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Assessing Culture Sensitivity Patterns of *Escherichia Coli* in Urinary Tract Infection Clinical Isolates; Implications for Antibiotic Therapy

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Abstract

Urinary tract infections (UTIs) a pathogenic infection that occur in any part of the urinary system, most commonly in the lower urinary tract affecting the bladder and urethra. They can also extend to the upper urinary tract, including kidney infection (pyelonephritis), prostate infection in men, and urethral infections in females. The current study was carried out in DHQ Timergara lower Dir, with n=44 culture sensitivity reports evaluated to assess thse sensitivity and resistance pattern of antibiotics to *Escherichia Coli,* in which male n=28(63.3%) and female n=16(36.4). Various age groups of patients participate in the study, age ranges are 1-9 Y n=3, 11-19 Y n=8, 20-29 Y n=9, 30-39 Y n=4, 40-49 Y n=3, 50-59 Y n=5, 60-69 Y n=10, and 70-79 Y n=2. Ciprofloxacin out of 41, sensitive to 48.8%, intermediate 14.6%, resistant to 36.6%, levofloxacin out of 41 sensitive to 65.8%, intermediate 9.7%, resistant to 24.3%, nitrofurantoin sensitive to 51.4%, intermediate 14.3%, and resistant to 34.3%. Antibiotics like piperacillin/tazobactam and meropenem appear more effective and may be preferred in empirical therapy for infections caused by resistant organisms. Continuous monitoring through susceptibility testing is essential to adapt treatment protocols and combat rising antimicrobial resistance. The findings emphasize the necessity for regular monitoring of antibiotic susceptibility patterns to inform clinical decision-making effectively. Given the high rates of resistance observed, clinicians should consider local resistance data when selecting empirical therapy for UTIs. Additionally, the study advocates for more judicious use of antibiotics to preserve their efficacy and combat the rising tide of resistance.

Keywords; Urinary Tract infections, AMR, Complicated urinary tract infections, CSTs, Antibiotic therapy.

1.0 INTRODUCTION

Urinary tract infections (UTIs) are infections that occur in any part of the urinary system, most commonly in the lower urinary tract affecting the bladder and urethra. They can also extend to the upper urinary tract, including kidney infection (pyelonephritis), prostate infection in men, and urethral infections in females [1]. Although the symptoms of UTIs vary depending on the specific type of infection, several symptoms like burning sensation during urination, dark smelled urine, blood in urine, the urgency of urination, pain or pressure in the back or lower abdomen, fever or chills, nausea or vomiting, may commonly appear [2].

Bacterial infections primarily cause those, *Escherichia coli (E. coli)*, typically found in the gut, is frequently the main offender. In addition, structural anomalies in the urinary tract, diabetes, multiple sclerosis, stroke, spinal cord injury, weakening of the immune system, menopause, pregnancy [3], kidney stones, multiple sexual partners, catheter use, obstructions, and urinary surgery are examples of medical conditions contributing to UTIs [4]. If left untreated, UTIs can result in several complications like recurrent infections, permanent kidney damage, urethral stricture which is the narrowing of the urethra particularly in men, and sepsis which is a life-threatening response to infection. [5]. Urine analysis to check organisms causing infection, urine culture to determine the type of organism, cystoscopy (looking at the bladder and urethra), and CT or MRI scans to evaluate abnormalities in the urinary tract are all used to diagnose UTIs [6].

UTIs are extremely prevalent, impacting millions of individuals annually across the globe. The population and environment impact the prevalence [7]. The prevalence of community-associated UTIs (CAUTIs) is approximately 0.7%, and the primary risk factors for the illness are age, previous UTI history, sexual activity, and diabetes. In the US, the frequency of healthcare-associated UTIs ranges from 12.9-19.6%, while in Europe and developing countries, it can reach up to 24%. The prevalence in urology departments is 5.1% [8]. Each year, UTIs cause about 7 million office visits and 1 million visits to emergency rooms in the United States. Compared to men, women are much more likely to get UTIs. By the age of 24, almost one in three women will experience at least an episode requiring antibiotics, and nearly half will experience a UTI at some point in their lives [9]. Pregnant women, older adults, individuals with spinal cord injuries, diabetes, immunodeficiency, and urologic abnormalities are among the specific high-risk groups. Over a million catheter-associated UTIs are diagnosed in hospitals and assisted living facilities annually, making them the most prevalent nosocomial infections [10]. Uropathogenic *E. Coli* (UPEC) is the most frequent causative agent, followed by *Candida species, Enterococcus species, Proteus mirabilis, Staphylococcus saprophyticus, Klebsiella pneumoniae,* and others [11].

UTIs can result in significant morbidity, mortality, and financial burden, particularly when they are exacerbated by risk factors that raise the possibility of sepsis and kidney damage. Hospital admissions for sepsis are frequently related to UTIs [3]. Urosepsis resulting from complex UTIs has a 10% mortality rate. Untreated kidney infections can result in scarring, declined function, hypertension, and even renal failure. The mother and fetus are more susceptible to complications such as preterm labor, low birth weight, preeclampsia, and septic shock when they have a pregnancy-related UTI [3, 5]. Mens complicated UTIs can lead to major side effects such as bacteremia, prostatitis, orchitis, and epididymitis. Complicated UTIs account for over 626,000 admissions per year to hospitals in the United States, or roughly 1.8% of all hospitalizations. 50% of women are experiencing at least once in their lifetime suffer from UTIs. Recurrent infections raised the cost and utilization of healthcare. When untreated UTIs worsen and necessitate hospitalization and intravenous antibiotics, medical expenses may increase dramatically. [12].

German bacteriologist Therefore *Escherichia* initially identified the Bacterium coli commune and characterized *E. coli* in 1885. The bacteria were isolated from the healthy baby feces. Before 1950, the bacteria were considered a benign resident of warm-blooded animals and people's gastrointestinal tracts. Gram-negative, facultatively anaerobic, non-spore-forming, rapid, rod-shaped bacteria with a diameter of 2-3 µm is called *E. coli*. Humans, animals, and fowl frequently have *E. coli* in their digestive systems. It invades a human infant's gastrointestinal tract right away after birth. The interaction between *E. coli* and its host is positive, but it has the potential to turn opportunistic and spread diseases.

AMR toward uropathogenic bacteria is a major challenge in UTI management. Lower and middle-income countries are more prone to resistance, because of the irrational use of antimicrobials for common and minor infections. However, its prevalence and resistance pattern are changing day by day, so monitoring patient susceptibility toward antimicrobials during UTI management is extremely important [13].

Urinary infections in eastern Nepal, India, and Bangladesh have shown an increasing resistance to commonly used medications. The types of organisms that cause UTIs, along with their patterns of antibiotic resistance and sensitivity, vary by region. Therefore, it is essential to regularly investigate these resistance and sensitivity patterns. Additionally, the causative agents and their levels of resistance to the most frequently used drugs for treating UTIs may have changed over time. To ensure the optimal use of conventional antibiotics, public health officials should conduct regular assessments of the local incidence of uropathogens and their susceptibility profiles [14, 15].

The current study aimed to assess the latest prevalence of *E. Coli* and its antibiotic susceptibility in UTI patients, while analyzing the antimicrobial susceptibility patterns observed in a tertiary care hospital.

2.0 MATERIALS AND METHODS

2.1 Data collection

A total of n=44 culture sensitivity reports were collected during the data collection period from January 1, 2024, to February 29, 2024. This data collection was conducted with the official permission of the chief pharmacist and the ward in charge. The data collector, who was well-educated, received ethical guidance from the university prior to the collection process. The data was gathered with the consensus of physicians, nurses, and patient attendants.

2.2 Study setting and design

The retrospective study was carried out in the District Headquarter Hospital Timergara, Dir Lower. The study was specially conducted in medical DHQ Timergara, Lower Dir, KP Pakistan.

2.2 Inclusion and Exclusion Criteria

All the patients were excluded

- Hospital stay time of less than 01 day
- Having an insufficient or lost medical record

All the patients were included that were

- Already discharged from hospital
- Patients with complete medical records
- Patients having at least one antibiotic prescribed
- Patients who have culture sensitivity test report

2.3 Antibiotic consumption

The main focus was shifted toward the following.
A. Total Number of antibiotics
B. Monotherapy or Combination Therapy
C. Hospital Longevity
D. Average stay in the hospital
E. Antibiotic at which the Patient was discharged
F. Switching over (if any)

2.4 Data analysis

The collected data was analyzed by using Graph Pad Prism Microsoft Excel for tabulating and graphical presentation of data. Pharma Guide and Pharmapedia Pakistan were used for the generic names of the drugs.

2.5 Limitations

The collected data was from 44 patients, including male and female patients. Culture sensitivity test is an expensive procedure and takes almost 48-72 hours.

3.0 RESULTS AND DISCUSSION

The current study was carried out in DHQ Timergara lower Dir, with n=44 culture sensitivity reports evaluated to assess the sensitivity and resistance pattern of antibiotics to *E. Coli*. In which CSTs collected from male patients were, n=28(63.3%) and female pateinets were, n=16(36.4), as shown in Table 1.

3.1 Age-wise distribution

Various patients of different age groups who participated in the study, Various age groups patients participate in the study, age ranges are 1-9 n=3, 11-19 n=8, 20-29 n=9, 30-39 n=4, 40-49 n=3, 50-59 n=5, 60-69 n=10, and 70-79 n=2 (Table 2).

Table 1. Total CSTs collected from male and female patients

Gender	Number of patients (n)	Percentage (%)
Male CSTs collected	28	63.6
Female CSTs collected	16	36.4
Total	44	

Table 2. CSTs collecetd among age range of patients (male/female)

Age ranges (Years)	Number of patients (n)
1-9	3
10-19	8
20-29	9
30-39	4
40-49	3
50-59	5
60-69	10
70-79	2
Total	44

3.2 Clinical Isolates and their Susceptibility Reports

The Table 3, presents the susceptibility of various bacterial isolates to different antimicrobial agents, illustrated in Fig 1. It details the total number of isolates tested, along with the percentage of isolates categorized as susceptible, intermediate, or resistant to each agent. This information is crucial for understanding the effectiveness of antibiotics against specific pathogens and guiding treatment decisions.

Ciprofloxacin was tested on 41 total isolates, out of which 48.8% of the isolates were sensitive, 14.6% were intermediate, while 36.6% were resistant to ciprofloxacin. Similarly, in case of levofloxacin the total isolates were 41, out of which 65.8% showed sensitivity, 9.7% were intermediate while 24.3% showed resistance. The total nitrofurantoin tested isolates were 35 out of which 51.4% showed sensitivity while 14.3% were intermediate and 34.3% showed resistance. In case of ampicillin 11.3% of the 44 isolates were susceptible, 6.8% were intermediate, while 81.8% showed resistance. The high resistance rate in case of ampicillin shows that it is highly ineffective against the tested isolates. For amoxicillin/Clavulanate, a susceptibility rate of 23.8% was observed among the 44 isolates, 14.3% isolates were intermediate while 61.9% of the isolates showed resistance.

Moderate susceptibility suggests that while there is some effectiveness, substantial resistance still remains. Piperacillin/Tazobactam were tested on 44 isolates, 72.7% of the total isolates showed sensitivity, and 13.6% were intermediate while 13.6% exhibited resistance. This combination suggests strong efficacy against the isolates. Cefixime was tested on 38 isolates out of which 42.1% were sensitive, 10.5% were intermediate and 47.3% showed resistance. This treatment indicates variable effectiveness since resistance is almost equal to susceptibility.

For ceftriaxone, a susceptibility of 37.8% was observed out of 37 isolates, 8.1% were intermediate, while 54.0% of the isolates showed resistance to ceftriaxone. The resistance rate of more than 50% suggests limited utility in treatment. Cefotaxime showed nearly similar results to ceftriaxone with a susceptibility of 40.6% and resistance rate of 43.7%. The susceptibility rate of 27.6% to cefepime indicates significant resistance. While, Meropenem and Imipenem were relatively more susceptible (68.4% and 56.4% respectively), suggesting that they are among the more effective options available.

Table 3. Percentage of antibiotics prescribed, and CSTs on isolate susceptible, intermediate, and resistant

Antimicrobial agent	**Total no. of isolates**	**% Isolates (Susceptible)**	**% Isolates (Intermediate)**	**% Isolates (Resistant)**
Ampicillin	44	11.3	6.8	81.8
Amoxicillin/Clavulanate	42	23.8	14.3	61.9
Piperacillin/Tazobactam	44	72.7	13.6	13.6
Cefixime	38	42.1	10.5	47.3
Ceftriaxone	37	37.8	8.1	54.0
Cefotaxime	32	40.6	12.5	43.7
Cefepime	29	27.6	24.1	48.2
Cefoperazone	37	40.5	27.0	32.4
Cefuroxime	44	61.4	20.5	18.2
Cefaclor	27	26.0	14.8	59.2
Ceftazidime	30	30.0	13.3	56.7 6
Ertapenem	39	71.7	12.8	15.3
Amikacin	39	74.3	10.2	15.4
Gentamicin	42	66.6	7.1	26.2
Nalidixic Acid	41	9.7	17.1	73.2
Ciprofloxacin	41	48.8	14.6	36.6
Moxifloxacin	40	42.5	15.0	42.5
Levofloxacin	41	65.8	9.7	24.3
Tobramycin	25	28.0	20.0	52.0
Ofloxacin	35	34.3	17.1	48.6
Fosfomycin	42	50.0	21.4	28.6

Nitrofurantoin	35	51.4	14.3	34.3
Trimethoprim/Cotrimoxazole	37	24.3	21.6	54.0
Doxycycline	35	34.3	11.4	54.3
Meropenem	38	68.4	7.9	23.7
Imipenem	39	56.4	10.2	33.4

The data illustrates in Fig 2, a concerning trend of high resistance rates among common antibiotics, particularly ampicillin and its derivatives. Antibiotics like piperacillin/tazobactam and meropenem appear more effective and may be preferred in empirical therapy for infections caused by resistant organisms. Continuous monitoring through susceptibility testing is essential to adapt treatment protocols and combat rising antimicrobial resistance.

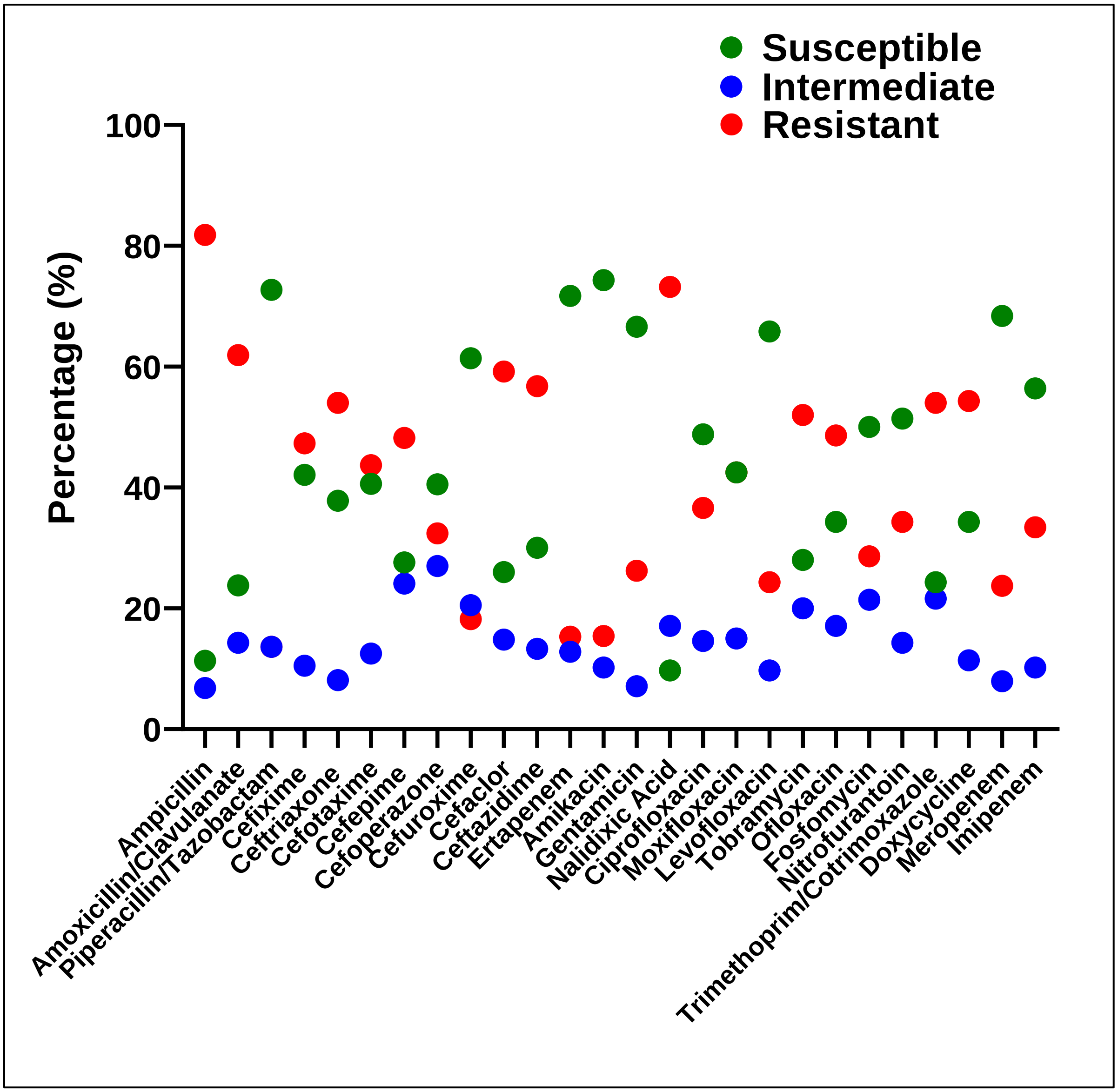

Fig. 1: *Sensitivity, Resistance, and Intermediate Pattern of Antibiotics*

Ciprofloxacin out of 41, sensitive to 48.8%, intermediate 14.6%, resistant to 36.6%, levofloxacin out of 41 sensitive to 65.8%, intermediate 9.7%, resistant to 24.3%, nitrofurantoin sensitive to 51.4%, intermediate 14.3%, and resistant to 34.3%.

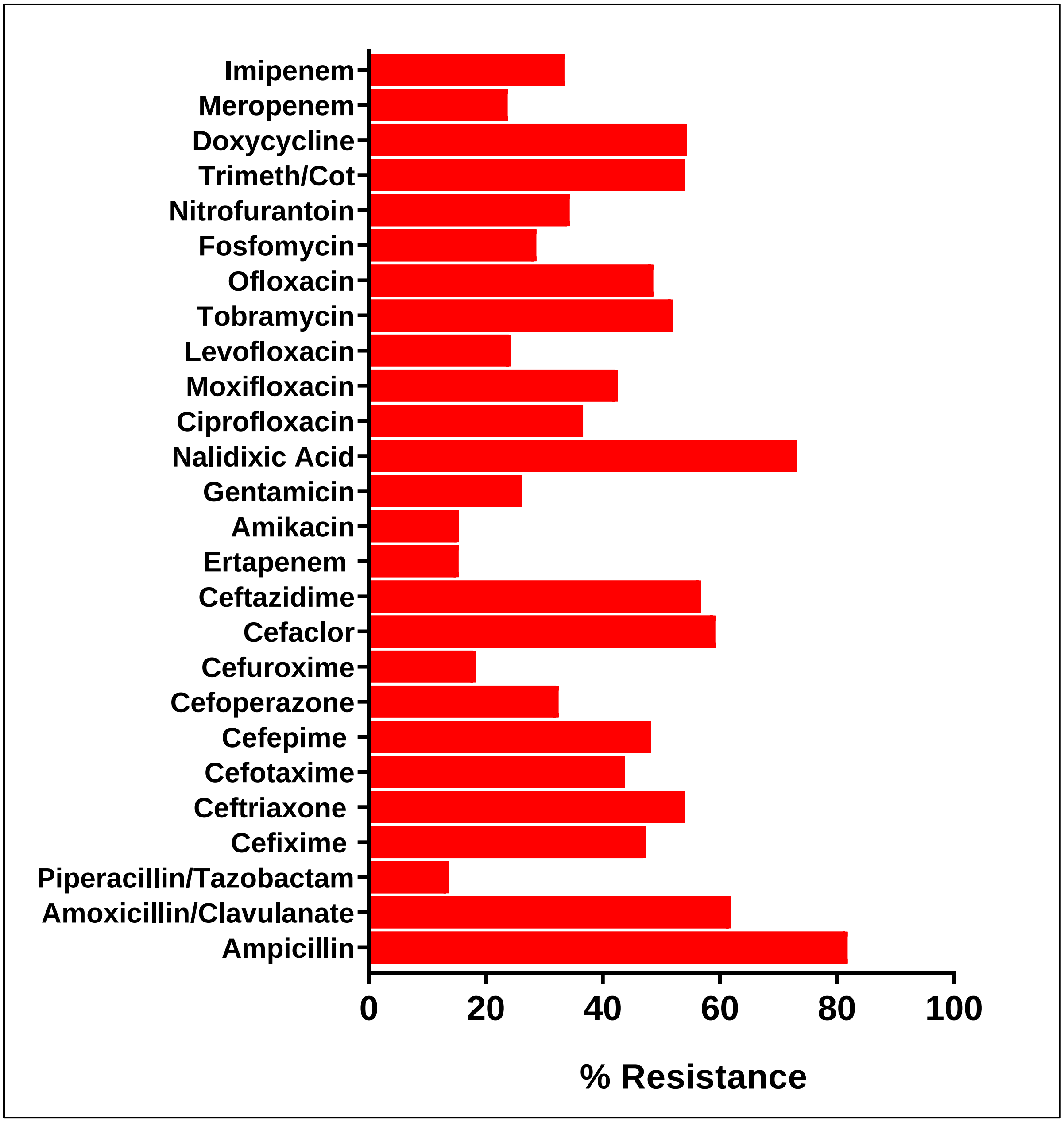

Fig. 2: *Percentage of Antibiotics resistance*

3.3 Discussion

The current study was conducted at DHQ Timergara in Lower Dir, evaluating 44 culture sensitivity reports to assess the sensitivity and resistance patterns of antibiotics against Escherichia coli. Among the participants, there were 28 males (63.3%) and 16 females (36.4%). The study included various age groups, with the following age distribution: 1-9 years (n=3), 11-19 years (n=8), 20-29 years (n=9), 30-39 years (n=4), 40-49 years (n=3), 50-59 years (n=5), 60-69 years (n=10), and 70-79 years (n=2). Ampicillin, Total Isolates 44, Susceptible 11.3%, Intermediate 6.8%, Resistant 81.8%. High resistance indicates that ampicillin is largely ineffective against the tested isolates. Amoxicillin/Clavulanate, Total Isolates: 42, Susceptible 23.8%, Intermediate 14.3%, Resistant 61.9%. Moderate susceptibility suggests some effectiveness, but significant resistance remains. Piperacillin/Tazobactam, Total Isolates 44, Susceptible 72.7%, Intermediate: 13.6%, Resistant 13.6%. This combination shows strong efficacy against the isolates. Cefixime, Total Isolates: 38, Susceptible: 42.1%, Intermediate: 10.5%, Resistant: 47.3%. Resistance is nearly equal to susceptibility, indicating variable effectiveness. Ceftriaxone, Total Isolates 37, Susceptible 37.8%, Intermediate 8.1%, Resistant 54.0%. More than half are resistant, suggesting limited utility in treatment. Cefotaxime shows similar results to ceftriaxone with a susceptibility rate of 40.6% and a resistance rate of 43.7%. Cefepime shows a susceptibility of only 27.6%, indicating significant resistance. While Meropenem and Imipenem both agents show relatively high susceptibility rates (68.4% and 56.4%, respectively), suggesting they are among the more effective options available. Ciprofloxacin out of 41, sensitive to 48.8%, intermediate 14.6%, resistant to 36.6%, levofloxacin out of 41 sensitive to 65.8%, intermediate 9.7%, resistant to 24.3%, nitrofurantoin sensitive to 51.4%, intermediate 14.3%, and resistant to 34.3%.

A recent study aimed to extract antibiotic-resistant and ESBL-producing *E. coli* from 200 UTI patients at HMC Hospital in Peshawar. A total of 121 *E. coli* isolates were subjected to antibiotic sensitivity testing, revealing notable resistance levels to several antibiotics. The findings showed a resistance rate of 1.85% to meropenem, with a corresponding sensitivity of 98.14%; a resistance rate of 9.25% to Tazocin and a sensitivity of 85.18%; and a significant resistance rate of 87.96% to ciprofloxacin, with only 12.03% sensitivity. Additionally, fosfomycin exhibited a resistance level of 3.70% and a sensitivity of 95.37%. Resistance was also observed for cefotaxime, augmentin, ceftazidime, and cefepime [16].

A 6-month cross-sectional study was conducted involving 146 patients with urinary tract infections (UTIs) to investigate the prevalence of multidrug-resistant (MDR) *E. coli* infections. Among the participants, 65 (44.5%) were male, and 81 (55.5%) were female. The average age of the included cases was 46.87 ± 8.70 years. Additionally, 90 patients (61.6%) resided in rural areas, while 56 patients (38.4%) lived in urban areas. MDR *E. coli* was detected in 69 patients, accounting for 47.3% of the study population [17].

Ilyas et al. conducted a study on multidrug-resistant (MDR) *E. coli* and *Klebsiella pneumoniae* at Holy Family and Khalifa Gul Nawaz Hospitals in Pakistan from June to November 2023. The aim was to assess the prevalence and β-lactamase enzyme production of these pathogens. A total of 350 midstream urine samples were collected from patients suspected of having urinary tract infections (UTIs). Among these samples, 85 showed significant bacteriuria, including 62 cases of *E. coli* and 23 cases of *Klebsiella pneumoniae*. Notably, 62.35% of the isolates were found to be multidrug-resistant (MDR). The preferred treatments identified in the study were Imipenem, Meropenem, and Nitrofurantoin [18].

A study conducted by Ali et al. examined the antibacterial susceptibility of *E. coli* isolates from hospitalized patients with UTIs. The results indicated that imipenem demonstrated significant efficacy, with a susceptibility rate of 73.42%. Additionally, cephalosporins, such as cefpirome, showed a susceptibility rate of 44.94%. Conversely, high resistance rates were observed against Sulfamethoxazole/Trimethoprim (71.52%), Amoxicillin-Clavulanic Acid (67.72%), and Nalidixic Acid (66.46%). These findings underscore the need for targeted therapy and highlight the potential effectiveness of Imipenem.

The data reveals a troubling trend of high resistance rates among common antibiotics, especially ampicillin and its derivatives. Antibiotics such as piperacillin/tazobactam and meropenem seem to be more effective, making them preferable choices for empirical therapy in cases of infections caused by resistant organisms. Ongoing monitoring through susceptibility testing is crucial for adapting treatment protocols and addressing the growing issue of antimicrobial resistance.

Uropathogenic *E. coli* is the leading cause of both community-acquired and hospital-acquired UTIs. Other significant contributors include *Staphylococcus*, *Klebsiella*, *Enterobacter*, *Proteus*, and *Enterococci* species. Key factors such as age, gender, geographical location, sexual activity, diabetes mellitus, and prior UTI history directly influence the nature of UTIs, the involved pathogens, and the patterns of antibiotic resistance observed. Furthermore, the ability of *E. coli* to produce biofilms ensures its persistence within the urinary system, complicating treatment efforts. As a result, these infections are notoriously difficult to cure and are a major source of antibiotic resistance [19].

Treating urinary tract infections (UTIs) caused by ESBL-producing *E. coli* is significantly more costly than treating infections from ESBL-negative strains. Therefore, understanding the prevalence of ESBL production in urine *E. coli* isolates is essential for making informed choices about antimicrobial treatments. In a thorough study with 583 patients, researchers identified uropathogens in 400 urine samples (68.6%), including 134 *E. coli* isolates. Alarmingly, of the tested uropathogenic *E. coli* (UPEC), 80 isolates (59.7%) were found to produce ESBLs. Notably, over half of these ESBL producers exhibited multidrug resistance (62%). However, there is a silver lining: all were found to be susceptible to meropenem. The majority of *E. coli* isolates fell into four distinct phylogenetic groups: B2 (52.5%), F (21.25%), and Clade I or II (12.5%). This information is critical for our ongoing efforts to combat resistant infections effectively and efficiently [20].

From 2012 to 2021, a compelling case-control study examined 27,747 individuals (22,800 females and 4,947 males) of all ages diagnosed with urinary UTIs caused by *E. coli* at a clinical microbiology laboratory, reflecting nearly two-thirds of Iceland's population. Alarmingly, the percentage of samples containing extended-spectrum beta-lactamase (ESBL)-producing *E. coli* surged from 2.6% in 2012 to 7.6% in 2021 ($p < 0.001$). This study identified 1,207 individuals (4.4%) with ESBL-positive strains, including 905 women (4.0%) and 302 men (6.1%). Key risk factors for these infections include male sex, older age, type of institution (such as hospitals or nursing homes), hospital-associated UTIs, a Charlson comorbidity index score of 3 or greater, and a history of cystitis or hospitalization in the previous year. Notably, recent prescriptions for certain antibiotics or proton pump inhibitors (PPIs) also played a role (odds ratio [OR] 1.51). Ciprofloxacin particularly emerged as a significant risk factor for ESBL-producing *E. coli* infections, with an odds ratio of 2.45. These findings underscore the pressing need for awareness and proactive measures in managing UTIs to control the rise of drug-resistant infections.[21].

4.0 CONCLUSION

The antibiotic susceptibility profile reveals alarming trends, with shockingly high resistance rates to widely used antibiotics like ampicillin and ciprofloxacin. Thankfully, sensitivity to polymyxin B and carbapenems remains robust, but we must not ignore the rising threat posed by multidrug-resistant strains. This pressing situation demands immediate action, revising empirical treatment guidelines and implementing strict antibiotic stewardship practices are essential to prevent treatment failures. Our findings highlight a critical need for routine monitoring of antibiotic susceptibility patterns to empower effective clinical decision-making. With resistance rates so high, it is vital for clinicians to factor in local resistance data when choosing empirical therapies for UTIs. Moreover, we must emphasize the judicious use of antibiotics to safeguard their efficacy and combat the escalating crisis of antibiotic resistance. Together, we can make a difference in preserving the effectiveness of these crucial medications.

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CONFLICT OF INTEREST

All the authors declare that, they have no conflict of interest.

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