Original Article

# Antibiotic Sensitivity and Resistance Patterns in Complicated Urinary Tract Infections in Peshawar, Pakistan



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## ABSTRACT

**Objective:** To study the patterns of antibiotic sensitivity and resistance in complicated urinary tract infections.
**Study Design:** Cross sectional study
**Place and Duration of Study:** This study was conducted at the department of Urology at the Institute of Kidney Diseases, Peshawar, Pakistan, from May 1, 2023 to October 31, 2023.
**Methods:** We collected 137 urine samples from patients diagnosed with complicated UTIs and culture and sensitivity tests were performed using standard microbiological techniques.
**Results:** Among the positive urine samples, E.coli was found in 78 (56.9%), Klebsiella pneumoniae in 16 (11.7%) and Pseudomonas areuginosa in 14 (10.2%) of the positive cultures, respectively. Gram negative bacteria were highly sensitive to several antibiotics, including Fosfomycin (91.2%), Imipenem (84.0%), Meronem (83.3%), Amakicin (83.3%), Pipercillin/Tazobacrum (80.2%), and Nitrofuranroin (79.7%). However, they showed high resistance to Cefixime (85.5%), Ciprofloxacin (81.3%), and Co-amoxiclav (75.0%). On the other hand, Gram positive bacteria were highly sensitive to Piperaxillin/Tazobactum (100%), Imipenem (75.0%), and Meropenem (62.5%). Gram-positive bacteria showed high resistance to Cefixime and Moxifloxacin (100%), Ceftriaxone (78.6%) and Ciproflaxacin (75.0%).
**Conclusion:** E.coli was the most common uropathogen in patients with complicated UTIs. Nitrofurantoin, meropenem, imipenem, and amikacin were found to be effective against the majority of the bacteria. Conversely, most of the bacterial strains exhibited resistance to commonly prescribed antibiotics such as ciprofloxacin and cefixime.


**Key Words:** Complicated UTIs, Antibiotic sensitivity, Resistance patterns, Uropathogens

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## INTRODUCTION

Urinary tract infection (UTI) is a frequent bacterial infection that enters the sterile urinary system via the urethra. These germs live on skin and rectum. Bladder infection (cystitis) is the most prevalent UTI. UTIs may also be kidney infections, called pyelonephritis[1]. Affected individuals' symptoms, indicators, and urinalysis are used to diagnose[2]. UTI symptoms vary on the causal agent, infection severity, and immunological response[3].

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UTIs are simple or complex[4]. All UTIs in males, pregnant women, immunocompromised patients, and those with fevers, stones, sepsis, urinary blockage, catheters, or kidney involvement are complicated. Bacteria—gram positive and negative—cause UTIs[5]. Most UTIs are caused by Escherichia coli, Klebsiella pneumonia, Staphylococcus, Streptococcus, and Proteus species. Several studies have linked UTIs to gender, age, prior UTI, catheterization, and hospitalisation, and poor economic position[6,7].

When UTI is suspected, urine dipstick and microscope are the major diagnostic techniques[8]. Aseptically collecting midstream pee and culture reveals the organism and its antibiotic sensitivity. However, empirical UTI treatment has caused antibiotic resistance in the pathogenic organisms[9].

Over 6 billion dollars are spent on UTIs annually, affecting almost 150 million individuals[10].UTI therapy is threatened by antibiotic resistance, as various investigations have indicated[11,12]. Uropathogen antibiotic susceptibility varies by healthcare facility (primary, tertiary, or other), environment, and geography. Misuse of antimicrobials may also cause

antimicrobial resistance and Clostridium difficile colitis[13].

Khatoon et al. studied. UTI was identified in 65.1% of Pakistani pee test patients[14]. 23% were caused by gram-positive bacteria, 76.9% by gram-negative bacteria. Gram-negative bacteria Escherichia coli caused 48.8% of UTIs. The most frequent gram-positive bacterium was Staphylococcus aureus (17.30%). In 2017, gram-negative bacteria caused 82.86% of UTIs in Peshawar[15], with Escherichia coli being the most frequent (65.02%). The most frequent gram-positive bacterium was S.aureus (40.48%). More than 82% sensitive meropenem and imipenem. In a Peshawar investigation from November 2020 to May 2021 [17], E. Coli had the greatest prevalence (47.80%) and 100% Amikacin and Meropenem sensitivity.

UTI therapy should be tailored and based on local microorganism sensitivity data[16]. UTI bacteria are becoming antimicrobial-resistant[11,12]. However, there is no contemporary research on uropathogen trends and antibiotic sensitivity in Peshawar, Pakistan. Thus, this research examined the antimicrobial susceptibility of popular medications in Peshawar patients with severe UTIs. Uropathogens from difficult UTI outpatients in a tertiary care hospital were microbiologically and antimicrobially analysed. This research will help doctors choose medications for complex UTIs based on local susceptibility patterns.

# METHODS

A six-month cross-sectional research was undertaken at the Urology outpatients department of the Institute of Kidney Diseases, Peshawar, from May 1 to October 30, 2023. Before starting, the hospital ethical review board authorised the trial. Using an expected frequency of 9.85% for Pseudomonas aureginosa and a confidence level of 95%, the OpenEpi sample size calculator generated 137. Complex UTI patients 16 or older were included in the research. The sampling method was sequential non-probability. Patient exclusion criteria included catheterization, DJ stent implantation, immunocompromised, recent hospital admission, and antibiotic use within 24 hours. Patients gave informed written permission before joining the trial.

Mid-stream urine samples were collected in sterile containers and quickly processed in the microbiology lab. If delayed, samples were held at 4°C. The samples were grown overnight on blood agar and MacConkey medium with a standard loop at 37°C. Growth of > 105 CFU/mL was deemed serious bacteriuria.

Both disc diffusion and VITEK-2 compact system direct Antimicrobial Susceptibility Testing (AST) were used for antibiograms. The uropathogens were tested for sensitivity to Piperacillin-Tazobactum, Ciprofloxacin, Levofloxacin, Moxifloxacin, Co trimoxizole, Co amoxiclav, Amikacin, Gentamicin, Fosfomycin, Nitrofurantoin, Ceftriaxone, Cefixime, Meropenem, Imipenem, and Colistin. Intermediately sensitive isolates were resistant to those drugs.

IBM SPSS for Windows version 26 was used to determine UTI causative organisms and uropathogen sensitivity and resistance patterns using Google Forms data.

# RESULTS

The study included 137 samples, 60 (43.8%) male and 77 (56.2%) female. The mean patient age was 43.99 with a S.D. of 16.55 and ranged from 16 to 80. There were 112 (81.8%) gram-negative and 25 (18.2%) gram-positive bacteria. 60 (53.6%) of the gram-negative bacteria were obtained from females and 52 (46.4%) from men. Gram-positive bacteria were recovered from 17 (68.0%) females and 8 (32.0%) men. The most common uropathogen in our research was E.coli (56.9%), followed by Klebsiella pneumoniae (11.7%) and Staphlococcus aureus (10.9%).

**Table No. 1: Culture reports results**

| Uropathogens | Frequency | Percent |
|---|---|---|
| Escherichia coli | 78 | 56.9 |
| Klebsiella pneumoniae | 16 | 11.7 |
| Pseudomonas aerugenosa | 14 | 10.2 |
| Burkholderia cepacia | 3 | 2.2 |
| Enterobacter | 1 | 0.7 |
| Staphlococcus aureus | 15 | 10.9 |
| Streptococcus pyogenes | 1 | 0.7 |
| Enterococcus | 9 | 6.6 |
| Total | 137 | 100.0 |

**Table 2: Antibiotics sensitivity and resistant pattern in gram negative bacteria**

| Antibiotics | | E coli | | K Pneumoniae | | P Aerugenosa | | Enterobacter | | B Cepacia | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Co amoxiclav | Sensitive | 22 | 28.2% | 2 | 12.5% | 1 | 16.7% | 0 | 0.0% | 0 | 0.0% |
| | Resistant | 56 | 71.8% | 14 | 87.5% | 5 | 83.3% | 0 | 0.0% | 0 | 0.0% |
| Co trimoxizole | Sensitive | 23 | 31.5% | 4 | 25.0% | 0 | 0.0% | 1 | 100.0% | 2 | 66.7% |
| | Resistant | 50 | 68.5% | 12 | 75.0% | 3 | 100.0% | 0 | 0.0% | 1 | 33.3% |
| Ceftriaxone | Sensitive | 19 | 24.4% | 1 | 6.3% | 0 | 0.0% | 1 | 100.0% | 0 | 0.0% |
| | Resistant | 59 | 75.6% | 15 | 93.8% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% |
| Ciprofloxacin | Sensitive | 20 | 26.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% |
| | Resistant | 57 | 74.0% | 16 | 100.0% | 13 | 100.0% | 1 | 100.0% | 0 | 0.0% |
| Levofloxacin | Sensitive | 14 | 26.9% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% |
| | Resistant | 38 | 73.1% | 8 | 100.0% | 4 | 100.0% | 1 | 100.0% | 3 | 100.0% |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Moxifloxacin | Sensitive | 8 | 24.2% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% |
| | Resistant | 25 | 75.8% | 4 | 100.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% |
| Nitrofurantoin | Sensitive | 53 | 88.3% | 5 | 41.7% | 0 | 0.0% | 1 | 100.0% | 0 | 0.0% |
| | Resistant | 7 | 11.7% | 7 | 58.3% | 1 | 100.0% | 0 | 0.0% | 0 | 0.0% |
| Fosfomycin | Sensitive | 73 | 96.1% | 9 | 64.3% | 0 | 0.0% | 1 | 100.0% | 0 | 0.0% |
| | Resistant | 3 | 3.9% | 5 | 35.7% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% |
| Cefixime | Sensitive | 8 | 17.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% |
| | Resistant | 39 | 83.0% | 8 | 100.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% |
| Piperacillin / Tazobactum | Sensitive | 67 | 89.3% | 9 | 56.3% | 8 | 57.1% | 1 | 100.0% | 0 | 0.0% |
| | Resistant | 8 | 10.7% | 7 | 43.8% | 6 | 42.9% | 0 | 0.0% | 0 | 0.0% |
| Amikacin | Sensitive | 74 | 94.9% | 10 | 62.5% | 5 | 38.5% | 1 | 100.0% | 0 | 0.0% |
| | Resistant | 4 | 5.1% | 6 | 37.5% | 8 | 61.5% | 0 | 0.0% | 0 | 0.0% |
| Colistin | Sensitive | 4 | 100.0% | 4 | 66.7% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% |
| | Resistant | 0 | 0.0% | 2 | 33.3% | 6 | 100.0% | 0 | 0.0% | 0 | 0.0% |
| Imipenem | Sensitive | 73 | 94.8% | 10 | 66.7% | 5 | 38.5% | 1 | 100.0% | 0 | 0.0% |
| | Resistant | 4 | 5.2% | 5 | 33.3% | 8 | 61.5% | 0 | 0.0% | 0 | 0.0% |
| Meropenem | Sensitive | 72 | 94.7% | 11 | 68.8% | 3 | 25.0% | 1 | 100.0% | 3 | 100.0% |
| | Resistant | 4 | 5.3% | 5 | 31.3% | 9 | 75.0% | 0 | 0.0% | 0 | 0.0% |
| Gentamicin | Sensitive | 43 | 55.8% | 4 | 25.0% | 3 | 23.1% | 0 | 0.0% | 0 | 0.0% |
| | Resistant | 34 | 44.2% | 12 | 75.0% | 10 | 76.9% | 1 | 100.0% | 0 | 0.0% |

**Table No. 3: Antibiotics sensitivity and resistant pattern in gram positive bacteria**

| **Antibiotics** | | **Staphylococcus Aureus** | | **Enterococcus** | | **Streptococcus pyogenes** | |
|---|---|---|---|---|---|---|---|
| Co amoxiclav | Sensitive | 4 | 26.7% | 3 | 75.0% | 0 | 0.0% |
| | Resistant | 11 | 73.3% | 1 | 25.0% | 0 | 0.0% |
| Co trimoxizole | Sensitive | 7 | 46.7% | 0 | 0.0% | 0 | 0.0% |
| | Resistant | 8 | 53.3% | 0 | 0.0% | 0 | 0.0% |
| Ceftriaxone | Sensitive | 2 | 15.4% | 0 | 0.0% | 1 | 100.0% |
| | Resistant | 11 | 84.6% | 0 | 0.0% | 0 | 0.0% |
| Ciprofloxacin | Sensitive | 3 | 30.0% | 1 | 11.1% | 1 | 100.0% |
| | Resistant | 7 | 70.0% | 8 | 88.9% | 0 | 0.0% |
| Levofloxacin | Sensitive | 3 | 75.0% | 0 | 0.0% | 0 | 0.0% |
| | Resistant | 1 | 25.0% | 4 | 100.0% | 0 | 0.0% |
| Moxifloxacin | Sensitive | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% |
| | Resistant | 1 | 100.0% | 0 | 0.0% | 0 | 0.0% |
| Nitrofurantoin | Sensitive | 0 | 0.0% | 7 | 100.0% | 0 | 0.0% |
| | Resistant | 5 | 100.0% | 0 | 0.0% | 0 | 0.0% |
| Fosfomycin | Sensitive | 3 | 60.0% | 1 | 25.0% | 0 | 0.0% |
| | Resistant | 2 | 40.0% | 3 | 75.0% | 0 | 0.0% |
| Cefixime | Sensitive | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% |
| | Resistant | 3 | 100.0% | 0 | 0.0% | 0 | 0.0% |
| Piperacillin/Tazobactum | Sensitive | 10 | 100.0% | 0 | 0.0% | 0 | 0.0% |
| | Resistant | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% |
| Amikacin | Sensitive | 3 | 50.0% | 0 | 0.0% | 0 | 0.0% |
| | Resistant | 3 | 50.0% | 0 | 0.0% | 0 | 0.0% |
| Colistin | Sensitive | 2 | 50.0% | 0 | 0.0% | 0 | 0.0% |
| | Resistant | 2 | 50.0% | 0 | 0.0% | 0 | 0.0% |
| Imipenem | Sensitive | 9 | 75.0% | 0 | 0.0% | 0 | 0.0% |
| | Resistant | 3 | 25.0% | 0 | 0.0% | 0 | 0.0% |
| Meropenem | Sensitive | 5 | 62.5% | 0 | 0.0% | 0 | 0.0% |
| | Resistant | 3 | 37.5% | 0 | 0.0% | 0 | 0.0% |
| Gentamicin | Sensitive | 1 | 16.7% | 1 | 100.0% | 0 | 0.0% |
| | Resistant | 5 | 83.3% | 0 | 0.0% | 0 | 0.0% |

# DISCUSSION

We examined the causal agents of UTI and antibiotic susceptibility in patients at the Institute of Kidney

Diseases, Peshawar's urology outpatient clinic. Gram-negative bacteria were the most prevalent uropathogen in positive urine culture samples (82.87%). These findings match Pakistani research[14,15,17].

We found Fosfomycin responsive in 91.2% of gram-negative bacteria. In the earlier Peshawar research, Meropenem and Imipenem had sensitivity of over 82.60% against gram-negative bacteria, whereas fosfonycin had sensitivity of over 73.91%[15].

According to Peshawar research, E. Coli causes the most UTIs, followed by K. Pneumoniae and Enterococcus[15,17]. Staph aureus was the third most frequent UTI causer in our research, after E. Coli and K. Penumoniae. Positive urine cultures included 6.6% enterococcus. Klebsiella was 84.6%, E.coli 68.5%, Enterobacter species 36.84%), and Proteus mirabilis 28.55% in Karachi[18]. These findings vary from our research.

E.coli is 100% sensitive to colistin, followed by Fosfomycin (96.1%), Amikacin (94.8%), and Meropenem (94.7%). A earlier Peshawar research indicated that E.coli was most responsive to Meropenem (89.39%), Imipenem (87.12%), and Fosfomycin (83.33%)[16]. Another research found that E.coli was 100% sensitive to Meropenem and Amikacin, 98.97% to Fosfomycin, Piperacillin/Tazobactum, and Imipenem[17].

Klebsiella pneumoniae was Meropenem-sensitive the most. E.coli has the greatest Meropenem sensitivity in Pakistan (16)(18). Staphylococcus aureus was most sensitive to Piperacillin/Tazobactum (100%), followed by Levofloxacin (75.0%) and Imipenem (75.0%). Shehbaz Ahmad et al. found 100% Meropenem, Imipenem, Fosfomycin, and amikacin sensitivity in stpah areus[17].

Our investigation demonstrated E.coli resistant to Cefixime (83.0%), Ceftriaxone (76.5%), Moxifloxacin (75.8%), and Ciprofloxacin (74.0%). Klebsiella pneumoniae was 100% resistant to Ciprofloxacin, Moxifloxacin, Levofloxacin, and Cefixime. Staph aureus was 100% resistant to Moxifloxacin, Nitrofurantoin, and Cefixime. In Peshawar[17], Ahmad et al. found E.coli 100% resistance to Piperacillin, followed by Cefotaxime, ceftazidime, doxyxycline (95.88%), and Ciprofloxacin (93.81%). They found Klebsiella 100% resistant to Piperacillin, 97.30% to Cefotaxime and ceftazidime, and 89.19% to ciprofloxacin. Stap aureus was 100% resistant to Erythormycin, Ciprofloxacin, Cefotaxime, Ceftazidime, and Piperacillin/Tazobactam.

Limitation: This research was done at one centre, hence the results may not reflect Peshawar, Pakistan. However, the study's cross-sectional methodology gives a snapshot in time, which may help discover trends and patterns.

# CONCLUSION

Our study concluded that E. Coli was the most prevalent uropathogen, followed by K pneumoniae and S aureus. Nitrofurantoin, meropenem, imipenem, and amikacin were found to be effective against the majority of the bacteria. However, most of the bacterial strains were resistant to commonly used antibiotics such as ciprofloxacin and cefixime. All the antibiotics showed varying patterns of sensitivity and resistance. Therefore, it is highly recommended to diagnose UTI routinely and identify the bacteria causing UTI to determine the most effective antibiotic treatment to avoid the development of antibiotic resistance.

**Author's Contribution:**

| | |
|---|---|
| Concept & Design of Study: | Akhtar Nawaz |
| Drafting: | Hafiz Asad Ullah Jan, Waqas |
| Data Analysis: | Siddique Akbar, Muhammad Saad Hamid |
| Revisiting Critically: | Akhtar Nawaz, Hafiz Asad Ullah Jan |
| Final Approval of version: | Akhtar Nawaz |

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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