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Burden of Carbapenem Resistant Urinary Isolates of E. coli and Klebsiella at Tertiary Care Hospital

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ABSTRACT

Background: Urinary tract infections are a significant cause of morbidity worldwide, with *Escherichia coli* and *Klebsiella* spp. Being the predominant causative agents. The emergence of carbapenem-resistant Enterobacteriaceae (CRE) poses a grave public health threat due to limited treatment options.

Methods: A cross-sectional study was conducted from October 2023 to September 2024 in the Department of Microbiology at Sharda University. Urine samples from suspected UTI patients were processed using standard microbiological techniques. Isolates were identified using biochemical methods, and antimicrobial susceptibility testing was performed using the Kirby-Bauer disc diffusion method as per CLSI guidelines.

Results: In the present study, out of 8154 urine samples, 1166 were culture positive, among which *E. coli* 712 (61.06%) and *Klebsiella* spp. 128 (10.97%) were the predominant isolates. Of these, 190 (26.68%) of E. coli and 54 (42.18%) of *Klebsiella* species exhibited resistance to carbapenems.

Conclusion: The increasing burden of carbapenem resistance in urinary pathogens underscores the need for antimicrobial stewardship, rapid diagnostic tools, and infection control practices in healthcare settings.

Keywords: *Carbapenem, Resistant, Urinary Isolates, E.coli, Klebsiella, UTI*

1. INTRODUCTION

Urinary tract infections (UTIs) rank as some of the most prevalent bacterial illnesses in humans, second only to respiratory infections [1]. They involve any region of the urinary system—kidneys, ureters, bladder, or urethra—and it is widespread across all age categories, especially common in older adults due to weakened immunity and reduced physical activity. Globally, UTIs contribute to about 150–200 million cases annually, with an estimated 40% of women and 12% of men having at least one symptomatic episode during their lives [2]. The frequency of UTIs rises as individuals grow older. Fluctuations in hormones, structural abnormalities in the urinary tract, weakened immune defences, loss of bladder control, physical limitations, poor nutrition, and coexisting diseases are key risk factors for UTIs among the aged [3].

UTIs are generally categorized as either uncomplicated, where no structural or neurological urinary tract issues exist, or complicated, where underlying health problems predispose individuals to persistent or recurrent infections. The bacterial origin of UTIs is well recognized, with *Escherichia coli* identified as the leading causative organism in 50–80% of instances [4].

There is a growing incidence of multidrug-resistant urinary pathogens, such as carbapenemase-producing Enterobacterales and Acinetobacter species, especially in hospital-acquired complicated UTIs [5]. International protocols suggest several antimicrobials for UTI therapy, such as nitrofurantoin, trimethoprim-sulfamethoxazole, fosfomycin, pivmecillinam, fluoroquinolones, and beta-lactam antibiotics.

Nonetheless, excessive and inappropriate antibiotic usage has resulted in resistance among UTI pathogens, particularly ESBL-producing Gram-negative bacteria, which are resistant to most drugs except carbapenems, and these resistant strains are becoming more prevalent [6]. The primary mechanism behind carbapenem resistance is the synthesis of carbapenemase enzymes, which break down carbapenems and other beta-lactam antibiotics [7].

This study aims to assess the prevalence of carbapenem-resistant *E.coli* and *Klebsiella* urinary isolates in our institution.

2. MATERIAL AND METHODS

A cross-sectional study was performed in the Central Laboratory at the School of Medical Sciences and Research (SMS&R), Sharda Hospital, Greater Noida, over a period of 12 months from October 2023 to September 2024. The research aimed to assess the prevalence and burden of carbapenem-resistant urinary isolates of Escherichia coli and Klebsiella species. The study protocol was meticulously designed and received approval from the Institutional Ethics Committee, ensuring compliance with ethical research standards.

Inclusion criteria: All urine samples received for culture and sensitivity tests in the bacteriology section.

Department of Microbiology, Central Laboratory.

Exclusion criteria: Duplicate samples

PROCEDURE:

All urine samples received were processed for culture and antimicrobial sensitivity according to the standard procedures.

Sample collection – Microscopic examination - Inoculation – Identification – Colony morphology (Gram stain)- Biochemical test { catalase test , cytochrome oxidase test , motility test [Hanging drop] , Indole production , Nitrate reduction test , Methyl red, Voges-proskauer test, Citrate utilization, Urease hydrolysis test , Triple sugar iron agar , Semi-solid agar [mannitol salt agar] , Oxidative -fermentative test , Decarboxylases test } - Antimicrobial Susceptibility Testing (Kirby Bauer method).

TABLE 1: Demographic characteristics of patients with the study isolates

Demographics	
Total Samples (n)	8154
Gender	
Male	3448 (42.28%)
Female	4706 (57.71%)
Male: Female	0.7:1
Median Age (years)	34
Inpatient Department (IPD)	5017(61.52%)
Outpatient Department (OPD)	3137(38.47%)

3. RESULTS

A total of 8154 urine samples were received for culture and sensitivity, out of which 6405 showed No Growth, 583 showed Mixed Growth, and 1166 samples showed growth. Out of their 1166 samples, only 840 samples showed growth of *E.coli* and *Klebsiella*.

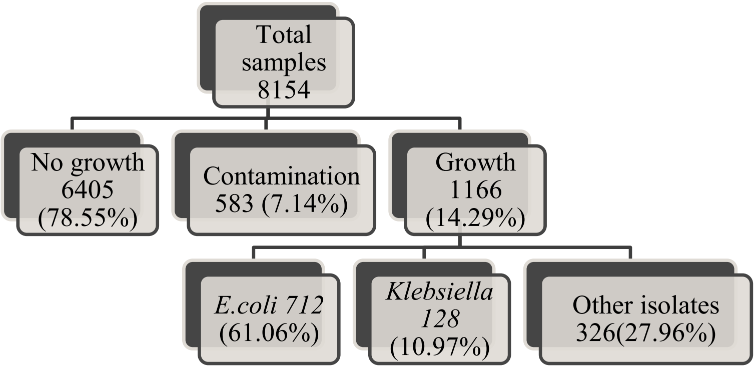

Figure 1: Flow chart depicting the result of the culture of urine samples

TABLE 2: Carbapenem resistance in *E.coli* and *Klebsiella* urinary isolates

Organism	Total isolates (n=1166)	Carbapenem resistance [n (%)]
E.coli	712 (61.06%)	190 (26.68%)
Klebsiella	128 (10.97%)	54 (42.18%)

TABLE 3: Age-wise distribution of carbapenem-resistant *E.coli*&*Klebsiella* isolates

AGE	*E.coli* (190)		*Klebsiella* (54)	
	MALE (%)	FEMALE (%)	MALE (%)	FEMALE (%)
Below 10	6(3.15%)	10(5.26%)	1(1.85%)	2(3.70%)
11-20	9(4.73%)	16(8.42%)	2(2.70%)	1(1.85%)
21-30	12(6.31%)	25(13.15%)	6(11.11%)	4(7.40%)
31-40	8(4.21%)	13(6.84%)	4(7.40%)	4(7.40%)
Above 40	31(16.31%)	60(31.57%)	16(29.62%)	14(25.92%)

Predominance of CRE was found in the age group above 40 (49.60%), followed by 21-30 years (19.26%), 31-40 years (11.88%), and the least resistance was found in below 10 years (7.7%)

TABLE 4: Antibiotic susceptibility pattern of *E.coli*&*Klebsiella* isolates

	E.coli		*Klebsiella*	
Antibiotics	**Sensitive(%)**	**Resistant(%)**	**Sensitive (%)**	**Resistant (%)**
Gentamicin	66.29	33.71	57.81	42.19
Amoxyclav	35.25	64.75	34.37	65.63
Cefepime	39.04	60.96	42.19	57.69
Cefotaxime	20.93	79.07	38.28	61.72

Cefuroxime	19.52	8.48	34.38	65.63
Imipenem	73.03	26.97	57.03	42.97
Meropenem	73.59	26.41	57.03	42.97
Amikacin	55.76	44.24	45.31	54.69
Ciprofloxacin	24.86	75.14	37.50	65.63
Cotrimoxazole	39.18	60.82	51.56	48.44
Aztreonam	39.75	60.25	41.41	58.59
Nitrofurantoin	90.03	9.97	55.47	44.53
Fosfomycin	90.45	9.55	72.66	27.34

The disk diffusion method determined the antibiotic susceptibility profile of all the bacterial isolates (n=1166) as per CLSI guidelines (2024).For *E. coli*, we found it was highly sensitive to Fosfomycin (90.44%) and Nitrofurantoin (90.02%). It was also quite sensitive to Carbapenems (imipenem & meropenem, 73.31%), Gentamicin (66.29%), and Amikacin (55.75%). However, Aztreonam, Amoxiclav, and cephalosporins were the least effective antibiotics against *E. coli*.

Similarly, *Klebsiella* showed high sensitivity to Fosfomycin (72.66%) and Nitrofurantoin (55.47%). Carbapenems (imipenem & meropenem, 57.81%), Gentamicin (57.81%), and Cotrimoxazole (51.56%) were also effective. Like *E. coli*, Aztreonam, Amikacin, Amoxiclav, and cephalosporins were the least effective against *Klebsiella.*

The AST patterns of carbapenem-resistant E. coli and Klebsiella are shown in Tables 5 and 6, respectively.

Fosfomycin demonstrated the maximum sensitivity to both organisms, followed by Nitrofurantoin. The sensitivity of both these drugs was greater for *E. coli* than for *Klebsiella*.

TABLE 5:- Antibiotic susceptibility pattern of carbapenem-resistant *E.coli* (n =190)

Antibiotics	Sensitive	%
Gentamicin	81	42.63
Amoxiclav	3	1.57
Cefepime	7	3.68
Cefotaxime	2	1.05
Cefuroxime	4	2.10
Amikacin	66	34.73
Ciprofloxacin	6	3.15
Cotrimoxazole	23	12.10
Aztreonam	11	5.78
Nitrofurantoin	165	86.84
Fosfomycin	173	91.05

The carbapenem-resistant isolates of *E.coli* exhibited high sensitivity to Fosfomycin and Nitrofurantoin, followed by Aminoglycosides {Gentamicin & amikacin}. Conversely, the least sensitive drugs were Cotrimoxazole, Aztreonam, Amoxiclav & cephalosporins.

TABLE 6: Antibiotic susceptibility pattern of carbapenem-resistant *Klebsiella* (n = 54)

Antibiotics	Sensitive	%
Gentamicin	9	16.66
Amoxiclav	0	0
Cefepime	3	5.55
Cefotaxime	2	3.7
Cefuroxime	1	1.85
Amikacin	4	7.4
Ciprofloxacin	0	0
Cotrimoxazole	8	14.81
Aztreonam	2	3.7
Nitrofurantoin	13	24.07

The carbapenem-resistant isolates of *Klebsiella* exhibited high sensitivity to Nitrofurantoin, Gentamicin& Cotrimoxazole. Conversely, the least sensitive drugs were Amikacin, Aztreonam, Amoxiclav & cephalosporins.

TABLE 7: Distribution of MDR *E.coli* and *Klebsiella*

Organism	Total isolates (n=1166)	MDR(%)
E.coli	712 (61.06%)	73(10.25)
Klebsiella	128 (10.97%)	45(35.16)

The study revolves around pathogenic bacteria, which are characterized as MDR. MDR organisms are resistant to more than three classes of antimicrobial agents.

4. DISCUSSION

Urinary tract infection (UTI) is one of the most common infectious illnesses worldwide, affecting nearly 10% of the population during their lifetime. Both Gram-positive and Gram-negative bacteria are responsible for causing UTIs. Various anatomical and physiological changes increase susceptibility. UTIs remain a major public health issue, with approximately 150 million cases annually and a global economic burden exceeding $6 billion[8]. Urinary tract infections (UTIs) present significant challenges due to their high incidence and often complex diagnosis. UTIs must be distinguished from conditions with overlapping symptoms, such as pelvic inflammatory disease in females and benign prostatic hyperplasia in males[9].

A combination of clinical assessment and laboratory tests aids in the prompt and precise identification of urinary tract infections. While urine culture remains the definitive standard for diagnosis and guiding targeted treatment, it is labor-intensive, costly, and requires specialized facilities, prompting some clinicians to use urinalysis, which is less specific but quick and economical. Overdiagnosis is frequent, leading to unnecessary antibiotic use and escalating antimicrobial resistance. Carbapenem-resistant organisms in urine pose a significant threat, particularly in healthcare settings of developing nations, highlighting the need for ongoing surveillance to contain the spread of CRE[10].

Our investigation aimed to assess antimicrobial resistance patterns in a tertiary care setting. Out of 8,154 urine specimens analyzed, 1166 (14.29%) exhibited significant bacteriuria, a lower prevalence compared to the 48.57% reported by Pratiksha et al. [11] in their cohort. In our study, females comprised 57.71% of culture-positive cases, while males accounted for 42.28%, which aligns with the findings of Mustafa et al.[12]. This higher incidence among females is consistent with existing knowledge, likely attributable to anatomical and physiological factors such as a shorter urethra and its proximity to the anus, facilitating ascending infections.

In terms of age distribution, our study found the highest incidence of *Escherichia coli* and *Klebsiella* infections among individuals over 40 years, whereas M. Suwaiba et al. reported peak prevalence in the 31–40 age group. Despite this variation, both studies highlight adulthood as a period of increased vulnerability to UTIs[13]. The elevated rates in older adults in our cohort may be associated with factors such as comorbidities, post-menopausal changes, or prostatic enlargement, all of which can promote urinary stasis and subsequent infection.

E. coli was the predominant uropathogen in our study, comprising 61.06% of isolates, followed by *Klebsiella* species at 10.97%. This is consistent with findings from other studies, such as Adesola et al.[14] where E. coli was also the leading isolate, despite differences in exact percentages. Such variations in prevalence may be influenced by regional factors, antibiotic prescribing habits, hygiene standards, and accessibility to healthcare services

Carbapenem resistance remains a significant issue, with 29.05% of isolates in our study exhibiting resistance, closely matching rates reported by Namita Jaggi et al. and Pratiksha et al. [15]. This consistency underscores the widespread emergence of carbapenem-resistant uropathogens and highlights the urgent need for judicious antibiotic use and robust antimicrobial stewardship.

*E.coli*isolates displayed high resistance to Cefuroxime (80.47%), Cefotaxime (79.07%), Ciprofloxacin (75.14%), Amoxiclav (64.74%), Cotrimoxazole and Cefepime (60.95%), and Aztreonam (60.25%), but lower resistance to Amikacin (44.24%), Gentamicin (33.70%), Carbapenem (26.68%), Nitrofurantoin (9.97%), and Fosfomycin (9.55%). These patterns are consistent with previous research, such as Mays B. Jalil et al.[16].

Klebsiella species showed high resistance to Cefuroxime and Amoxiclav (65.63%), Ciprofloxacin (62.50%), Cefotaxime (61.72%), Aztreonam (58.59%), Cefepime (57.81%), and Amikacin (54.69%), with moderate resistance to Cotrimoxazole (48.4%), Nitrofurantoin (44.53%), Gentamicin and Carbapenem (42.19%). These findings align with other regional and international studies, though resistance rates vary, likely due to differences in study populations, geographic factors, and antibiotic usage patterns[17]. Indiscriminate antibiotic use without medical supervision remains a key driver of rising resistance[18].

Multiple studies have identified surgical interventions, dialysis, catheterization, mechanical ventilation, poor functional status, residence in long-term care facilities, recent healthcare exposure, hospitalization, and prior use of broad-spectrum antibiotics as risk factors for CRE colonization or infection. In our study, all patients with carbapenem-resistant urinary tract infections (CR-UTIs) had at least one such risk factor. The prevalence of CR-UTI among Gram-negative UTIs was 29.04%, consistent with findings by Eshwarappa M, Gangula RS, and the ICMR Annual Surveillance Report 2022[19].

Carbapenem-resistant E. coli isolates exhibited the highest susceptibility to Fosfomycin (91.05%) and Nitrofurantoin (86.84%), with markedly lower sensitivity to other agents. This pattern mirrors results from Ibrahim et al. Similarly, carbapenem-resistant Klebsiella isolates were most sensitive to Fosfomycin (53.70%), with limited susceptibility to other antibiotics, again consistent with previous reports[20].

In this study, multidrug-resistant (MDR) E. coli accounted for 10.25% of isolates, and MDR Klebsiella for 35.16%. This contrasts with Suhartono et al., who reported a higher proportion of MDR E. coli compared to Klebsiella, whereas our findings indicate greater MDR prevalence in *Klebsiella*[21].

Carbapenem-resistant urinary tract infections (CR-UTIs) are increasingly common, challenging to manage, and associated with significant morbidity and mortality, with CRE isolation linked to 29%–52% of all-cause hospital deaths. Assessing outcomes is complicated by the retrospective nature of most studies and difficulties in differentiating infection from colonization. Effective containment of carbapenem-resistant organisms requires comprehensive strategies, including robust infection control, active surveillance, antimicrobial stewardship, and the development of novel therapeutic options.

The high prevalence of multidrug-resistant *Klebsiella* and *E. coli* strains, particularly those resistant due to carbapenemase production, poses a significant challenge for treatment and patient outcomes. Accurate detection of carbapenem resistance is crucial, and this study discovered that both the mCIM and MHT are effective diagnostic tools[22,23].

5. CONCLUSION

Urinary tract infections (UTIs) are among the most frequently diagnosed infections in both outpatient and inpatient settings, contributing to considerable morbidity and occasional mortality. This study aimed to assess the prevalence of carbapenem-resistant urinary isolates of Escherichia coli and Klebsiella in a tertiary care hospital over 12 months at the Department of Microbiology, School of Medical Sciences & Research, Sharda University.

Among 712 E. coli isolates, 26.6% were carbapenem-resistant, while 42.1% of 128 *Klebsiella* isolates exhibited carbapenem resistance. UTIs were more common in females across all age groups, with the highest incidence in the 21–30 year age group. *E. coli* was the predominant isolate (61.06%) but showed lower carbapenem resistance (26.68%) compared to *Klebsiella* (10.97% of isolates, 42.18% resistance).

Of the 244 carbapenem-resistant isolates, multidrug resistance was significantly higher in *Klebsiella* (35.16%) than in *E. coli* (10.25%).

These findings underscore the urgent need for stringent infection control measures and ongoing surveillance to address the rising burden of carbapenem-resistant organisms. Variability in resistance patterns across regions and over time highlights the necessity for further multicenter studies to inform effective interventions.

6. DECLARATIONS

Conflicts of interest: There is no conflict of interest associated with this study

Consent to participate: There is consent to participate.

Consent for publication: There is consent for the publication of this paper.

Authors' contributions: Each author listed above contributed significantly to carrying out the research

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