coli (16%). Грамположительные изоляты проявили устойчивость к ципрофлоксацину (54,5%), эритромицину (53,2%) и кларитромицину (52,56%), но были универсально чувствительны к ванкомицину. Грамотрицательные изоляты проявили устойчивость к ципрофлоксацину (75%), цефуроксиму (85%) и цефотаксиму (54,43%), при этом имипенем и сульбактам-цефоперазон продемонстрировали высокую чувствительность.

Заключение
DFU преимущественно поражают людей в возрасте около 50 лет, при этом язвы связаны с длительностью диабета, приверженностью лечению и уходом за ранами. Мужчины страдают чаще, чем женщины. Ванкомицин продемонстрировал 100% эффективность против грамположительных изолятов, тогда как линезолид был эффективен в 92% случаев, способствуя выздоровлению многих пациентов. Наличие изолятов с множественной лекарственной устойчивостью подчеркивает необходимость индивидуальной антибактериальной терапии.

Ключевые слова: Чувствительность к антибиотикам, язва диабетической стопы, множественная лекарственная устойчивость, микробиологический профиль

Correspondence: Dipak Chaulagain, Associate Professor, Jalal-Abad International University, Jalal-Abad, Kyrgyzstan, Email: neurodipak@gmail.com

Introduction

Diabetes mellitus is a group of metabolic disorders defined by chronic hyperglycemia resulting from impaired insulin secretion, insulin action, or both [1]. Uncontrolled diabetes leads

to long-term complications, including nephropathy, retinopathy, peripheral neuropathy, microtubule dysfunction, and vasculopathy [2, 3]. Peripheral neuropathy and vasculopathy significantly increase the risk of developing diabetic foot ulcers (DFUs), chronic wounds prone to infection due to reduced blood supply [4]. These ulcers are associated with severe outcomes, such as amputations and Charcot joint deformities, and are a leading cause of hospitalization among diabetic patients [5].

Diabetes is classified into several types. Type 1 diabetes, often termed juvenile diabetes, arises from autoimmune destruction of pancreatic beta cells, primarily affecting children and young adults [6]. Secondary diabetes mimics Type 1 but results from pancreatic damage due to disease or injury rather than autoimmunity [7]. Type 2 diabetes, the most common form, is characterized by insulin resistance and typically affects middle-aged and older adults, though its incidence is rising among younger populations due to obesity [8]. Pharmacological management includes insulin, amylin analogs, oral agents, and GLP-1 receptor agonists [9].

DFUs are polymicrobial infections, often involving gram-positive and gram-negative bacteria, including MDR strains [10]. Common gram-negative isolates include E. coli, Klebsiella pneumoniae, and Proteus mirabilis, while Pseudomonas aeruginosa exhibits notable antibiotic resistance [11, 12]. Microbiological profiling and antibiotic sensitivity testing are critical for effective treatment and preventing progression to deeper tissues, which may necessitate amputation [13]. DFUs are graded from 1 (superficial) to 5 (extensive gangrene) per the Wagner classification, with higher grades linked to increased amputation risk [14]. Approximately 60% of non-traumatic lower limb amputations are attributed to DFUs [15], with re-amputation and mortality rates significantly impacting quality of life [16, 17].

This study investigates the microbiological patterns and antibiotic sensitivity profiles of DFUs in a cohort from the Malakand Division, Pakistan, to inform clinical management and reduce adverse outcomes.

Materials and Methods

A cross-sectional, descriptive study was conducted across multiple hospitals in the Malakand Division, Pakistan, including Saidu Teaching Hospital and Central Hospital, Saidu Sharif, Swat. Data were collected from 138 DFU patients and supplemented by hospital records of over 500 patients. Diagnostic, microbiological, and culture sensitivity tests were performed at Amreek Hospital and Anwar Hospital, Mingora, Swat.

Ulcer samples were obtained using sterile surgical tools, placed in saline within sterilized containers, and transported to the laboratory. Gram staining was followed by culturing on nutrient agar at 37°C for 24 hours. Primary growth was sub-cultured for purification, and antibiotic sensitivity was assessed using strips on agar plates incubated for an additional 24 hours. Sensitivity was categorized as resistant (R), sensitive (S), or intermediate (I) based on microbial growth inhibition. Microbial identification involved cultural characteristics (colony morphology, color, odor) and biochemical tests (e.g., catalase, coagulase, indole, TSI). Advanced identification was performed using Analytical Profile Indexing (API) strips processed by automated software. Blood cultures utilized a Bactec lytic machine. Protocols adhered to international standards (CLSI, EUCAST, FDA) [18].

Results

The study observed 138 patients over one year, with demographic data summarized in Table 1. The cohort comprised 65% males and 45% females, with a mean age of 45.7 ± 10 years,

diabetes duration of 8.7 ± 3 years, and ulceration duration of 4 ± 2 years. Type 2 diabetes predominated (97.83%), with only 2.17% having Type 1.

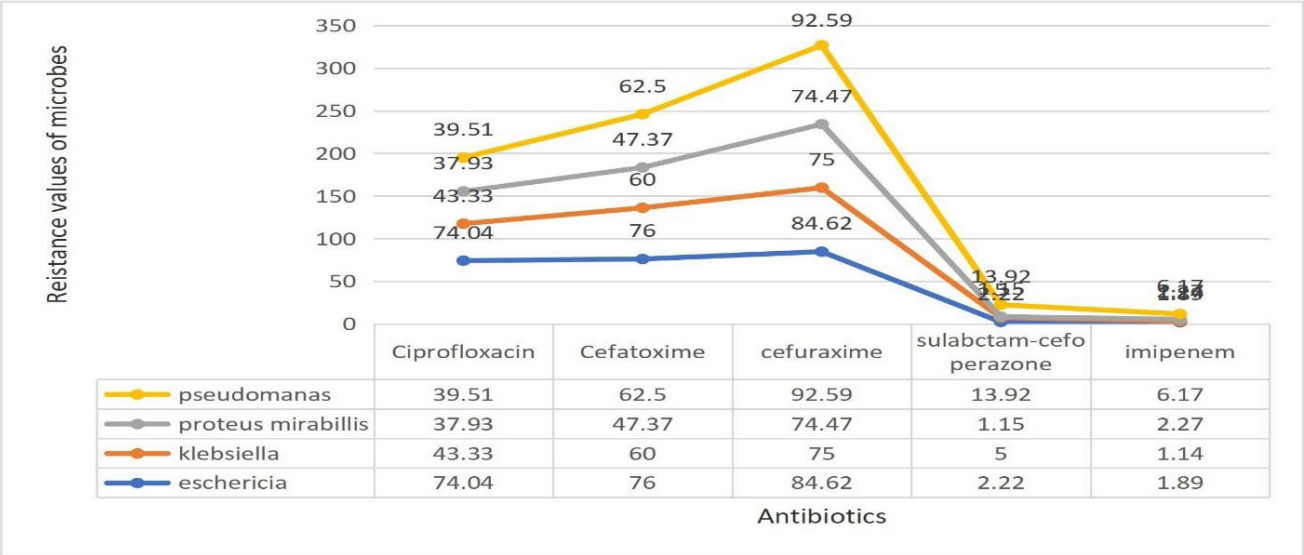
• *Table 1: Baseline Characteristics of Patients*

VARIABLES	MEAN ± S. D
Total patients	138
Age	45.7 ± 10
Duration of diabetes	8.7 ± 3
Duration of ulcer	4 ± 2
Gender	
Male	65%
Female	45%
Type 1 diabetes	3 (2.17%)
Type 2 diabetes	135 (97.83%)

From 150 specimens (92% pus, 8% blood), 455 aerobic bacteria were isolated, averaging 3.03 isolates per specimen. MDR and MRSA strains were prevalent. Among gram-positive isolates, S. aureus (25.4%) was most common, followed by Streptococcus, coagulase-negative staphylococci, and Enterococcus. Among gram-negative isolates, E. coli (16%) predominated, followed by K. pneumoniae, P. mirabilis, and P. aeruginosa. Antibiotic sensitivity patterns are presented in Table 2 and Table 3.

• *Table 2: Antibiotic Sensitivity of Gram-Positive Aerobes (%)*

Antibiotics	Staphylococcus Aureus	Streptococcus	Enterococcus
Amikacin	85	-	-
Clarithromycin	47	47.8	47.4
Linezolid	99	-	-
Vancomycin	99	100	100
Clindamycin	65	59	-
Ciprofloxacin	45	45.4	45.2
Levofloxacin	19	-	-
Erythromycin	45.8	47.8	46.8



• *Table 3: Antibiotic Resistance of Gram-Negative Isolates (%)*

Gram-positive isolates showed resistance to ciprofloxacin (54.5%), erythromycin (53.2%), and clarithromycin (52.56%), but were 100% sensitive to vancomycin. Gram-negative isolates exhibited high resistance to ciprofloxacin (75%), cefuroxime (85%), and cefotaxime (54.43%), with imipenem and sulbactam-cefoperazone being the most effective.

Of the 138 patients, 13 underwent amputation due to gangrene, and 3 required re-amputation due to ulcer progression.

Discussion

Diabetes mellitus, a disorder of insulin dynamics, predisposes patients to severe complications, including DFUs, driven by peripheral neuropathy and vasculopathy [1, 4, 5]. DFUs are a major public health concern, with 14–20% of patients requiring amputation and 35–40% facing re-amputation, reducing life expectancy by up to 60% [10, 16, 17]. This study confirms that DFUs are polymicrobial, with S. aureus and E. coli as dominant isolates, consistent with global findings [11, 12, 19]. Regional variations in microbial profiles may reflect differences in antibiotic use and environmental exposure [13, 20].

The cohort's baseline characteristics align with prior studies, though additional metrics like BMI and HbA1c could enhance risk profiling [10, 21]. Ulcer severity ranged from Grade 1 (superficial) to Grade 5 (extensive gangrene), with higher grades necessitating amputation due to delayed or inappropriate treatment [14]. Vancomycin's 100% efficacy against gram-positive isolates and linezolid's 92% success rate highlight their therapeutic value, corroborating other research [10, 21]. Gram-negative isolates showed significant resistance, with imipenem emerging as a key option [12].

Risk factors for amputation included gangrene, prior DFU history, osteomyelitis, smoking, and male sex, consistent with meta-analyses [17, 22]. Non-significant factors included hypertension and HbA1c levels [16]. These findings underscore the importance of early intervention and culture-guided therapy.

Conclusion

DFUs predominantly affect individuals around 50 years old, with males at higher risk. Ulceration correlates with diabetes duration, treatment adherence, and wound care. S. aureus and E. coli

are the leading pathogens, with MDR strains posing treatment challenges. Vancomycin and linezolid are highly effective against gram-positive isolates, while imipenem excels against gram-negative bacteria. Amputation risk escalates with delayed referral, improper antibiotic use, and poor diabetes control. These insights emphasize the need for timely, evidence-based management to improve outcomes.

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