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# ASSESSMENT OF ANTIBIOTIC RESISTANCE TRENDS OF THE COMMUNITY ACQUIRED URINARY PATHOGENS

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## Abstract
Urinary tract infections (UTIs) are primary source of infections linked to healthcare settings describing as a significant factor in the overuse and abuse of antibiotics. Antibiotic-resistant forms of UTIs have emerged, contributing to the significant public health burden. With an emphasis on gender-based variations, this study investigates the frequency and patterns of antibiotic resistance of pathogens such as *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Enterococcus faecium*. This retrospective observational research was carried out between October 2023 to March 2024 in tertiary care hospital in Islamabad after getting a proper institutional ethical approval. The isolates of *E. coli* showed significant resistance (100%) to co-trimoxazole, ampicillin, and amoxicillin, however colistin was still effective (0% resistance). Female isolates of *Klebsiella pneumoniae* had strong resistance to ampicillin, amoxicillin, and augmentin (100%), as well as high resistance to ciprofloxacin (88.5%) and co-trimoxazole (91.4%). Male isolates of *Pseudomonas aeruginosa* exhibited whole resistance to many antibiotics, while female isolates exhibited reduced resistance (33.3%) overall, with the exception of co-trimoxazole (100%). Male isolates of *Enterococcus faecium* was completely resistant to a number of antibiotics, with an 83.3% resistance rate to ciprofloxacin and cefepime. Gender-specific treatment techniques are necessary due to the high rates of antibiotic resistance, which pose substantial obstacles in the treatment of illnesses. Despite Colistin effectiveness, the findings of this study underscore the vital necessity of creating novel antimicrobial medicines and strengthening antimicrobial stewardship initiatives.

**Keywords:** Antibiotic resistance, *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa*, antimicrobial stewardship

## 1. Introduction

A common source of antibiotic prescriptions in the community, particularly in poor nations, urinary tract infections (UTIs) account for a considerable amount of morbidity and mortality worldwide (1). The physiology and anatomy of the female urethra make women more susceptible to urinary tract infections particularly by uropathogenic *Escherichia coli* (2). The greatest cause of antibiotic resistance is urinary tract infections (UTIs), which are linked to 25–40% of the antibiotics used in basic care. *E. coli* is the predominant bacterium responsible for almost 80% of urinary tract infections, infecting 8–10 million individuals yearly in the United States (3). The World Health Organization ranks antibiotic resistance, along with climate change, terrorist acts, and conflicts, as the primary contributors to the danger to world security (4).

After carbapenems, macrolides, and vancomycin, which exhibit a rapid and concerning rise in resistance, aminoglycosides and the trimethoprim-sulfamethoxazole combination have an average but growing resistance (5). UTIs are becoming one of the major global public health concerns due to the rise in drug-resistant bacteria and the incidence of bacterial resistance. According to reports, UTIs rank second in primary care treatment frequency and top among infections observed in hospital settings (6). In 1997, a review of National Ambulatory Medical Care and National Hospital Ambulatory Medical Care revealed that UTIs are responsible for over 100,000 hospital admissions, 1 million ER visits, and 7 million outpatient visits. Compared to males, women have UTIs more frequently (7). UTIs are a primary source of infections linked to healthcare settings and a significant factor in the overuse and abuse of antibiotics. Antibiotic-resistant forms of UTIs have emerged, contributing to the significant public health burden of UTIs in Asia, where the frequency is as high as 14% in pregnant women and 9.8% overall (8).

The most frequent etiological cause for UTIs is a gram-negative bacillus, with *E. coli* being responsible for almost 80% of acute UTIs (9). In a 2012 research conducted in a provincial medical college hospital in Bangladesh, 443 suspected UTI patients were found to have considerable uropathogenic bacterial growth in their urine samples, accounting for 43% of the patients. More than 75% of *E. coli* that cause UTIs are resistant to third-generation cephalosporins, according to a recent research (10). UTIs afflict patients of all ages, from newborns to the elderly, and are currently among the most prevalent illnesses seen in clinical settings. *Escherichia coli* is the most often reported bacterial cause of urinary tract infections (UTI), with *Klebsiella pneumoniae, Proteus mirabilis,* and *Pseudomonas aeruginosa* following closely behind (11).

The main goal of this study was to analyze antibiotic resistance trends in UTI pathogens among patients in a tertiary care hospital in Islamabad, Pakistan. In order to improve treatment results and slow the development of resistant strains, the ultimate objective was to inform and improve antibiotic stewardship methods. Enhancing and educating people about antibiotic stewardship initiatives was another important goal (12-13).

This work is important because it fills in a crucial knowledge gap in antibiotic resistance trends in bacteria that cause UTIs in a tertiary care setting in Islamabad, Pakistan. Through the identification and analysis of the resistance profiles of the most frequently isolated UTI bacteria, this study offers insightful information that can improve and provide guidance for local antibiotic stewardship initiatives. These understandings are essential for creating focused interventions to maximize the use of antibiotics, which will eventually enhance patient care and stop the spread of resistant strains.
The fact that data for this study came from just one tertiary care hospital in Islamabad is a significant restriction. The findings' applicability to other healthcare settings in the area or nation may be limited by this single-center methodology. The resistance trends identified might be influenced by differences

in patient demographics, healthcare procedures, and antibiotic prescription patterns among various institutions. As a result, even while the study offers insightful localized information, larger, multi-hospital investigations are required to confirm and build upon these results, guaranteeing that they are inclusive of a larger population.

## 2. Materials and methods

### 2.1 Study design, duration and ethical approval

Antibiotic resistance trends in UTI patients at a Quaid e Azam International Hospital, a tertiary care hospital in Islamabad were examined using a retrospective observational research methodology. Urine analysis records together with accompanying culture and sensitivity reports for patients diagnosed with UTIs over the last six months were obtained and compiled for the data collection, which took place at a tertiary care hospital in Islamabad. The study was carried out between October 2023 to March 2024. Following the Institutional Review Board's approval of the study protocol (191/pharm/GU, dated 01/07/2022) the investigation got underway.

### 2.2 Inclusion and Exclusion Criteria

Only those patients whose culture sensitive test i.e. double disc synergy (DDS) test was performed over the last six month were included in the study. Those with no culture sensitive test although UTI patients were excluded (14).

### 2.3 Sample Size

200 individuals with a diagnosis of urinary tract infection (UTI) who had completed culture sensitivity testing, including the double disc synergy test, within the preceding six months made up the study's sample.

## 3. Statistical Analysis

Using both descriptive and inferential statistics, the statistical analysis for this study was conducted using IBM SPSS (Statistical Package for the Social Sciences) version 20. A 5% level of significance ($\alpha = 0.05$) and a 1% confidence interval (99% CI) were used in the highly rigorous statistical study.

## 4. Results

### 4.1 Prevalence of Etiological species

The majority of cases were caused by *E. coli* (61% the greatest percentage prevalence) compared to various pathogens. This suggests that *E. coli* was the most prevalent causative agent among the pathogens identified. *Klebsiella pneumoniae* was the second most prevalent causal agent, accounting for 30% of cases. *Pseudomonas aeruginosa* was a less frequent causal agent, as indicated by its percentage prevalence of 6%. Of all the pathogens mentioned, *Enterococcus faecium* had the lowest percentage prevalence (3%), indicating that it was the least frequent etiological agent and Figure 1 below displayed all these.

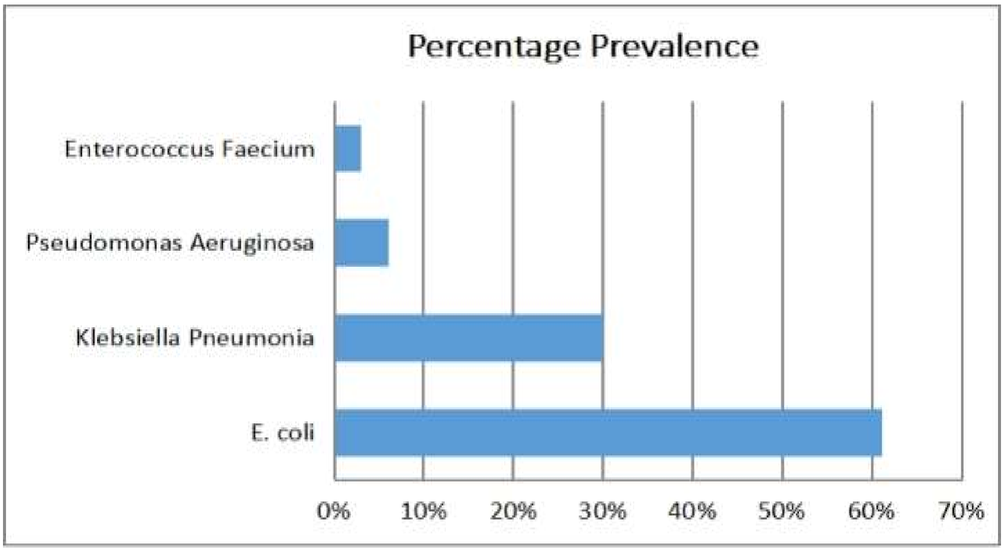


Figure 1. Percentage Prevalence of community acquired UTIs Causative agent (n=200)

### 4.2 Gender based prevalence of causative agents

The information presented in the Figure 2 provides a gender-specific breakdown of the percentage prevalence of different causal factors. Some significant tendencies are shown by this data. With 18.5% of cases in the male population, *E. Coli* was the most common causal agent. Closely behind, with 12.5% prevalence, was *Klebsiella pneumonia*. Three percent of cases in males were caused by *Pseudomonas aeruginosa* and *Enterococcus faecium* combined. All things considered, 37% of the examined causal agents were male isolates. On the other hand, the total prevalence in the female population was substantially greater at 63%. *E. coli* continues to be the most common cause. *Pseudomonas aeruginosa* continued to have a 3% prevalence whereas 17.5% of cases in females were caused by *Klebsiella pneumoniae*. The data unambiguously showed that females were more vulnerable to the causal agents under analysis, with *E. coli* presenting the highest risk. Further research is necessary to determine the underlying causes of the gender imbalance in prevalence rates, since this might have significant effects on targeted public health initiatives and individualized medical treatments (15).

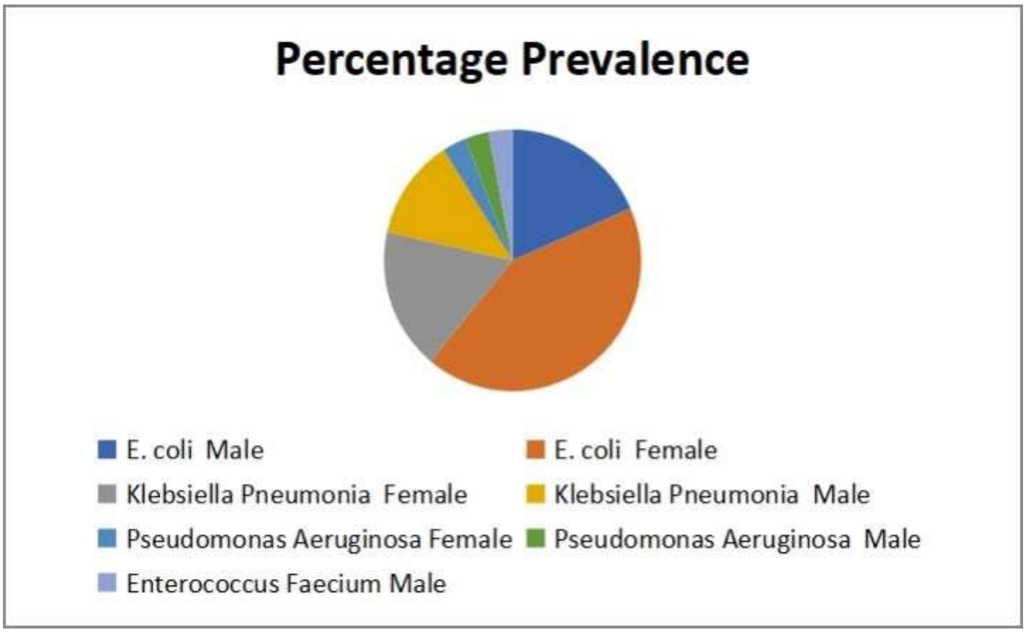


Figure 2. Gender based % age prevalence of various causative agents (n=200)

### *4.3* Antibiotic Resistance Pattern of *E.coli*

Serious concerns were revealed by the antibiotic resistance profiles of the isolates of *Escherichia coli*. Alarmingly high resistance rates were seen in male patients ( Figure 3), with 86.48% and 97.3%, respectively, to ciprofloxacin and ampicillin, augmentin, and amoxicillin. Significant resistance was also shown by ceftriaxone and cefepime (83.73%). On the other hand, reduced resistance rates were noted for nitrofurantoin (13.5%), fosfomycin (8%), and sulzone (2.7%). Notably, antibiotics used as a last option such as colistin, imipenem, meropenem, amikacin, and tazocin exhibited zero percent resistance (16). With 100% resistance to ampicillin, amoxicillin, and augmentin, as well as high resistance to cefepime (89.4%) and ciprofloxacin (76.4%), the situation for female patients was similarly dire (Figure 4). Lower resistance was seen in nitrofurantoin (3.5%), fosfomycin (7.05%), and sulzone (5.8%). Antibiotics used as a last resort, such as imipenem, meropenem, colistin, and amikacin, exhibited extremely low rates of resistance (2.3% or 0%), indicating that they are still effective therapeutic choices (17). A statistical significance observed between male and female isolates when tested against chi square test ( $p<0.01$).

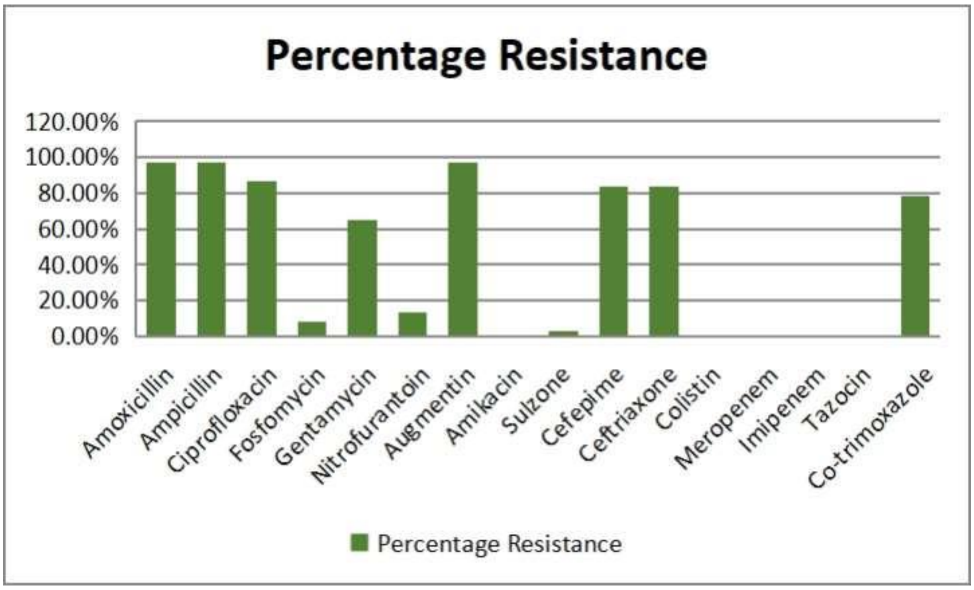


Figure 3. Antibiotic Resistance Pattern of *E.coli* in males (n=37)

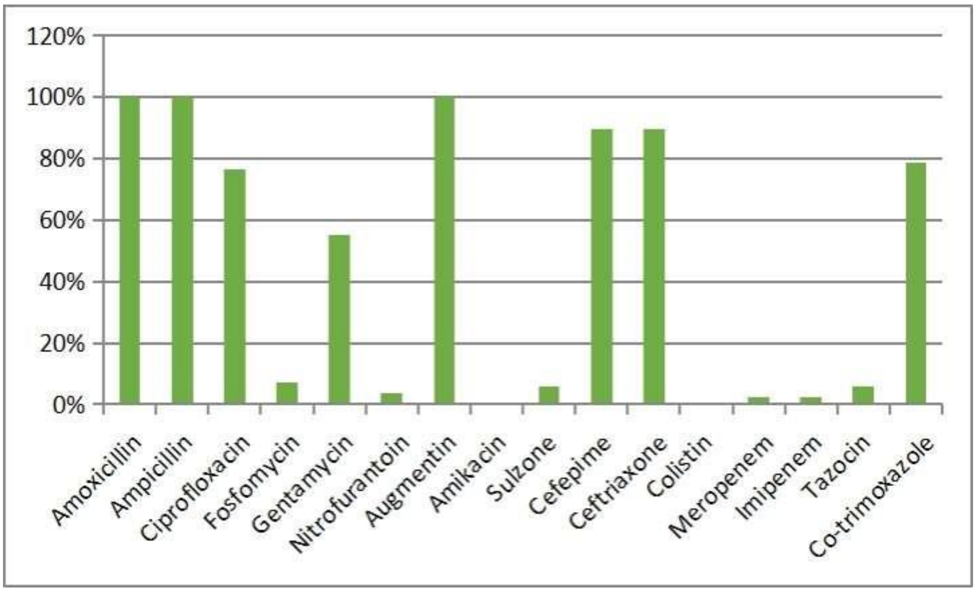


Figure 4. Antibiotic Resistance Pattern of *E.coli* in females (n=85)

### *4.4* Antibiotic Resistance Pattern of *Klebsiella pneumonia*

Serious concerns were highlighted by the antibiotic resistance profiles of *Klebsiella pneumoniae* isolates for both male and female patients (Table 1). The prevalence of resistance in males to cefepime, ceftriaxone, ampicillin, ciprofloxacin, augmentin, and co-trimoxazole was concerningly high. There was also notable resistance to nitrofurantoin (76%), fosfomycin (72%), and meropenem/imipenem (64%). Gentamycin displayed the least amount of resistance (4%), followed by Sulzone and Tazocin (36% and 56%, respectively). Colistin was still a therapy option with zero resistance (18). The resistance rates were even worse for females: ciprofloxacin (88.5%), co-trimoxazole (91.4%), cefepime/ceftriaxone (80%), gentamycin (77.1%), nitrofurantoin (68.5%), Sulzone (68.5%), meropenem/Tazocin (71.4%), and imipenem (51.4%) were all highly resistant. For females, the resistance rates were 100% to ampicillin, amoxicillin, and augmentin. With a 42.8% rate of resistance, fosfomycin might have some therapeutic benefits. Colistin exhibited zero resistance and still effective (19). These results highlight the pressing need for the creation of novel antibiotics, the application of multimodal strategies, and comprehensive antimicrobial stewardship plans in order to combat the growing threat of antibiotic resistance in *Klebsiella pneumoniae* and other critical pathogens, especially in susceptible groups such as male patients. Chi square test showed statistical significance between male and female isolates ( $p<0.05$).

### *4.5* Antibiotic Resistance Pattern of *Pseudomonas aeru'ginosa*

There were notable variations in the antibiotic resistance profiles of *Pseudomonas aeruginosa* isolates between male and female patients (Table 1). Concerningly, all males were resistant to co-trimoxazole, ceftriaxone, ampicillin, amoxicillin, and augmentin at 100%. Ciprofloxacin and cefepime resistance rates were similarly significant (83.3% each). Although there are few options for treatment, antibiotics with reduced resistance (50–66.6%) include gentamycin, fosfomycin, nitrofurantoin, amikacin, Sulzone, Tazocin, and meropenem/imipenem. Notably, colistin had zero resistance (20). On the other hand, *Pseudomonas aeruginosa* isolates from female patients showed reduced overall resistance, averaging 33.3% for the majority of antibiotics, indicating a greater range of possible treatments. Co-trimoxazole was 100% resistant, whereas other antibiotics such as ciprofloxacin, ampicillin, and amoxicillin exhibited less resistance. Colistin still had 100% success rate in treating females and was a good last-resort option (21). The increasing threat of antibiotic resistance in *Pseudomonas aeruginosa* and other critical pathogens, especially in vulnerable populations like male patients, highlights the urgent need for comprehensive antimicrobial stewardship strategies, the development of new antibiotics, and the implementation of multifaceted approaches.

### 4.6 Antibiotic Resistance Pattern of *Enterococcus faecium* in Males

The information supplied in the table 1 revealed a worrying pattern of antibiotic resistance for *Enterococcus faecium*, a major disease linked to healthcare. The most startling discovery was the complete resistance to co-trimoxazole, ceftriaxone, ampicillin, amoxicillin, and augmentin (a mixture of amoxicillin and clavulanic acid). This suggested that these widely used antibiotics were essentially useless against *Enterococcus faecium* infections. This is especially troubling because these antibiotics are frequently employed as first lines of therapy for different *Enterococcus* illnesses linked to the faecium, including bloodstream infections, endocarditis, and urinary tract infections. The data also revealed significant rates of resistance to cefepime (83.3%) and ciprofloxacin (83.3%), which further reduced the range of treatments that were possible for *Enterococcus faecium* infections. Additionally, the data pointed to a few drugs that had comparatively lower levels of resistance, which could be useful substitutes for therapeutic therapy. The resistance rates of 50–66.6% for fosfomycin, gentamycin, nitrofurantoin, amikacin, Sulzone, Tazocin (a mixture of piperacillin and tazobactam), and meropenem/imipenem indicated that these could be better choices against *Enterococcus faecium* infections. Interestingly, the data showed that the antibiotic used as a last resort, colistin, had a 0% resistance rate, indicating that it could still be a viable treatment for *Enterococcus faecium* infections for the time being (22).

**Table 1.** Antibiotic Resistance profile of different Uropathogens

| Drugs | *E. coli* (males) | *E. coli* (Females) | *Klebsiella pneumonia* (males) | *Klebsiella pneumonia* (females) | *Pseudomonas aeruginosa* (males) | *Pseudomonas aeruginosa* (females) | *Enterococcus faecium* (males) |
|---|---|---|---|---|---|---|---|
| Amoxicillin | 97.3% | 100% | 100% | 100% | 100% | 33.3% | 100% |
| Ampicillin | 97.3% | 100% | 100% | 100% | 100% | 33.3% | 100% |
| Ciprofloxacin | 86.48% | 76.4% | 100% | 88.5% | 83.3% | 33.3% | 83.3% |
| Fosfomycin | 8% | 7.05% | 72% | 42.8% | 50% | 33.3% | 50% |
| Gentamycin | 64.8% | 55.2% | 4% | 77.1% | 50% | 33.3% | 50% |
| Nitrofurantoin | 13.5% | 3.5% | 76% | 68.5% | 50% | 33.3% | 50% |
| Augmentin | 97.3% | 100% | 100% | 100% | 100% | 33.3% | 100% |
| Amikacin | 0% | 0% | 44% | 51.4% | 50% | 33.3% | 50% |
| Sulzone | 2.7% | 5.8% | 36% | 68.5% | 50% | 33.3% | 50% |
| Cefepime | 83.73% | 89.4% | 100% | 80% | 83.3% | 33.3% | 83.3% |
| | | | | | | | |
| Ceftriaxone | 83.73% | 89.4% | 100% | 80% | 100% | 33.3% | 100% |
| Colistin | 0% | 0% | 0% | 0% | 0% | 0% | 0% |
| Meropenem | 0% | 2.3% | 64% | 71.4% | 66.6% | 33.3% | 66.6% |
| Imipenem | 0% | 2.3% | 64% | 51.4% | 66.6% | 33.3% | 66.6% |
| Tazocin | 0% | 5.8% | 56% | 71.4% | 50% | 33.3% | 50% |
| Co-trimoxazole | 86% | 78.8% | 100% | 91.4% | 100% | 100% | 100% |
| **Total Sample Size (n=200)** | | | | | | | |
| Sample Size | n=37 | n=85 | n=25 | n=35 | n=06 | n=06 | n=06 |

## 5. Discussion

This retrospective observational analysis was carried out at Quaid e Azam International hospital Islamabad, Pakistan to investigate the antibiotics resistance trends of community acquired urinary tract infections to emphasize the exploration of any viable resistance free antibiotic as well as highlighting the implementation of antibiotics stewardship program as a sole possible intervention to minimize the likelihood of antibiotics resistance. With a 61% case rate, *Escherichia coli* (*E. coli*) was the most common causal agent in our investigation of urinary tract infections. Compared to the 33.2% recorded in a study of 283 hospital-acquired UTIs, this prevalence was significantly greater. The tendency of *E. coli* being the predominant pathogen, despite the increasing percentage, is in line with earlier research (23). *Klebsiella pneumoniae* was found in 30% of our study, but it was found in 16.6% of the study in hospital-acquired UTIs, (23). Once more, even if our results showed a higher percentage, the order of prevalence made sense in light of the earlier research.

Our study found that *Pseudomonas aeruginosa* caused 6% of UTIs, which is in line with the trend but somewhat less than the 8.8% reported in the comparative study (23). This discrepancy might be explained by the fact that our investigation focused on infections obtained in the community as opposed to the comparative study's focus on illnesses acquired in hospitals. In our investigation, *Enterococcus faecium* was detected in 3% of cases, while in the hospital-acquired UTIs, study, *Enterococcus spp.* was responsible for 25.9% of cases (24). The observed statistical disparity implies a more robust correlation between *Enterococcus species* and infections linked to healthcare, an entity that was not as prevalent in the subjects under investigation. Overall, our results showed that *E. coli* was the primary cause of UTIs and showed a consistent pattern with other research involving *E. coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*. The significance of customized antimicrobial stewardship programs and local surveillance in addressing regional differences in pathogen incidence is highlighted by these findings.

According to our study's gender analysis, 81% of UTI patients were female, suggesting that UTIs are more common in women. This result is consistent with a study carried out in Pakistan's Kohat district, where the frequency of UTIs was reported to be 13.8% in females and 8.9% in males (25). The gender distribution in both research emphasizes how more vulnerable women are to UTIs, which may be related to anatomical and physiological variations. In contrast, a study conducted in Saudi Arabia found lower resistance in *E. coli* from human urine samples: norfloxacin (80%), amoxicillin and ampicillin (70%), trimethoprim/sulfamethoxazole (55%), ciprofloxacin and ofloxacin (50%), and (30–25%) in various cephalosporins (26). Despite these differences, the trend of high resistance to these antibiotics is consistent across both studies. Our study also found lower rates of resistance to sulzone (2.7%), fosfomycin (8%), and nitrofurantoin (13.5%), and no resistance was observed for imipenem, colistin, meropenem, amikacin, and tazocin. 81% of UTI cases in our study were in females, according to gender-specific analysis, while *E. coli* had 100% ampicillin, amoxicillin, and augmentin resistance. This is consistent with the Saudi study, which found that females had a higher prevalence and resistance to UTIs (26).

In both male and female patients in our study, *Klebsiella pneumoniae* showed startlingly high rates of resistance to several medicines. Male patients had reduced resistance to gentamycin, sulzone, and tazocin, but significant resistance to cefepime, ceftriaxone, co-trimoxazole, ampicillin, ciprofloxacin, and augmentin. Colistin faced no opposition. The ampicillin, amoxicillin, and augmentin resistance in female patients was 100%, while the resistance to ciprofloxacin, co-trimoxazole, cefepime/ceftriaxone, gentamycin, nitrofurantoin, sulzone, meropenem/tazocin, and imipenem was high. The resistance to fosfomycin was decreased and the efficacy of colistin was maintained. A different region's study, however, found lower resistance rates. 100% susceptibility to amikacin and 100% resistance to clarithromycin were demonstrated by *Klebsiella pneumoniae*. Lower rates of resistance were seen for the following antibiotics: ampicillin (20%), cefalotin (75%), co-trimoxazole (43.9%), ceftriaxone (32%), ciprofloxacin (30.9%), ampicillin (20%), and cefotaxime (24%). High sensitivity was observed for amikacin, meropenem, and cefepime (27). The necessity for localized data to inform treatment methods is highlighted by the possibility that regional variations in antibiotic use, healthcare procedures, and patient demographics are the cause of the differences between the studies.

Based on our analysis of *Pseudomonas aeruginosa* isolates, we have shown that male patients exhibited 100% resistance to co-trimoxazole, ceftriaxone, ampicillin, amoxicillin, and augmentin, indicating extreme antibiotic resistance. The resistance rates to cefepime and ciprofloxacin are likewise substantial (83.3%). Conversely, for female patients, the majority of other antibiotics have a much lower resistance rate (33.3%), even though co-trimoxazole resistance is still 100%. In contrast, the resistance rates generally were found to be lower in the Czech study on hospital wastewater. Resistance rates to ciprofloxacin, gentamicin, and meropenem were 30.5%, 28.8%, and 27.2%, respectively. Resistance to ceftazidime, amikacin, piperacillin-tazobactam, and aztreonam was lower. (28). The variations in antibiotic use patterns, healthcare environments, and regional resistance profiles could be the cause of the disparities observed throughout the research. of particular environmental and medical variables on patterns of resistance. The Czech study illustrated a more modest resistance scenario, stressing the influence of unique environmental and healthcare elements on resistance patterns, whereas our study pointed to major resistance difficulties, especially for male patients.

Globally, UTIs place a significant financial and emotional strain on people as well as health resources, and successfully treating UTIs is a difficult task in practice. Antimicrobial stewardship programs have been developed with the goal of minimizing the unintended consequences of antibiotic overuse, such as antibiotic-related adverse events and the emergence of resistant bacterial strains. These programs seek to optimize clinical outcomes while reducing inappropriate antibiotic use. First-line therapy with fosfomycin trometamol, nitrofurantoin, or pivmecillinam is recommended as first-line antimicrobial therapy for uncomplicated UTIs. Strategies are available to reduce the dependence on antimicrobial use in uncomplicated UTIs, including methenaminehippurate, cranberry extract, D-mannose, probiotics, intravesical GAG therapy, and prophylactic vaccination. Appropriate non-antimicrobial strategies aimed at reducing the incidence of rUTIs should also be considered (29). By choosing the right antibiotic and dose schedule and avoiding overuse of antibiotics, clinicians may be able to enhance patient outcomes while lowering the risk of toxicity and resistance. Giving IV antibiotics like ceftriaxone and imipenem/cilastatin for mild to moderate infections in afebrile patients without or with a slight elevation in WBC was the most frequently reported inappropriate antibiotic prescription. β-lactams were the most inappropriate antibiotic recommended for adult patients in a research on UTI patients attending an academic emergency department (30).

A variety of intervention techniques were employed, including instructional sessions, the establishment of local ASB teams, audit and feedback, guidelines, and the introduction of multidisciplinary quality circles. (31) Children with congenital uropathies should consider non-pharmacological measures to avoid UTI recurrence. The main objective for physicians and caregivers should be to restore both normal bowel function and a proper micturition pattern to restore bladder function. There is not enough data to recommend certain medications and doses as first-choice preventative regimens. Due to the fact that each nation has a unique regimen and set of medications, some medications are successful in one nation but resistive in another (32). In order to address gender-specific vulnerabilities and infection patterns, the study also highlights the significance of customized public health programs and medical practices. To combat growing problem of antibiotic resistance, a coordinated strategy including medical experts, researchers, legislators, and public awareness campaigns is necessary. To maintain the efficacy of currently available medications and safeguard the public's health, this strategy should concentrate on creating novel treatments, improving the use of already available antibiotics, and stopping the development of resistant bacteria (33).

## 6. Conclusion

The results of this study highlight the critical need to manage antibiotic resistance, especially when it comes to infections brought on by *E. coli* and *Klebsiella pneumoniae*. Interestingly, the overall infection rate was greater in females (63%) than in males (37%), with *E. coli* infections being substantially more common in females. The results showed a worrying pattern of 100% resistance in females and 97.3% resistance in males to popular medicines as ampicillin, augmentin, and amoxicillin. Nonetheless, antibiotics used as a last option, such as imipenem and colistin, continued to be effective. This underscores the vital necessity of creating novel antimicrobial medicines and strengthening antimicrobial stewardship initiatives.

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