



## Prevalence of ESBL Producing and Carbapenem-resistant E. Coli in Urinary Tract Infection from Tertiary Care Hospital

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### Declaration

#### Authors' Contribution

All authors equally contributed to the study and approved the final manuscript

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### ABSTRACT

**Background:** Urinary tract infections are the most common kind of nosocomial infection. E. coli is the leading cause of UTIs and show resistance to carbapenem. **Objective:** The aim of this study was to determine the Prevalence of ESBL Producing and carbapenem-resistant E. coli in urinary tract infection from tertiary care hospital. **Material and Method:** The present cross sectional study was conducted at the d Institute of Kidney Diseases Hayatabad Peshawar after taking permission from the ethical board of the institute. A total of 324 mid-stream urine samples were collected in sterile, closed containers from patients presenting with UTI complications. Culturing was done on standard laboratory techniques. Gram staining, microscopy, and biochemical testing were used to identify and confirm the presence of Escherichia coli. The Kirby-Bauer disc diffusion technique was used on Mueller-Hinton agar to determine antibiotic susceptibility. For screening purposes of ESBL generation, E. coli isolates were tested for resistance to cephalosporin and/or aztreonam. A crucial hole or shoulder zone formed by the combination of amoxicillin, clavulanic acid, and one of the surrounding cephalosporin or aztreonam was identified as an ESBL producer. E. coli strains resistant to imipenem, meropenem, or both were designated carbapenem-resistant. Data was analyzed using SPSS version 21 and presented in the tables and figures. **Results:** A total of 324 urine samples were processed out of which 260 (80.2%) showed bacterial growth. UTIs were most common in female 140(53.8%) as compared to male 120(46.1%) . Out of the total culture positive, the most prevalent uropathogen was E.coli 150(57.6%) followed by Klebsiella 60(23%, Proteus 26(10%) and Pseudomonas species 24(9.2%) correspondingly The E.coli isolates were sensitive to Meropenem 95%, Imipenem 94%, amikacin 89% , Fosfomycine 88% and Nitrofurantoin 72% while exhibited the highest resistance to ampicillin (88%), followed by ofloxacin 70%, ciprofloxacin 65%, ceftriaxone 65%, and co-trimoxazole 64% . Out of the total 150 E.coli bacteria 100(66.6%) were extended spectrum  $\beta$  - lactamases producers and 50(33.3%) were not producers. Among ESBL isolates 10(6.6%) were carbapenem resistant and 4(2.6%) were carbapenem-resistant but not ESBL producers. **Conclusion:** The current study reported high prevalence of ESBL-producing E. coli, but carbapenem-resistant E. coli was less prevalent in urinary tract infections.

### INTRODUCTION

One of the major health issue in the world is Antimicrobial resistance (AMR), resulting in seven thousand mortalities per year.<sup>1</sup> The use of antibiotics in a variety of industries, including agriculture and the food sector, has led to the spread of antibiotic resistance genes (ARGs) in human microbes to soil occupants, posing a serious risk to public health and posing difficulties for medical professionals.<sup>2</sup> Plasmid-mediated ESBLs are a complicated category of more common and rapidly evolving enzymes.<sup>3</sup> Except for

carbapenems and antibiotics containing ESBL inhibitors, these enzymes hydrolyze a broad range of 3 and 4 generation cephalosporin and other  $\beta$ -lactam antibiotics.<sup>4</sup> According to reports, 62.9–100% of *E. coli* strains that produce ESBLs are found in Asia.<sup>5-6</sup> Novel ARGs that encode resistance to carbapenems have been discovered thus limiting the treatment options. Super bugs are microorganisms that possess resistance genes. The Enterobacteriaceae (CRE) are posing a challenge to the empirical hypothesis.<sup>1</sup> The frequency of CRE ranges from

4.6 to 44.4% in developing countries.<sup>7-8</sup> Urinary tract infections (UTIs) are mostly caused by a lack of anatomical resources.<sup>9</sup> This is due to the fact that UTI therapy in nations with limited resources is typically based on clinical trials and susceptibility testing. Furthermore, a lack of education and poverty are two variables for growing trends of unsuitable antibiotic dose and incomplete course of treatment, which contribute to an increase in the number of prescriptions for antibiotics.<sup>10</sup> The most common bacteria belong to enterobacteriaceae are *Escherichia coli*, *Klebsiella*, *Enterobacter*, *Citrobacter*, and *Proteus*.<sup>11</sup> *Escherichia coli* is the most prevalent uropathogen in both hospitals and the community.<sup>12</sup> Urinary tract infections are the most prevalent bacterial infections globally, affecting around 150 million individuals yearly.<sup>13</sup> Contribute significantly to community development and healing systems.<sup>14</sup> To improve the efficacy of new antibiotics, monitoring extremely resistant organisms is the best way. Therefore, the current study was carried out to determine the Prevalence of ESBLs Producing and carbapenem-resistant *E. coli* in urinary tract infection from tertiary care hospital.

## MATERIAL AND METHOD

The present cross sectional study was conducted at the Institute of Kidney Diseases Hayatabad Peshawar from November 2024 to April 2025 after taking permission from the ethical board of the institute. A total of 324 mid-stream urine samples were collected in sterile, closed containers from patients presenting with UTI complications. The samples were immediately brought to the microbiology laboratory for further evaluation. Culturing was done on MacConkey agar via standard laboratory techniques. Incubation was done at 37°C under aerobic conditions for a period of 24 to 48 hours. Bacterial growth was assessed using the Kass criteria, with colony-forming units (CFU) of 10<sup>5</sup> or more per milliliter of urine indicating infection.<sup>15</sup> Gram staining, microscopy, and biochemical testing were used to identify and confirm the presence of *Escherichia coli*. The Kirby-Bauer disc diffusion technique was used on Mueller-Hinton agar to determine antibiotic susceptibility. The inhibition zones were evaluated after 48 hours of incubation at 37°C and interpreted using the 2019 CLSI (Clinical and Laboratory Standards Institute) criteria. Antibiotics such as Amikacin (AKN), Ceftazidime (CAZ), Ampicillin (AMP), Ciprofloxacin (CIP), Ceftriaxone (CRO), Fosfomycin (FOS), Ofloxacin (OXF), Cefixime (CFM), Gentamicin (CN), Cotrimaxazole (SXT), Nitrofurantoin (F), Cefepime (Fep), Aztreonam (ATM), Meropenam (Mem), Fosfomycin (FOS), and others were tested. Bacterial strains were classified into three groups: resistant (R), sensitive (S), or intermediate (I) based on their inhibitory zone diameter measurements. *Escherichia coli* strain TCC 25922 used as a quality control strain for regular AST testing. For screening purposes of ESBL generation, *E. coli* isolates were tested for resistance to cephalosporin and/or aztreonam. The double disc synergy test (DDST) validated ESBL generation. A crucial hole or shoulder zone formed by the combination of amoxicillin, clavulanic acid, and one of the surrounding cephalosporin or aztreonam was identified as an ESBL producer. *E. coli* strains resistant to

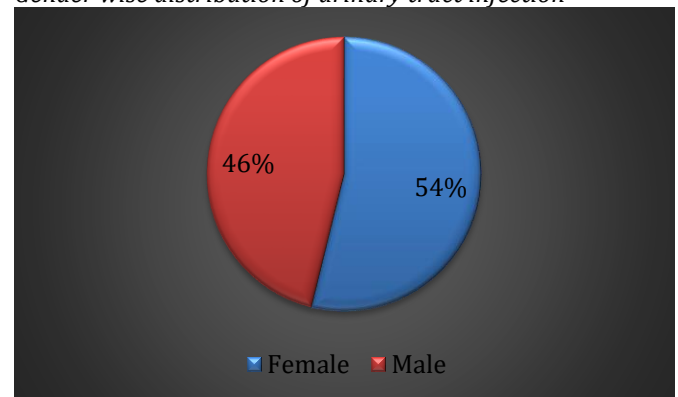
imipenem, meropenem, or both were designated carbapenem-resistant. The isolates have been confirmed using minimum inhibitory concentrations (MICs) with Etest of imipenem and meropenem. Data was analyzed using SPSS version 21 and presented in the tables and figures.

## RESULTS

A total of 324 urine samples were processed out of which 260 (80.2%) showed bacterial growth. UTIs were most common in female 140(53.8%) as compared to male 120(46.1%) as presented in **figure 1**. The mean age of the study population was 37.64±14.02 years. The age groups of 21–40 years had the highest prevalence of UTIs, 200 (76%), followed by those aged ≥41–60 years, 60 (23 %). Out of the total culture positive, the most prevalent uropathogen was *E.coli* 150(57.6%) followed by *Klebsiella* 60(23%, *Proteus* 26(10%) and *Pseudomonas* species 24(9.2%) correspondingly as presented in **table 1**. The *E.coli* isolates were sensitive to Meropenem 95%, Imepenem 94%, amikacin 89%, Fosfomycine 88% and Nitrofurantoin 72% while exhibited the highest resistance to ampicillin (88%), followed by ofloxacin 70%, ciprofloxacin 65%, ceftriaxone 65%, and co-trimoxazole 64% as presented in **table 2**. Out of the total 150 *E.coli* bacteria 100(66.6%) were extended spectrum β-lactamases producers and 50(33.3%) were not producers. Among ESBL isolates 10(6.6%) were carbapenem resistant and 4(2.6%) were carbapenem-resistant but not ESBL producers as presented in **figure 2**.

**Figure 1**

Gender wise distribution of urinary tract infection



**Table 1**

uropathogen distribution in positive culture collected from the urine samples of the study population

Bacteria	Percentage
<i>E.coli</i>	57.6%
<i>Klebsiella</i>	23%
<i>Proteus</i>	10%
<i>Pseudomonas</i> species	9.2%

**Table 2**

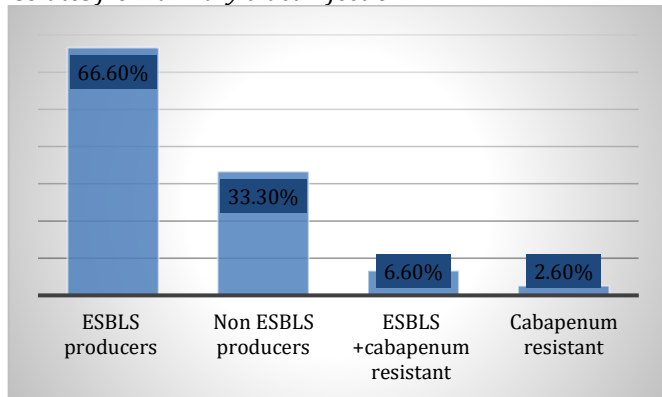
Antibiogram of *E.coli* isolates N=150

Antibiotic	Sensitive	Intermediate	Resistance
Meropenem	95%	Nil	5%
Imepenem	94%	Nil	6%
Amikacin	89%	1%	10
Nitrofurantoin	72%	2%	26%
Ampicillin	10%	2%	88%
Ofloxacin	15%	10%	75
Ciprofloxacin	20%	15%	65%

Ceftriaxone	20%	15%	65%
Co-trimoxazole	30%	6%	64
Cepifime	55%	5%	40%
Co-Amoxi clave	60%	10%	30%
Aztreonam	48%	2%	50%
Gentamicin	52%	Nil	48%
Fosfomycine	88%	2%	10%

## Frequency 2

of ESBLs producing and carbapenem-resistant *E. coli* isolates from urinary tract infection



## DISCUSSION

Urinary tract pathogens cause around 150 million infections globally each year. UTIs are the most common kind of nosocomial infection, accounting for 35%. *E. coli* is the leading cause of UTIs, particularly in less severe cases.<sup>17</sup> This is the most prevalent condition following respiratory infections. The kidneys, ureters, bladder, and urethra are together known as the urinary tract. *Escherichia coli* is the most common bacterium responsible for UTIs. Every year, around 35% of healthy women get UTI symptoms, whereas 5% experience painful urination (dysuria). Women have a higher frequency of UTIs than males.<sup>18</sup> Carbapenemase synthesis in Enterobacteriaceae has a significant impact on human health worldwide. Carbapenemases can degrade  $\beta$ -lactam antibiotics, including carbapenems.<sup>19</sup> The current study was carried out to determine the Prevalence of ESBLs Producing and carbapenem-resistant *E. coli* in urinary tract infection from tertiary care hospital. In our study UTIs were most common in female 53.8%, as compared to male 46.1%. Our findings are similar to the study conducted by Alanazi et al, in Saudi Arabia they reported high prevalence of UTIs in women of all ages as compared to males.<sup>20</sup> Enterobacteriaceae, particularly *E. coli*, are the

predominant uropathogens among both Gram-positive and Gram-negative bacteria.<sup>12</sup> Globally, antibiotic-resistant uropathogens are on the rise.<sup>20</sup> Increasing the incidence of ESBLs generating *E. coli* can have major clinical effects.<sup>21</sup> The present study found a greater incidence of *E. coli* ESBL producers (66.6%), which reduces the practical use of cephalosporin in UTI. The incidence of ESBL producers varies globally and depends on variables such as environmental factors, antibiotic usage, and infection control measures. Poor infection control can lead to the spread of ESBLs, which are plasmid-mediated. The frequency of this bacterium has previously been observed to range from 40% to 84.2%.<sup>6-20</sup> Carbapenem-resistant Enterobacteriaceae infection rates are low in the population. A research found 13.7% of carbapenem-resistant *E. coli* in Pakistan, which differs from current findings due to the inclusion of indoor pathogens and different locations.<sup>22</sup> In our study *E. coli* exhibited the highest resistance to ampicillin and ceftriaxone. Aminoglycosides and fluoroquinolones are routinely recommended for UTIs. However, *E. coli* resistance to these medicines is similar to that of  $\beta$ -lactam antibiotics. *E. coli* exhibited the highest resistance to ofloxacin and ciprofloxacin in the current study. However, resistance to amikacin was lower than gentamicin. A previous research revealed similar results.<sup>23</sup> Kalal et al. (2022) studied the antibiotic susceptibility of *E. coli* isolates from infections of the urinary tract in a tertiary care hospital in India. The study found substantial resistance rates to popular antibiotics including ceftriaxone & ciprofloxacin which aligns with our findings. However, they found slightly low resistance to ceftazidime, indicating regional differences in antimicrobial resistance trends.<sup>24</sup> This study highlights the importance of strong antimicrobial stewardship programs and ongoing resistance surveillance for effective treatment regimens. This work adds to the growing body of evidence supporting specific approaches to address antibiotic resistance by emphasizing careful application of antibiotics and adjusting empirical therapy depending on local susceptibility.

## CONCLUSION

The current study reported high prevalence of ESBL-producing *E. coli*, but carbapenem-resistant *E. coli* was less prevalent in urinary tract infections.

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