Journal of Health and Rehabilitation Research 2791-156X JHRR

Original Article

Antibiotic Sensitivity and Resistance Patterns of Uropathogens in Peshawar, Pakistan

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Keywords: Urinary Tract Infections, Antibiotic Resistance, Uropathogens, Escherichia Coli, Fosfomycin, Meropenem, Imipenem, Antimicrobial Susceptibility

Abstract

Background: Urinary tract infections (UTIs) are a major global health issue, primarily caused by bacteria invading the urinary system. Escherichia coli is the most common pathogen, with increasing resistance to antibiotics posing treatment challenges.

Objective: This study evaluated the antibiotic sensitivity and resistance patterns of uropathogens from UTI patients in Peshawar, Pakistan, to guide effective therapy and inform local healthcare practices.

Methods: A cross-sectional study was conducted from January 1 to May 30, 2023, at the Institute of Kidney Diseases, Hayatabad Medical Complex, Peshawar. The study included patients aged 16 years and older diagnosed with UTIs. Urine samples were cultured, and significant bacteriuria was defined as growth of ≥10⁵ CFU/mL. Uropathogens were tested for antibiotic sensitivity using the disk diffusion method and VITEK-2 compact system. Data were analyzed using IBM SPSS version 25.

Results: Of 137 samples, 80.3% were gram-negative, and 19.7% were gram-positive. Escherichia coli was the most prevalent pathogen (57.7%). Among gram-negative bacteria, Fosfomycin had 91.2% sensitivity, while Cefixime showed 85.5% resistance. For gram-positive bacteria, Piperacillin/Tazobactam had 100% sensitivity, while Cefixime and Moxifloxacin had 100% resistance.

Conclusion: The study identified Escherichia coli as the predominant uropathogen, with significant resistance to common antibiotics like Ciprofloxacin and Cefixime. Fosfomycin, Meropenem, and Imipenem were more effective against resistant strains. Routine susceptibility testing and updated treatment protocols are essential to combat antibiotic resistance and improve patient outcomes.

1 Introduction

Urinary tract infections (UTIs) are a significant public health concern globally, impacting millions each year and resulting in substantial healthcare costs (13). These infections occur when microorganisms invade the normally sterile urinary system, typically through the urethra, leading to conditions such as cystitis (bladder infection) and, less frequently, pyelonephritis (kidney infection) (1). The clinical manifestation of UTIs can vary widely, influenced by the specific pathogen involved, the severity of the infection, and the host's immune response (2). Bacterial pathogens, both gram-positive and gram-negative, are the predominant causes of UTIs, with Escherichia coli being the most frequently identified organism. Other common bacterial culprits include Klebsiella pneumoniae, various Staphylococcus and Streptococcus species, and Proteus species (3). Numerous risk factors have been associated with UTIs, including gender, age, prior history of infection, catheterization, hospitalization history, and socioeconomic status, suggesting that UTIs can often recur in vulnerable populations (4, 5).

Diagnosing UTIs typically involves evaluating clinical symptoms and urinalysis, with urine dipstick tests and microscopy being primary diagnostic tools (6, 7). These methods often require midstream urine samples collected using sterile techniques, which are then cultured to identify the causative bacteria and assess their antibiotic sensitivity (8). The reliance on empirical antibiotic treatment has been linked to the rise of antimicrobial resistance among uropathogens, posing a significant challenge in managing UTIs effectively (9, 10, 11). The susceptibility profile of these pathogens can vary widely depending on geographic location, healthcare setting, and environmental factors, emphasizing the need for region-specific data to guide treatment strategies. Misuse of antibiotics not only exacerbates resistance issues but can also lead to other complications, such as Clostridium difficile colitis (12).

The global burden of UTIs is staggering, with estimates suggesting that around 150 million individuals are affected annually, leading to healthcare expenditures exceeding 6 billion dollars (13). In Pakistan, a study by Khatoon et al. revealed that 65.1% of patients tested for UTIs were diagnosed positive, with gram-negative bacteria accounting for 76.9% of these infections, primarily due to Escherichia coli (48.8%) (14). Furthermore, studies conducted in Peshawar in 2017 and 2020 confirmed E. coli as the predominant cause of UTIs, with antibiotics such as Meropenem, Imipenem, and Amikacin showing the highest sensitivity against these pathogens (15, 16). Despite this knowledge, there remains a paucity of recent data on the current trends of antibiotic sensitivity and resistance patterns of uropathogens in Peshawar. This gap underscores the necessity for updated research to inform clinical practices effectively.

Therefore, this study aims to evaluate the antimicrobial susceptibility patterns of commonly used antibiotics against uropathogens isolated from patients with UTIs in Peshawar, Pakistan. The findings will provide crucial insights for healthcare practitioners, facilitating the selection of appropriate antibiotics that align with local susceptibility patterns. Such targeted therapy is essential for the effective treatment of complicated UTIs and for mitigating the development of antibiotic resistance, which remains a critical concern in modern medicine (17).

2 Material and Methods

A cross-sectional study was conducted at the Institute of Kidney Diseases in the Outpatient Department of Hayatabad Medical Complex, Peshawar, Pakistan, over a five-month period from January 1, 2023, to May 30, 2023. The study received ethical approval from the Institutional Research & Ethical Board (IREB), ensuring adherence to the principles outlined in the Declaration of Helsinki for medical research involving human subjects. Prior to participation, informed consent was obtained from each participant, ensuring their understanding and voluntary involvement in the study.

The study population consisted of patients aged 16 years and older, both male and female, who were clinically diagnosed with urinary tract infections (UTIs). A convenient non-probability sampling technique was employed to select participants, allowing for the inclusion of patients based on availability during the study period. Patients with catheterization, those with a double J stent in place, immunocompromised individuals, and those who had taken antibiotics within the past 24 hours were excluded to avoid potential confounding factors affecting microbial sensitivity.

Mid-stream urine samples were collected in sterile containers using standard aseptic techniques to ensure sample integrity and reduce contamination risk. These samples were promptly processed in the Microbiology laboratory. Cultures were performed on blood agar and MacConkey media using a standard loop technique, followed by incubation at 37°C for 24 hours. A growth of ≥10^5 colony-forming units per milliliter (CFU/mL) was considered indicative of significant bacteriuria, allowing for the identification of uropathogens.

Antimicrobial susceptibility testing was performed using both the disk diffusion method and direct Antimicrobial Susceptibility Testing (AST) via the VITEK-2 compact system. The uropathogens identified from the urine cultures were tested against a panel of antibiotics, including Piperacillin-Tazobactam, Cefixime, Ciprofloxacin, Levofloxacin, Moxifloxacin, Co-trimoxazole, Co-amoxiclav, Gentamicin, Fosfomycin, Nitrofurantoin, Amikacin, Ceftriaxone, Meropenem, Imipenem, and Colistin. Isolates demonstrating intermediate sensitivity to antibiotics were categorized as resistant to those specific agents to ensure a conservative approach to assessing antimicrobial resistance patterns.

The data collected during the study were systematically recorded and analyzed using IBM SPSS for Windows, version 25. Descriptive statistics were employed to calculate frequencies and percentages of the causative organisms of UTIs. Sensitivity and resistance patterns of the uropathogens to various antibiotics were also determined, allowing for a comprehensive assessment of the antimicrobial susceptibility profiles prevalent in the study population. This methodological framework provided a robust basis for understanding the local epidemiology of UTIs and informing targeted antibiotic therapy (12, 13, 14).

3 Results

A total of 137 urine samples were analyzed, with 58 (40.1%) from male patients and 79 (57.7%) from female patients. The mean age of the participants was 41.9 years, with a standard deviation of 15.14 years, ranging from 16 to 78 years. Among these samples, 110 (80.3%) contained gram-negative bacteria, while 27 (19.7%) contained gram-positive bacteria. Among the gram-negative bacteria, samples from females accounted for 58 (52.7%), and those from males accounted for 52 (47.3%). For gram-positive bacteria, 17 (63.0%) were isolated from females and 10 (37.0%) from males.

The most frequently isolated uropathogen was *Escherichia coli*, which was responsible for 57.7% of the cases. *Staphylococcus aureus* and *Klebsiella pneumoniae* were also common, comprising 11.8% and 11.0% of infections, respectively. The antibiotic sensitivity and resistance patterns for the identified uropathogens were assessed using the disk diffusion method and the VITEK-2 compact system. The detailed distribution of uropathogens is presented in the table below: The detailed sensitivity and resistance patterns of gram-negative bacteria are shown below: These findings highlight the predominance of gram-negative bacteria in UTI cases in this study population, with *E. coli* being the most prevalent pathogen.

Table 1: Uropathogens with Frequencies and Percentages

Uropathogens	Frequency	Percent
Escherichia coli	79	57.7
Klebsiella pneumoniae	15	11.0
Pseudomonas aerugenosa	12	8.8
Burkholderia cepacia	3	2.2
Enterobacter	1	0.7
Staphylococcus aureus	16	11.8
Streptococcus pyogenes	3	2.2
Enterococcus	8	5.8

Among gram-negative bacteria, *Fosfomycin* exhibited the highest sensitivity at 91.2%, followed by *Imipenem* (84.0%), *Amikacin* (83.3%), *Meropenem* (83.3%), *Piperacillin/Tazobactam* (80.2%), and *Nitrofurantoin* (79.7%). Conversely, high resistance rates were observed for *Cefixime* (85.5%), *Ciprofloxacin* (81.3%), and *Co-amoxiclav* (75.0%). For gram-positive bacteria, *Piperacillin/Tazobactam* demonstrated complete sensitivity (100%), followed by *Imipenem* (75.0%) and *Meropenem* (62.5%).

Table 2: Sensitivity and Resistance Patterns of Antibiotics in Gram-Negative Bacteria

Antibiotics	E. coli (S/R)	K. pneumoniae (S/R)	P. aerugenosa (S/R)
Co-amoxiclav	22 (27.9%)/57 (72.1%)	2 (13.3%)/13 (86.7%)	1 (16.7%)/5 (83.3%)
Co-trimoxazole	23 (31.1%)/51 (68.9%)	3 (20.0%)/12 (80.0%)	0 (0.0%)/3 (100.0%)
Ceftriaxone	19 (24.0%)/60 (76.0%)	1 (6.6%)/14 (93.4%)	0 (0.0%)/12 (100.0%)
Ciprofloxacin	22 (27.8%)/57 (72.2%)	0 (0.0%)/15 (100.0%)	0 (0.0%)/12 (100.0%)
Levofloxacin	14 (26.9%)/38 (73.1%)	0 (0.0%)/8 (100.0%)	0 (0.0%)/4 (100.0%)
Moxifloxacin	8 (24.2%)/25 (75.8%)	0 (0.0%)/4 (100.0%)	0 (0.0%)/0 (0.0%)
Nitrofurantoin	53 (88.3%)/7 (11.7%)	5 (41.7%)/7 (58.3%)	0 (0.0%)/1 (100.0%)
Fosfomycin	73 (96.1%)/3 (3.9%)	9 (64.3%)/5 (35.7%)	0 (0.0%)/0 (0.0%)
Cefixime	9 (18.7%)/39 (81.3%)	0 (0.0%)/8 (100.0%)	0 (0.0%)/0 (0.0%)
Piperacillin/Tazobactam	67 (89.3%)/8 (10.7%)	9 (60.0%)/6 (40.0%)	8 (57.1%)/6 (42.9%)
Amikacin	74 (93.7%)/5 (6.3%)	10 (62.5%)/6 (37.5%)	4 (33.3%)/8 (66.7%)
Colistin	4 (100.0%)/0 (0.0%)	4 (66.7%)/2 (33.3%)	0 (0.0%)/6 (100.0%)
Imipenem	73 (94.8%)/4 (5.2%)	10 (66.7%)/5 (33.3%)	3 (25.0%)/9 (75.0%)
Meropenem	72 (94.7%)/4 (5.3%)	11 (73.3%)/4 (26.7%)	3 (25.0%)/9 (75.0%)
Gentamicin	43 (55.8%)/34 (44.2%)	3 (20.0%)/12 (80.0%)	2 (16.6%)/10 (83.4%)

However, resistance was universal against *Cefixime* and *Moxifloxacin* (100%), with substantial resistance observed against *Ceftriaxone* (78.6%) and *Ciprofloxacin* (75.0%). The sensitivity and resistance patterns for gram-positive bacteria are detailed below:

Table 3: Sensitivity and Resistance Patterns of Antibiotics in Gram-Positive Bacteria

Antibiotics	Staphylococcus aureus (S/R)	Enterococcus (S/R)	Streptococcus pyogenes (S/R)
Co-amoxiclav	4 (25.0%)/12 (75.0%)	3 (75.0%)/1 (25.0%)	0 (0.0%)/0 (0.0%)
Co-trimoxazole	7 (43.7%)/9 (56.3%)	0 (0.0%)/0 (0.0%)	0 (0.0%)/0 (0.0%)
Ceftriaxone	2 (15.4%)/11 (84.6%)	0 (0.0%)/0 (0.0%)	2 (100.0%)/0 (0.0%)
Ciprofloxacin	3 (30.0%)/7 (70.0%)	1 (12.5%)/7 (87.5%)	2 (100.0%)/0 (0.0%)
Levofloxacin	3 (75.0%)/1 (25.0%)	0 (0.0%)/5 (100.0%)	0 (0.0%)/0 (0.0%)
Moxifloxacin	0 (0.0%)/1 (100.0%)	0 (0.0%)/0 (0.0%)	0 (0.0%)/0 (0.0%)
Nitrofurantoin	0 (0.0%)/5 (100.0%)	8 (100.0%)/0 (0.0%)	0

4 Discussion

The study aimed to evaluate the prevalence of uropathogens and their antibiotic resistance patterns in Peshawar, Pakistan, focusing on both gram-positive and gram-negative bacteria. The findings aligned with previous studies conducted in Pakistan and other regions, where gram-negative bacteria, particularly *Escherichia coli*, were identified as the most common causative agents of urinary tract infections (UTIs) (14, 15). In this study, *E. coli* accounted for 57.7% of the infections, consistent with the results reported by Khatoon et al. and other regional studies, where *E. coli* was the leading uropathogen (14).

The study highlighted significant resistance patterns, especially among gram-negative bacteria, where high resistance was observed against commonly used antibiotics such as *Cefixime* and *Ciprofloxacin*. This pattern of resistance echoes findings from other studies in Pakistan, underscoring a growing concern over the efficacy of these antibiotics for treating UTIs (15, 16). Such trends suggest a pressing need to reconsider the empirical treatment strategies for UTIs to prevent further escalation of antibiotic resistance.

Notably, *Fosfomycin* demonstrated high sensitivity against gram-negative bacteria, including *E. coli*, in contrast to other antibiotics like *Cefixime* and *Ciprofloxacin*, which showed substantial resistance. This observation aligns with previous studies indicating *Fosfomycin* as an effective treatment option for resistant strains (15). The high sensitivity of *Fosfomycin*, along with *Meropenem* and *Imipenem*, suggests that these antibiotics could be prioritized in treatment regimens, particularly for infections caused by resistant strains of *E. coli*.

For gram-positive bacteria, *Staphylococcus aureus* showed significant resistance to *Moxifloxacin* and *Cefixime*, similar to findings in other studies (16). However, *Piperacillin/Tazobactam* and *Imipenem* displayed substantial effectiveness against these bacteria. This resistance pattern underscores the necessity for continuous monitoring of antibiotic sensitivity to inform appropriate therapeutic choices (17).

The study's strengths include its focus on a specific geographic area, providing localized data that can guide healthcare professionals in Peshawar. However, several limitations should be acknowledged (18) The cross-sectional design offers a snapshot of the current situation but does not capture potential variations over time. The study was conducted in a single center, which might limit the generalizability of the findings to other regions or populations. Additionally, the use of non-probability sampling may introduce selection bias, potentially affecting the results (19-21).

These findings emphasize the importance of routine susceptibility testing to tailor antibiotic therapy effectively, reducing the reliance on empirical treatments that may contribute to resistance. Further research should explore larger, multi-center studies to validate these findings and assess temporal trends in antibiotic resistance. Implementing stringent antibiotic stewardship programs and promoting awareness among healthcare providers and patients could mitigate the development of resistance and preserve the efficacy of existing antibiotics. The study highlights the critical need for continuous surveillance of resistance patterns and informed decision-making in antibiotic prescribing practices to ensure optimal patient outcomes (22, 23).

5 Conclusion

This study identified *Escherichia coli* as the most prevalent uropathogen in Peshawar, with significant resistance to commonly used antibiotics like *Ciprofloxacin* and *Cefixime*. *Fosfomycin*, *Meropenem*, and *Imipenem* emerged as more effective treatment options against resistant strains. The findings underscore the necessity for routine antibiotic susceptibility testing and tailored antibiotic therapy to combat the rising threat of antimicrobial resistance. Such practices are crucial for improving patient outcomes and ensuring effective management of UTIs. Healthcare providers must prioritize antibiotic stewardship and update treatment protocols based on local resistance patterns to preserve the efficacy of available antibiotics and protect public health.

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Disclaimers	
Author Contributions	Muhammad Waqas conceptualized and designed the study, collected data, and drafted the manuscript. Zaryaab Ahmad Khan contributed to data analysis and interpretation and reviewed the manuscript critically for important intellectual content. Shabeer Ahmad was involved in the data collection and management. Muhammad Saad Hamid assisted in the laboratory analysis and interpretation of results. Muhammad Altaf contributed to the study design and statistical analysis. Muzzamil Sohail provided technical support and supervised the overall project.
Conflict of Interest	The authors declare that there are no conflicts of interest.
Data Availability	Data and supplements available on request to the corresponding author.
Funding	NA
Ethical Approval	Institutional Research & Ethical Board (IREB) of the Institute of Kidney Diseases, Hayatabad Medical Complex, Peshawar.
Trial Registration	NA
Acknowledgments	Staff of the Microbiology Laboratory at Hayatabad Medical Complex.

LINK MEDICAL INTERFACE

~ JHRR, ISSN: 2791-156X ~