

Evolving trends in uropathogens and antimicrobial resistance: Five-year data from a tertiary care hospital

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Abstract

Background: Urinary tract infection (UTI) is one of the most common bacterial infections, with significant implications for antimicrobial resistance (AMR) management. Empiric treatment relies on current knowledge of local uropathogen prevalence and antimicrobial resistance pattern, which vary by region and over time. This study aimed to determine the distribution of bacterial pathogens causing UTIs and their antimicrobial resistance pattern over a five-year period (2019–2023) at a tertiary care hospital in coastal Karnataka. The findings are intended to support updates to the hospital's antibiotic policy and aid in the effective management of UTI cases.

Methods: A retrospective analysis was conducted on 1279 urine culture isolates processed between January 2019 and December 2023. Uropathogens were identified using standard microbiological techniques, and antimicrobial susceptibility testing was performed according to Clinical and Laboratory Standards Institute (CLSI) guidelines. Year-wise resistance trends were analyzed statistically.

Results: Gram-negative bacilli were the predominant uropathogens, with *Escherichia coli* being the most frequent isolate, followed by *Klebsiella pneumoniae*. Other Gram-negative and Gram-positive isolates included *Citrobacter koseri*, *Proteus mirabilis*, *Pseudomonas spp.*, *Acinetobacter spp.*, *Morganella morganii*, *Enterococcus spp.*, MSSA, and MRSA. Resistance to cephalosporins, piperacillin-tazobactam, and carbapenems showed an increasing trend over the five years. However, a significant reduction in resistance to oral antibiotics such as cotrimoxazole and nitrofurantoin was observed in 2023 compared to prior years.

Conclusion: The persistence of Gram-negative bacilli, particularly *E. coli*, as predominant uropathogens highlights their clinical significance. The observed decline in resistance to certain oral antibiotics offers a potential opportunity for their empiric use in uncomplicated UTIs. Continuous surveillance and antibiotic stewardship are essential to mitigate further escalation of antimicrobial resistance.

Keywords: urinary tract infection; antimicrobial resistance; uropathogens; trend analysis; empiric therapy; cotrimoxazole; nitrofurantoin

Introduction

Urinary tract infection (UTI) is one of the most common bacterial infections requiring medical attention, with its global burden continuing to rise. The prevalence of UTI varies based on gender, age, and geographic region [1]. A wide range of bacteria can cause UTIs, among which *Escherichia coli* (uropathogenic *E. coli*) is the leading causative agent of both uncomplicated and complicated UTIs, followed by other pathogens such as *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Enterococcus faecalis* [2].

Knowledge of prevalent uropathogens and their antimicrobial susceptibility patterns is essential for

guiding empiric therapy. However, the antibiotic susceptibility profiles of uropathogens have been

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changing over time, with an increasing trend of antimicrobial resistance (AMR) observed in various studies [3, 4]. Recent reports indicate an alarming rise in multi-drug resistant (MDR) uropathogens, particularly *E. coli* and *Klebsiella* spp., exhibiting high levels of resistance to cephalosporins and other commonly used antibiotics [5-7].

Treatment challenges intensify when uropathogens develop resistance to all tested antibiotics, leading to treatment failures. Reports of pan-drug resistant (PDR) *E. coli* strains further complicate the management of UTIs [8, 9]. In such scenarios, conventional antibiotic therapy becomes ineffective, necessitating the exploration of alternative treatment strategies. Emerging approaches, including antibiotic-sparing strategies and novel therapies such as plant-based therapeutics, are being investigated to target the survival mechanisms of drug-resistant uropathogens [10, 11].

Given these concerns, it is imperative to monitor the trends of antimicrobial resistance among uropathogens at regular intervals within specific geographical locations. Continuous surveillance enables healthcare providers to detect shifts in resistance patterns and adapt treatment protocols accordingly. Empiric treatment of UTIs is often guided by a hospital's antibiotic policy, which in turn relies on up-to-date data on local AMR trends. While similar studies have been conducted in other regions, there is a scarcity of recent data from this geographical area, and no prior studies have been reported from our institution on this topic.

Periodic assessment of prevalent uropathogens and their antimicrobial susceptibility profiles is essential for updating institutional antibiotic policies and ensuring effective management of UTI cases.

The present study was undertaken to analyze the distribution of bacterial pathogens causing UTIs and their antimicrobial resistance trends over the past five years in a tertiary care hospital in coastal Karnataka. This trend analysis will aid in refining empiric therapy guidelines and contribute to antimicrobial stewardship efforts.

Materials and methods

This retrospective descriptive study was conducted at the Kanachur Institute of Medical Sciences, Mangaluru, Karnataka, and included urine samples received in the Department of Microbiology from January 2019 to December 2023. The study was time-bound, and the sample size comprised all urine samples processed for culture and antimicrobial susceptibility testing during the specified period, adhering to defined inclusion

and exclusion criteria. This study got approval from Institutional Ethics Committee. A total of 1,279 samples meeting the selection criteria were included, and data regarding urinary tract infections (UTIs), pathogen isolation, and antimicrobial resistance patterns were retrieved from the microbiology diagnostic laboratory records.

Mid-stream urine samples received for culture from patients of all age groups were included if the patients presented with at least two of the following clinical symptoms: dysuria, urinary frequency, urgency, or suprapubic tenderness. Additionally, only samples yielding significant bacteriuria, defined as the growth of a single bacterial species with $\geq 10^5$ colony-forming units (CFU) per milliliter of urine as per Kass's semi-quantitative method along with pyuria, were considered for analysis. Samples were excluded if they exhibited bacterial growth of $< 10^5$ CFU/mL, showed mixed growth of two or more bacterial isolates, or if there was no growth on culture.

All urine samples were processed within 30 minutes of collection. Wet mount microscopy was performed to detect the presence of pus cells and bacteria. Semi-quantitative urine cultures were performed using a calibrated loop (0.001 mL) on Blood Agar and MacConkey Agar plates. The inoculated plates were incubated aerobically at 37°C for 18 to 20 hours, after which colony counts were determined. A colony count of $\geq 10^5$ CFU/mL was considered significant for bacteriuria. Bacterial isolates were identified based on colony morphology, Gram staining, and conventional biochemical tests as described in standard microbiological protocols [12].

Antimicrobial susceptibility testing (AST) was performed using the Kirby-Bauer disc diffusion method on Mueller-Hinton Agar, and results were interpreted according to the Clinical and Laboratory Standards Institute (CLSI) guidelines applicable for each respective year of the study period [13]. The selection of antibiotics tested was guided by CLSI recommendations and the clinical relevance of the antimicrobials in UTI management. Detection of extended-spectrum β -lactamase (ESBL) production among Gram-negative bacilli was carried out using the phenotypic two-disc synergy test. This involved placing a disc containing Cefotaxime (30 μ g) and another disc containing Cefotaxime + Clavulanic acid (30 μ g/10 μ g) & Ceftazidime (30 μ g) and another disc containing Ceftazidime + Clavulanic acid (30 μ g/10 μ g) 20 mm apart on a Mueller-Hinton Agar plate inoculated with a lawn culture of the test bacterial isolate. Interpretation (CLSI criteria): A ≥ 5 mm increase in zone diameter for either antibiotic + Clavulanic acid disk (compared to the antibiotic alone) confirms ESBL production [13].

Statistical analysis

Data collected were entered and organized in Microsoft Excel, categorized year-wise and organism-wise from 2019 to 2023. The prevalence rates of uropathogens and their antimicrobial resistance percentages were calculated. Statistical analysis was performed using the Chi-square test to assess the significance of changes in antimicrobial resistance trends over the five-year period. A p-value of less than 0.05 was considered statistically significant.

Results

Among the total of 1,279 urine samples analyzed, the occurrence of urinary tract infections (UTIs) was significantly higher in females (941 cases, 73.57%) compared to males (338 cases, 26.42%). The majority of affected individuals belonged to the adult age group (19–64 years), accounting for 872 cases (68%), followed by 247 cases (19.3%) in the geriatric age group and 160 cases (12.5%) in the paediatric population.

The distribution of bacterial isolates identified from urine cultures is depicted in Figure 1. Gram-negative bacilli formed the predominant group of uropathogens and included *Escherichia coli*, *Klebsiella pneumoniae*, *Citrobacter koseri*, *Proteus mirabilis*, *Pseudomonas spp.*, *Acinetobacter spp.*, and *Morganella morganii*. Among Gram-positive cocci, *Enterococcus spp.*, Methicillin-sensitive *Staphylococcus aureus* (MSSA), and Methicillin-resistant *Staphylococcus aureus* (MRSA) were isolated. Throughout the five-year study period, *E. coli* remained the most common causative agent of UTIs, followed by *Klebsiella pneumoniae*, as shown in the annual trend analysis (Figure 1).

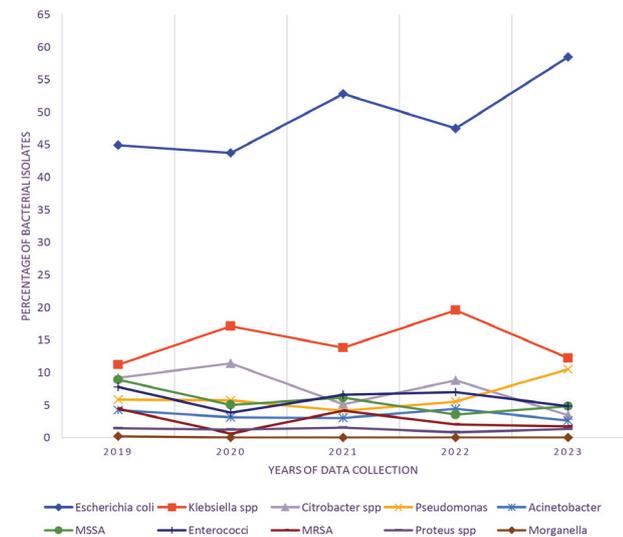


Figure 1: Frequency distribution of uropathogens and trend of bacterial isolates from urine over five years showing *Escherichia coli* as predominant in all five years.

The comparative antimicrobial resistance patterns of all bacterial isolates between 2019 and 2023 are detailed in Tables 1 and 2. Year-wise antimicrobial resistance data for *E. coli*, along with corresponding p-values, are presented in Table 3.

A five-year trend analysis of antimicrobial resistance in *E. coli* isolates (Figure 2) demonstrated a slight reduction in resistance to trimethoprim/sulphamethoxazole (cotrimoxazole), decreasing from 72 isolates (45%) in 2019 to 53 isolates (39.5%) in 2023. Similarly, resistance to nitrofurantoin declined from 14 isolates (8.7%) in 2019 to 5 isolates (3.7%) in 2023. In contrast, resistance to norfloxacin increased from 12 isolates (44%) in 2019 to 11 isolates (58%) in 2023. Notably, resistance to piperacillin/tazobactam rose from 11 isolates (6.8%) to 34 isolates (25.3%) over the same period. Resistance to meropenem also increased, from 2 isolates (1.2%) in 2019 to 14 isolates (10.4%) in 2023. The increase in resistance to piperacillin/tazobactam, third-generation cephalosporins (e.g., cefotaxime), aminoglycosides (amikacin and gentamicin), and carbapenems (imipenem and meropenem) was found to be statistically significant ($p < 0.05$). Among *E. coli* isolates, the proportion of extended-spectrum β -lactamase (ESBL) producers slightly decreased from 19 isolates (11.8%) in 2019 to 15 isolates (11.2%) in 2023.

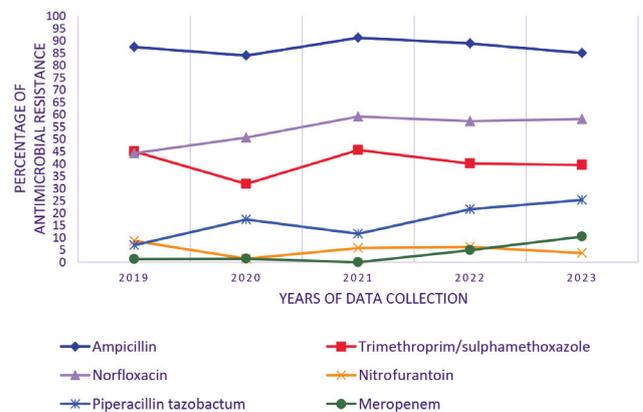


Figure 2: Trend of antimicrobial resistance of urinary isolates of *Escherichia coli* over five years.

Similarly, the trend analysis of antimicrobial resistance in *Klebsiella pneumoniae* isolates over five years a significant decrease in resistance to cotrimoxazole, which dropped from 14 isolates (35%) in 2019 to 6 isolates (21.4%) in 2023 ($p < 0.05$). Resistance to nitrofurantoin also showed a slight decline from 21 isolates (52.5%) in 2019 to 13 isolates (46.4%) in 2023. However, resistance to norfloxacin increased from 12 isolates (30%) to 11 isolates (39.3%), and resistance to cefotaxime rose from 17 isolates (42.5%) to 13 isolates

Table 1: Comparison of antimicrobial resistance (in percentage) of Gram-negative bacterial isolates from urine between year 2019 and year 2023.

Bacteria	<i>E.coli</i>		<i>K.pneumoniae</i>		<i>Citrobacter koseri</i>		<i>Proteus mirabilis</i>		<i>Pseudomonas spp</i>		<i>Acinetobacter spp</i>	
	2019	2023	2019	2023	2019	2023	2019	2023	2019	2023	2019	2023
Years	2019	2023	2019	2023	2019	2023	2019	2023	2019	2023	2019	2023
Amikacin	8.8	23.1	25	28.6	12.1	12.5	0	0	19	4.1	33.3	33.3
Ampicillin	87.5	85.1	95	92.9	87.8	100	60	66.6	IRa	IR	IR	IR
Amoxy-clav	54.4	45.5	52.5	35.7	60.6	62.5	60	33.3	IR	IR	IR	IR
Cefepime	41.9	51.5	40	28.6	45.4	12.5	60	0	6	20.8	40	33.3
Cefotaxime	64.4	75.4	42.5	46.4	51.5	37.5	60	33.3	IR	IR	66.6	83.3
Ceftazidime	60.0	64.9	42.5	39.3	48.4	25	60	0	33.3	25	46.6	50
Cotrimoxazole	45.0	39.5	35	21.4	36.3	37.5	60	33.3	IR	IR	40	0
Gentamicin	18.8	38.8	27.5	50.0	12.1	25	0	0	28.5	4.1	40	50
Imipenem	1.9	11.2	2.5	25.0	6	0	0	0	4.7	8.3	33.3	0
Meropenem	1.3	10.4	10	21.4	6	0	0	0	4.7	8.3	33.3	0
Nitrofurantoin	8.8	3.7	52.5	46.4	30.3	25	IR	IR	66.6	29.1	86.6	66.6
Norfloxacin	44.4	58.2	30	39.3	30.3	25	20	33.3	33.3	25	46.6	50
Piperacillin	NAb	NA	NA	NA	NA	NA	NA	NA	23.8	58.3	NA	NA
PTZc	6.9	25.4	20	28.6	12.1	0	0	0	4.7	12.5	40	16.6

Abbreviations: ^aIR- Intrinsic resistance, ^bNA- not applicable, ^cPTZ- Piperacillin/Tazobactam.

Table 2: Comparison of antimicrobial resistance (in percentage) of Gram-positive bacterial isolates from urine between year 2019 and year 2023.

Bacteria	MSSA		Enterococcus spp		MRSA	
	2019	2023	2019	2023	2019	2023
Years	2019	2023	2019	2023	2019	2023
Ampicillin	75	27.2	32.1	18.1	100	100
Amikacin	0	0	IRa	IR	0	0
Cefoxitin	0	0	IR	IR	100	100
Cotrimoxazole	12.5	0	IR	IR	43.7	75
Gentamicin	0	0	IR	IR	25	0
High level Gentamicin	NAb	NA	42.8	27.2	NA	NA
Nitrofurantoin	3.1	0	14.2	18.1	0	0
Norfloxacin	9.4	9	10.7	54.5	50	75
Vancomycin	NDc	ND	0	0	ND	ND

Abbreviations: ^aIR- Intrinsic resistance, ^bNA- not applicable ^cND- Not done.

(46.4%) during the study period. Statistically significant increases in resistance were observed for piperacillin/tazobactam and imipenem in *Klebsiella pneumoniae* isolates.

It was noted that resistance to nitrofurantoin was markedly higher in *Klebsiella pneumoniae* isolates (46.4%) compared to *E. coli* isolates (3.7%) in the year 2023.

Overall, the study observed a favourable trend with a decrease in resistance to certain oral antibiotics, namely cotrimoxazole and nitrofurantoin, by the end of the study period. This improvement could potentially be attributed to the reduced empirical usage of these antibiotics during recent years. Conversely, an alarming rise in resistance to broad-spectrum antibiotics such as cephalosporins, piperacillin-tazobactam, and carbapenems underscores the need for strict antimicrobial stewardship interventions.

Table 3: Year-wise antimicrobial resistance of *Escherichia coli* in number (percentage) and p value. P value < 0.05 is considered statistically significant.

Antibiotics	2019	2020	2021	2022	2023	chi square value	p value
Amikacin	14(8.7%)	9(13%)	11(10.6%)	27(16.6%)	31(23.1%)	14.136	0.006
Ampicillin	140(87.5)	58(84%)	94(91.2%)	144(88.8%)	114(85%)	3.1	0.541
Amoxy-clav	87(54.3%)	40(57.9%)	65(63.1%)	90(55.55)	61(45.5%)	7.841	0.0975
Cefepime	67(41.8%)	32(46.3%)	53(51.4%)	95(58.6%)	69(51.4%)	9.538	0.048
Cefotaxime	103(64.3%)	42(60.8%)	66(64%)	120(74%)	101(75.3%)	9.345	0.053
Ceftazidime	96(60%)	39(56.5%)	65(63.1%)	120(74%)	87(64.9%)	9.929	0.041
Cotrimoxazole	72(45%)	22(31.8%)	47(45.6%)	65(40.1%)	53(39.5%)	4.486	0.344
Gentamicin	30(18.7%)	19(27.5%)	29(28.1%)	44(27.1%)	52(38.8%)	14.685	0.005
Imipenem	3(1.8%)	4(5.79%)	0	8(4.9%)	15(11.1%)	12.027	0.007
Meropenem	2(1.2%)	1(1.4%)	0	8(4.9%)	14(10.4%)	15.584	0.001
Nitrofurantoin	14(8.7%)	1(1.4%)	6(5.8%)	10(6.1%)	5(3.7%)	6.091	0.192
Norfloxacin	71(44.3%)	35(50.7%)	61(59.2%)	93(57.4%)	78(58.2%)	9.096	0.058
Piperacillin/ tazobactam	11(6.8%)	12(17.3%)	12(11.6%)	35(21.6%)	34(25.3%)	23.208	0.0001
ESBL producers	19(11.8%)	0	5(4.8%)	24(14.8%)	15(11.1%)	6.334	0.096

Discussion

In the present study, the incidence of urinary tract infections (UTIs) was significantly higher in females compared to males, a finding consistent with several previous studies that reported a higher prevalence of UTIs among females due to anatomical and physiological factors [14, 15]. The distribution of uropathogens and their antimicrobial susceptibility patterns are known to vary over time and across different geographic regions. Our five-year trend analysis revealed that Gram-negative bacilli remained the predominant uropathogens, with *Escherichia coli* being the most frequently isolated organism, followed by *Klebsiella pneumoniae*. This distribution pattern aligns with findings from similar studies conducted in other regions [16, 17].

A concerning observation in our study is the rising antimicrobial resistance among uropathogens, particularly to piperacillin-tazobactam, cephalosporins, aminoglycosides, and carbapenems over the five-year study period. This trend mirrors the increasing levels of antimicrobial resistance reported in recent literature, reflecting a global challenge in the management of UTIs [18-21]. Previous studies have highlighted a consistent rise in resistance of uropathogenic *E. coli* to cephalosporins, cotrimoxazole, piperacillin-tazobactam, and carbapenems [22]. However, in contrast to these reports, our study demonstrated a notable reduction in resistance to cotrimoxazole and nitrofurantoin over the study period. This decline may be attributed to a reduction in the empirical use of these oral antibiotics

at our facility, emphasizing the positive impact of antibiotic stewardship practices.

An important observation in this study is the decreasing resistance trend of *E. coli* and *Klebsiella pneumoniae* isolates to oral antibiotics such as cotrimoxazole and nitrofurantoin between 2019 and 2023. This trend is encouraging, as it provides clinicians with more accessible and cost-effective options for the empiric treatment of uncomplicated UTIs. Reduced resistance to these oral agents could potentially minimize the need for hospitalization and limit the use of higher-generation antibiotics, thereby preventing further escalation of antimicrobial resistance.

A long-term study evaluating resistance trends over twelve years reported low resistance rates of *E. coli* to piperacillin-tazobactam, carbapenems, and nitrofurantoin, while high resistance was observed against ampicillin, cotrimoxazole, and cephalosporins [23]. Another study indicated that amikacin, gentamicin, and imipenem were among the most effective drugs against Gram-negative uropathogens, whereas nitrofurantoin, vancomycin, and chloramphenicol showed higher efficacy against Gram-positive isolates [24].

In our study, despite the lower number of *Klebsiella pneumoniae* isolates compared to *E. coli*, *Klebsiella* exhibited higher levels of antimicrobial resistance. This finding is in agreement with similar studies that have identified *Klebsiella pneumoniae* as a highly resistant uropathogen among Gram-negative isolates [25].

The findings of this study underscore the importance of prudent antibiotic usage. Restricting the use of broad-spectrum antibiotics such as cephalosporins and carbapenems to only multidrug-resistant cases and preferring oral agents like cotrimoxazole, nitrofurantoin, and norfloxacin for empiric therapy in uncomplicated cases may help curb the rise in resistance. The AMR data generated from this five-year analysis is instrumental in updating institutional antibiotic policies and guiding the selection of empiric therapy for UTIs.

A significant clinical implication of this study is the observed reduction in resistance to specific oral antibiotics, which is not commonly reported in other similar regional studies. This offers a positive outlook for managing UTIs with oral medications, potentially reducing hospitalization rates and limiting exposure to higher-end antibiotics. Sustained surveillance and strict adherence to antibiotic stewardship programs are essential to maintain and further improve this trend.

Limitations: This study was conducted in a single tertiary care center with a limited sample size, which may not fully represent the community's uropathogen profile. Multicenter studies involving larger populations are needed to obtain more generalizable and comprehensive data on antimicrobial resistance trends.

Conclusion

This five-year trend analysis highlights that Gram-negative bacilli, particularly *Escherichia coli* and *Klebsiella pneumoniae*, remain the predominant uropathogens causing UTIs. An alarming rise in resistance to cephalosporins, piperacillin-tazobactam, carbapenems, and fluoroquinolones was observed. However, a favourable decline in resistance to cotrimoxazole and nitrofurantoin suggests potential for effective oral therapy. Continuous surveillance, strict antibiotic stewardship, and judicious antibiotic use are crucial to control antimicrobial resistance. Periodic local resistance data will aid in updating empirical treatment guidelines and preserving antibiotic efficacy for future UTI management.

Conflicts of interest

Authors declare no conflicts of interest.

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