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Original Article

Microbiology Section

Evolving Resistance Patterns: A Retrospective Five-year Study of Urinary Pathogens and Antibiotic Efficacy

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ABSTRACT

Introduction: The rising incidence of antimicrobial resistance is a major source of concern, particularly in the absence of new antimicrobial agents. This infection arises when microorganisms (predominantly bacteria) infiltrate and multiply within the urinary tract.

Aim: To we present the changing antibiotic sensitivity patterns of urinary pathogens over the past five years (2019-2023) in a hospital located on the northeast coast of Tamil Nadu, India.

Materials and Methods: This retrospective study was performed at the Department of Microbiology, Chettinad Hospital and Research Institute, Tamil Nadu, India, from January 2019 to October 2023. Out of 39,592 urine samples, 9,940 samples with bacterial growth were included in the study, considering only those with positive bacterial growth. Exclusion criteria included samples with no bacterial growth, samples from patients who had received antibiotics before sample collection, and duplicate samples. The demographic parameters considered were age, gender and co-morbidities. Bacterial identification was performed using conventional microbiological methods, including Gram staining, catalase testing, oxidase testing and biochemical tests. Antibiotic resistance testing was conducted using the Kirby-Bauer disk diffusion technique, following the protocols established by the Clinical and Laboratory Standards Institute (CLSI). Statistical analysis was performed using the Chi-square test, with a p-value under <0.05 regarded as statistically significant.

Results: The study processed 39,592 urine samples, from which 9,940 (25.1%) pathogens were isolated. *Escherichia coli* (4,406; 44%) and *Klebsiella pneumoniae* (1,730; 17%) were the most common Gram-Negative Bacteria (GNB), while *Enterococcus* spp. (1,305; 13%) dominated among Gram-Positive Cocci (GPC). Notably, the efficacy of Amikacin (AK) against *E. coli*, *Citrobacter koseri* and *Pseudomonas aeruginosa* has declined over the last five years, as has the penicillin class of antibiotics, such as penicillin against *Staphylococcus aureus*. However, certain antibiotic classes like cephalosporins, aminoglycosides, Cotrimoxazole (COT), and Ciprofloxacin (CIP) exhibited improved efficacy against GNB. COT and Clindamycin (CD) also demonstrated notable effectiveness against *Staphylococcus aureus*, highlighting evolving antibiotic susceptibility patterns.

Conclusion: From 2019 to 2023, there was a noticeable decrease in the efficacy of amikacin against *E. coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, as well as a decrease in penicillin effectiveness against *S. aureus*. However, Imipenem (IMP), Meropenem (MRP), and Gentamicin (GEN) remained effective against GNB. Oxazolidinones, glycopeptides and sulfonamide antibiotics showed positive efficacy against GPC, highlighting their continued reliability in treating GPC infections.

Keywords: Drug resistance, *Escherichia coli*, Gram-negative bacteria, Microbial sensitivity test, Urinary tract infections

INTRODUCTION

Urinary Tract Infection (UTI) is a prevalent medical condition that can occur anywhere in the urinary system, encompassing the kidneys, ureters, urinary bladder and urethra. This infection arises when microorganisms (predominantly bacteria) infiltrate and multiply within the urinary tract [1]. UTIs manifest in various forms, with cystitis affecting the urinary bladder and causing symptoms such as frequent urination, urgency, a burning sensation during urination and cloudy or bloody urine. In contrast, pyelonephritis involves kidney infection and presents more severe symptoms like fever, flank pain, nausea and vomiting. Urethritis pertains to urethral infection, which can elicit discomfort and irritation during urination. This is the second most common infection in the general population after respiratory infections [2].

UTIs can be caused by bacteria originating from either community or healthcare settings. GNB, specifically those belonging to the Enterobacteriaceae family, are the most common type of organisms responsible for UTIs. *Escherichia coli* and *Proteus* species are among the predominant bacteria within the Enterobacteriaceae family, known for their substantial role in causing infections in both community and healthcare settings, followed by *Klebsiella pneumoniae*, *Citrobacter* species, *Enterobacter* species and *Serratia* [3,4]. In addition to the Enterobacteriaceae family, *Pseudomonas aeruginosa* can also be implicated in UTIs. Among various age groups, elderly hospitalised individuals exhibit the highest incidence, especially males, due to factors such as prostate enlargement, diminished antibacterial properties of prostate secretions and the use of catheters [4].

Antibacterial medications are crucial in managing bacterial infections in patients with UTIs. While certain bacteria exhibit innate resistance to even the latest antibacterial agents, the development of acquired antimicrobial resistance has been observed in most pathogens [5]. Antibiotic resistance has evolved into a major public health concern with serious implications for infection treatment. In the last decade, there has been a growing occurrence of both carriage and infection with multidrug-resistant organisms [6]. Antimicrobial resistance tends to be of greater significance in developing countries compared to developed ones. Studies conducted in India have reported an increasing resistance of urinary pathogens to commonly prescribed antibiotics [7,8].

Conducting consistent and regular surveillance of the local prevalence of uropathogens and their antibiotic susceptibility patterns is of significant public health value, promoting the responsible use of existing antimicrobial medications. Hence, this study aimed to address the gap in knowledge regarding the antibiotic resistance trends of urinary pathogens in Tamil Nadu, India, over the past five

years. It is novel as it provides an in-depth analysis of the temporal changes in antibiotic resistance among uropathogens, focusing on both Gram-negative and Gram-positive organisms. Unlike many studies that focus on isolated time points, this research offers a comprehensive understanding of the evolving resistance patterns over time, contributing valuable data to the local healthcare setting.

While numerous studies have explored antibiotic resistance in UTIs, this study uniquely contributes to the growing body of knowledge by focusing on local data from Tamil Nadu, a region that has seen significant variations in resistance patterns. By examining the trends in the resistance of commonly prescribed antibiotics, this study adds new insights into how local pathogens are evolving and how this influences treatment decisions.

MATERIALS AND METHODS

This retrospective study gathered information on urinary pathogens and their corresponding antibiotic resistance patterns identified in urine samples collected from patients at the Department of Microbiology, Chettinad Hospital and Research Institute in Tamil Nadu, India, from January 2019 to October 2023. Clearance for the study was granted by The Institutional Human Ethics Committee (CARE IHEC-II) of Chettinad Academy of Research and Education, Tamil Nadu (IHECII/0443/23).

Inclusion criteria: For this study, data were collected from urine samples with bacterial growth over the past five years, excluding those with no bacterial growth. A total of 9,940 clinically isolated urine samples exhibited bacterial growth, yielding various bacteria.

Exclusion criteria: Urine samples that showed no bacterial growth, samples from patients who received antibiotic treatment before urine sample collection, duplicate samples from the same patient within the same infection episode, and samples from patients with incomplete or missing clinical data were excluded from this study.

Sample size calculation: The sample size for this study was not calculated statistically but was instead based on a time-bound approach. All available subjects who met the inclusion criteria during the study period from January 2019 to October 2023 were included in the study. A total of 39,592 samples from patients presenting with UTIs during this period were included, ensuring a comprehensive representation of the population under investigation.

Isolation of urinary pathogens: Clean midstream catch urine samples were collected from the patients for culture. These samples were promptly inoculated onto Cystine-Lactose-Electrolyte-Deficient (CLED) agar and incubated for 24 hours at 37°C aerobically.

Identification of urinary pathogens: Identification is a multi-step process, starting with colony morphology assessment and preliminary examination. Regarding colony morphology, the size, shape, color, texture, elevation, and margins were evaluated. The preliminary tests included Gram staining, catalase testing, oxidase testing and a motility assessment (Hanging Drop method). Following this preliminary examination, the biochemical examination was carried out, involving Indole, Triple Sugar Iron (TSI) tests, citrate utilisation testing, urease testing, Mannitol Motility Medium (MMM) tests, Methyl Red (MR) testing and Voges-Proskauer (VP) testing. Non fermenting GNB, including *Flavobacterium meningosepticum*, *Ochrobactrum anthropi* and *Stenotrophomonas maltophilia*, were isolated and identified using a combination of standard biochemical tests. The identification process involved testing for specific characteristics such as oxidase activity, glucose fermentation and utilisation of specific sugars. Additional tests, including motility and urease production, were used to confirm the species-level identification of these non fermenters. After these steps, antibiotic susceptibility tests were conducted to determine the pathogens' responsiveness to specific antibiotics.

Antibiotic susceptibility test: Antibiotic resistance was assessed using the Kirby-Bauer disk diffusion technique, following the standards set by the CLSI [9]. This testing was conducted and interpreted according to the year of sample collection, spanning from 2019 to 2023. The antibiotics selected for assessing susceptibility in GPC included Penicillin (P) (10 U), Linezolid (LZ) (30 µg), GEN (10 µg), Nitrofurantoin (NIT) (300 µg), CD (2 µg), CIP (5 µg), Erythromycin (E) (15 µg), Tetracycline (TE) (30 µg), Cefazolin (CZ) (30 µg) and Ampicillin (AMP) (10 µg), all of which were tested using the Kirby-Bauer disk diffusion method. Additionally, Vancomycin (VA) and Teicoplanin (TEI) were assessed using the E-strip method, with Minimum Inhibitory Concentration (MIC) ranges of 0.5–32 µg/mL.

The GNB were subjected to antibiotic susceptibility testing for the following antibiotics: IMP (10/25 µg), Cefepime (CPM) (30 µg), CZ (30 µg), COT (1.25/23.75 µg), Fosfomycin (FOS) (200 µg), MRP (20/10 µg), Norfloxacin (NOR) (10 µg), CIP (5 µg), GEN (10 µg), Cefotaxime (CTX) (30 µg), Ceftazidime (CAZ) (30 µg), NIT (300 µg), Piperacillin-Tazobactam (PIT) (100/10 µg), Tobramycin (TOB) (10 µg), Cefuroxime (CXM) (30 µg), AMP (10 µg), and Amikacin (AK) (30 µg).

STATISTICAL ANALYSIS

The data were analysed using appropriate statistical methods to evaluate trends in antibiotic resistance over time. Descriptive statistics were used to summarise the data, including the mean, standard deviation and frequency distribution. A Chi-Square test using contingency tables assessed the association between antibiotic resistance patterns and different years, evaluating whether the observed variations in resistance and susceptibility were statistically significant. A p-value of <0.05 was considered statistically significant.

RESULTS

Of the 39,592 urine samples processed over the past five years, 9,940 (25.1%) samples yielded significant or probably significant growth of pathogenic bacteria, with an increased incidence of GNB at 8,449 (85%) compared to GPC at 1,491 (15%). Within the GNB, the Enterobacteriaceae comprised 7,075 (72%) isolates. A detailed list of all the isolated bacteria is provided in [Table/Fig-1].

Chi-square tests were applied to determine the association between years and the isolation frequency of bacterial species. The Chi-square values and corresponding p-values are reported. A p-value of <0.05 indicates statistical significance. Drug sensitivity percentages of strains of the most commonly isolated uropathogenic organisms are illustrated in [Table/Fig-2] for GNB and [Table/Fig-3] for GPC.

In the isolated GNB, certain genera exhibited a significant decrease in susceptibility to amikacin, a primary drug of choice for managing GNB infections. Similarly, in GPC, the effectiveness of the penicillin class, including penicillin, was observed to be reduced when used against *Staphylococcus aureus*. Resistance patterns across various organism-antibiotic pairs revealed statistically significant variations in resistance for *Escherichia coli* against amikacin (p-value <0.05) and *Pseudomonas aeruginosa* against amikacin (p-value <0.05).

Specifically, *E. coli* resistance to amikacin increased from 5.0% in 2019 to 10.1% in 2023, with a mean resistance of 7.6%±1.9. Meanwhile, sensitivity declined from 92.3% to 65.7% (Mean±SD: 82.6±10.7%), demonstrating a statistically significant trend (p-value <0.001, χ^2 test). *P. aeruginosa* exhibited fluctuating resistance patterns, peaking at 26.5% in 2023 compared to 18.1% in 2019 (Mean±SD: 16.1%±7.2), with a notable decline in sensitivity (p-value <0.001). Isolates classified as intermediate were not included in the resistance and sensitivity percentage calculations, as shown in [Table/Fig-4]. These findings highlight critical trends in antibiotic resistance, underscoring the need for targeted interventions and continuous monitoring of increasing resistance.

The study also analysed the resistance patterns of *Klebsiella pneumoniae* to COT over five years, revealing a significant decline in resistance from 50.1% in 2019 to 40.1% in 2023 (p-value <0.001,

	Organism	2019 (n=2497)	2020 (n=1553)	2021 (n=1698)	2022 (n=2175)	2023 (n=2017)	Total (n=9940)
Gram negative bacteria	*Escherichia coli*	1150 (12%)	709 (6%)	755 (7%)	947 (10%)	845 (9%)	4406 (44%)
	Klebsiella pneumoniae	445 (4%)	281 (3%)	311 (3%)	376 (4%)	317 (3%)	1730 (17%)
	Citrobacter freundii	81 (1%)	30 (0%)	14 (0%)	27 (0%)	16 (0%)	168 (1%)
	Citrobacter koserii	50 (1%)	25 (0%)	42 (0%)	67 (1%)	73 (1%)	257 (3%)
	Proteus mirabilis	36 (0%)	10 (0%)	10 (0%)	56 (1%)	58 (1%)	170 (2%)
	Enterobacter spp.	34 (0%)	20 (0%)	28 (0%)	52 (1%)	49 (1%)	183 (2%)
	Morganella morganii	18 (0%)	14 (0%)	14 (0%)	15 (0%)	14 (0%)	75 (1%)
	Proteus vulgaris	33 (0%)	15 (0%)	28 (0%)	15 (0%)	18 (0%)	109 (1%)
	Serratia spp.	1 (0%)	2 (0%)	0	2 (0%)	3 (0%)	8 (0%)
	Salmonella typhi	0	0	0	1 (0%)	2 (0%)	3 (0%)
	Pseudomonas aeruginosa	127 (1%)	68 (1%)	54 (1%)	88 (1%)	102 (1%)	439 (5%)
	Acinetobacter spp.	108 (1%)	77 (1%)	94 (1%)	117 (1%)	93 (1%)	489 (5%)
	Pseudomonas spp.	49 (0%)	70 (1%)	110 (1%)	34 (1%)	86 (1%)	349 (4%)
	Aeromonas spp.	12 (0%)	1 (0%)	0	0	1 (0%)	14 (0%)
	Providentia spp.	11 (0%)	0	3 (0%)	7 (0%)	5 (0%)	26 (0%)
	Flavobacterium meningosepticum	0	0	0	3 (0%)	2 (0%)	5 (0%)
	Ochrobactrum anthropi	0	0	0	0	1 (0%)	1 (0%)
Gram positive bacteria	*Enterococcus* spp.	290 (3%)	192 (2%)	213 (2%)	339 (3%)	271 (3%)	1305 (13%)
	S. aureus	31 (0%)	31 (0%)	17 (0%)	6 (0%)	31 (0%)	116 (1%)
	Staphylococcus saprophyticus	11 (0%)	6 (0%)	1 (0%)	6 (0%)	2 (0%)	26 (0%)
	Streptococcus spp.	8 (0%)	2 (0%)	3 (0%)	16 (0%)	14 (0%)	43 (1%)
	Coagulase negative staphylococci	1 (0%)	0	0	1 (0%)	2 (0%)	4 (0%)
	Streptococcus agalactiae	1 (0%)	0	0	0	12 (0%)	13 (0%)
	Stenotrophomonas maltophilia	0	0	1 (0%)	0	0	1 (0%)
No. of growth/Total no. of samples		2497/9847	1553/6237	1698/7326	2175/7875	2017/8307	9940/39592

[Table/Fig-1]: List of bacteria isolated from urine samples over five years 9940 (25.1%).

The most common urinary pathogen susceptibility percentage of antibiotic drugs over the years	Drugs	*E. coli* 4406 (44%)	*K. pneumoniae* 1730 (17%)	*P. mirabilis* 170 (2%)	*Acinetobacter* spp. 489 (5%)
	AMP	839 (19%)	Intrinsic resistance	100 (59%)	Intrinsic resistance
	AK	3668 (83%)	1176 (68%)	136 (80%)	459 (94%)
	CZ	1322 (30%)	640 (37%)	121 (71%)	24 (5%)
	CPM	1983 (45%)	899 (52%)	139 (82%)	401 (82%)
	CTX	1762 (40%)	813 (47%)	140 (82%)	313 (64%)
	Cefoxitin	2600 (59%)	1090 (63%)	Not reported	Intrinsic resistance
	CXM	1454 (33%)	709 (41%)	128 (75%)	34 (7%)
	CIP	1807 (41%)	849 (49%)	114 (67%)	426 (87%)
	COT	2203 (50%)	935 (54%)	88 (52%)	411 (84%)
	Fosfomycin	4328 (98%)	1246 (72%)	128 (75%)	Intrinsic resistance
	GEN	3349 (76%)	1223 (71%)	134 (79%)	449 (92%)
	IMP	3965 (90%)	1193 (69%)	160 (94%)	440 (90%)
	MER	4057 (92%)	1263 (73%)	166 (98%)	455 (93%)
	NIT	4098 (93%)	935 (54%)	Intrinsic resistance	215 (44%)
	NOR	3432 (78%)	865 (50%)	Not reported	Nor reported
	PIT	3934 (89%)	1176 (68%)	163 (96%)	469 (96%)
	TOB	4098 (93%)	1282 (74%)	158 (96%)	464 (95%)

[Table/Fig-2]: Percentage of antibiotic sensitivity against commonly isolated GNB over the past 5 years 8432 (85%).
AMP: Ampicillin; AK: Amikacin; CZ: Cefazolin; CPM: Cefepime; CTX: Cefotaxime; CXM: Cefuroxime; CIP: Ciprofloxacin; COT: Cotrimoxazole; GEN: Gentamicin; IMP: Imipenem; MER: Meropenem; NIT: Nitrofurantoin; NOR: Norfloxacin; PIT: PiperacillinTazobactam; TOB: Tobramycin

Chi-square test). The average resistance was 44.2±3.8%, while sensitivity increased from 44.0% to 58.7%, with a mean of 52.9±5.5%. Of the total 1,730 isolates, 772 were resistant, and 903 were sensitive, highlighting a shifting trend in antibiotic efficacy, as shown in [Table/Fig-5].

The most common urinary pathogen susceptibility percentage of antibiotic drugs over the years	Drug	*S. aureus* 116 (1%)	*Enterococcus* spp. 1305 (13%)
	AMP	88 (76%)	1072 (82%)
	CZ	86 (74%)	13 (1%)
	CIP	44 (38%)	418 (32%)
	CD	88 (76%)	Intrinsic resistance
	Chloramphenicol	86 (74%)	Not reported
	COT	101 (87%)	Intrinsic resistance
	E	62 (53%)	170 (13%)
	GEN	102 (88%)	1006 (77%)
	LZ	116 (100%)	1305 (100%)
	NIT	115 (99%)	1194 (91%)
	P	19 (16%)	849 (65%)
	TE	116 (100%)	1299 (99%)
	TEI (E-strip)	110 (95%)	326 (25%)
	VA (E-strip)	116 (100%)	1279 (98%)

[Table/Fig-3]: Percentage of antibiotic sensitivity against common GPC isolates over the past 5 years 1508 (15%).
AMP: Ampicillin; CZ: Cefazolin; CIP: Ciprofloxacin; CD: Clindamycin; COT: Cotrimoxazole; E: Erythromycin; GEN: Gentamicin; LZ: Linezolid; NIT: Nitrofurantoin; P: Penicillin; TE: Tetracycline; TEI: Teicoplanin; VA: Vancomycin

Citrobacter koseri exhibited a highly significant change in resistance patterns to Cefuroxime ($p=6.47\times10^{-12}$, $p<0.05$), suggesting a marked alteration in susceptibility during the study period, as indicated in [Table/Fig-6]. Resistance remained relatively stable, ranging from 8.0% in 2020 to 22.4% in 2022, with a mean resistance of 18.0±5.8%. Conversely, sensitivity to cefuroxime improved, increasing from 30.0% in 2019 to 76.7% in 2023, with an average sensitivity of 60.4±20.3%. A statistically significant difference in resistance trends (p-value <0.05, Chi-square test) indicates a gradual decline in resistance and improved susceptibility over time.

Organism	Drug	Year	Resistant (n)	Resistant (%)	Sensitive (n)	Sensitive (%)	Total (n)	Chi-square (χ^2) p-value
Escherichia coli	*Amikacin*	**2019**	58	5.0	1061	92.3	1150	χ^2=70.1 p≤0.001
		2020	47	6.6	636	89.7	709	
		2021	54	7.2	654	86.6	755	
		2022	83	8.8	739	78.0	947	
		2023	85	10.1	555	65.7	845	
Total			**327**		**3645**		**4406**	
Mean±SD			65.4±18.1	7.6±1.9	729.0±196.7	82.6±10.7	881.2±175.6	
Pseudomonas aeruginosa	*Amikacin*	**2019**	23	18.1	102	80.3	127	χ^2=43.4 p≤0.001
		2020	12	17.6	54	79.4	68	
		2021	4	7.4	48	88.9	54	
		2022	10	11.4	74	84.1	88	
		2023	27	26.5	45	44.1	102	
Total			**76**		**323**		**439**	
Mean±SD			15.2±9.5	16.1±7.2	64.6±23.7	75.3±17.8	87.8±28.6	

[Table/Fig-4]: Decreasing antibiotic efficacy of certain strains over 5 years.

Organism	Drug	Year	Resistant (n)	Resistant (%)	Sensitive (n)	Sensitive (%)	Total (n)	Chi-square (χ^2) p-value
Klebsiella pneumoniae	*Cotrimoxazole*	2019	223	50.1	196	44.0	445	χ^2=14.2 p≤0.001
		2020	124	44.1	148	52.7	281	
		2021	130	41.8	174	55.9	311	
		2022	168	44.7	199	52.9	376	
		2023	127	40.1	186	58.7	317	
Total			**772**		**903**		**1730**	
Mean±SD			154.4±42.3	44.2±3.8	180.6±20.7	52.9±5.5	346±65.2	

[Table/Fig-5]: Changing antibiotic resistance patterns of *Klebsiella pneumoniae* against COT over 5 years.

Organism	Drug	Year	Resistant (n)	Resistant (%)	Sensitive (n)	Sensitive (%)	Total (n)	Chi-square (χ^2) p-value
Citrobacter koserii	*Cefuroxime*	2019	9	18.0	15	30.0	50	χ^2=58.3 p≤0.001
		2020	2	8.0	17	68.0	25	
		2021	9	21.4	21	50.0	42	
		2022	15	22.4	52	77.6	67	
		2023	15	20.5	56	76.7	73	
Total			**50**		**161**		**257**	
Mean±SD			10±5.3	18.0±5.8	32.2±20.0	60.4±20.3	51.4±19.3	

[Table/Fig-6]: Changing antibiotic resistance patterns of *Citrobacter koserii* against CXM over 5 years.

The resistance patterns of *Staphylococcus aureus* to both CD and COT showed statistically significant changes over the study period ($p<0.05$, χ^2 test), indicating a positive shift in their efficacy, as seen in [Table/Fig-7]. Resistance to CD declined from 16.1% in 2019 to

Organism	Drug	Year	Resistant (n)	Resistant (%)	Sensitive (n)	Sensitive (%)	Total (n)	Chi-square (χ^2) p-value
Staphylococcus aureus	*Clindamycin (CD)*	2019	5	16.1	4	12.9	31	χ^2=43.3 p≤0.001
		2020	4	12.9	11	35.5	31	
		2021	2	11.8	13	76.5	17	
		2022	1	16.7	5	83.3	6	
		2023	2	6.5	27	87.1	31	
Total			**14**		**40**		**116**	
Mean±SD			2.8±1.6	12.7±4.1	12.9±9.2	59±33	23.2±11.3	
Staphylococcus aureus	*Cotrimoxazole (COT)*	2019	7	22.6	16	51.6	31	χ^2=12.8 p=0.01224
		2020	6	19.4	25	80.6	31	
		2021	1	5.9	15	88.2	17	
		2022	1	16.7	5	83.3	6	
		2023	0	0	31	100	31	
Total			**15**		**92**		**116**	
Mean±SD			3±3.2	12.8±9.5	18.4±9.9	80.7±17.9	23.2±11.3	

[Table/Fig-7]: Changing antibiotic resistance patterns of *Staphylococcus aureus* over 5 years.

6.5% in 2023, with a mean resistance of 12.7±4.1%, while sensitivity improved substantially from 12.9% in 2019 to 87.1% in 2023 (mean sensitivity: 59±33%). Similarly, resistance to COT steadily decreased from 22.6% in 2019 to complete susceptibility (0%) in 2023, with a mean resistance of 12.8±9.5% and mean sensitivity of 80.7±17.9%.

These findings highlight a statistically significant trend (p-value=0.01224, χ^2 test) toward increased susceptibility, suggesting that both antibiotics may still hold therapeutic potential in managing *S. aureus* infections. For *S. aureus*, penicillin resistance averaged 48.8±43.9% over five years but dropped sharply to 6.5% in 2023, indicating a potential shift in antibiotic efficacy, as shown in [Table/Fig-8].

Organism	Drug	Year	Resistant (n)	Resistant (%)	Sensitive (n)	Sensitive (%)	Total (n)	Chi-square (χ^2) p-value
Staphylococcus aureus	*Penicillin*	**2019**	25	80.6	6	19.4	31	χ^2=60.4 p≤0.001
		2020	24	77.4	6	19.4	31	
		2021	14	82.4	2	11.8	17	
		2022	0	0.0	6	100	6	
		2023	2	6.5	29	93.5	31	
Total			**65**		**49**		**116**	
Mean±SD			13±11.7	49.3±42.2	9.8±10.8	48.8±43.9	23.2±11.3	

[Table/Fig-8]: Changing penicillin resistant patterns of *Staphylococcus aureus* over 5 years.

Despite certain classes of antibiotics losing their effectiveness against various genera, some other antibiotic classes have maintained their efficacy at a high level over the last five years in both types of organisms. Carbapenems, including IMP and MRP, remained effective against many GNB, particularly within the Enterobacteriaceae family. GEN, which belongs to the aminoglycoside class, also demonstrates strong efficacy against GNB.

In GPC, various antibiotic classes have consistently proved to be effective against pathogens. Notably, the Glycopeptide class, represented by teicoplanin and vancomycin, the Oxazolidinone class, encompassing LZ, and NIT still stand as reliable options. Moreover, AMP, a member of the penicillin class, has demonstrated strong efficacy specifically against *Staphylococcus saprophyticus*. Interestingly, this appears to be the only bacterial species for which the drug is consistently effective.

DISCUSSION

The UTIs exert a significant burden on the healthcare system due to their escalating prevalence in both community and hospital environments. The identification of pathogens and the selection of appropriate antibiotics are essential for effectively treating patients with bacterial UTIs. This current study has presented variations in antimicrobial resistance patterns over the past five years.

Present study findings indicate that GNB are more frequently isolated than GPC, with *Escherichia coli* being the predominant pathogen among GNB. This aligns with global trends reported by Karlowsky JA et al., which highlight *E. coli* as a leading uropathogen. However, a concerning observation was the declining sensitivity of *E. coli* to amikacin, from 92.3% in 2019 to 65.7% in 2023. This trend reflects the growing antimicrobial resistance observed globally, further stressing the need for regular susceptibility testing [10].

Similarly, antibiotics from the penicillin class, long regarded as the first line of defense against GPC, have shown reduced efficacy over time. Notably, Penicillin's reduced effectiveness against *Staphylococcus aureus*, as reported in this study, was consistent with the observations of Joshua IA et al. This highlights the critical need to reassess the use of older antibiotics in the face of rising resistance [11].

Among the GNB, present study found that COT and CIP, widely used against the Enterobacteriaceae family, retained substantial efficacy. These results are comparable to studies by Al-Tawfiq JA et al., and Sader HS et al., which noted similar susceptibility patterns [12,13]. The class of Cephalosporins displayed high sensitivity overall, with Cefuroxime (CXM) showing remarkable improvement against *Citrobacter koserii*, increasing from a sensitivity rate of 30% in 2019 to 76.7% in 2023. This striking change aligns with findings from Liu L et al., in China, who reported an analogous rise in CXM efficacy against Citrobacter koserii [14].

GEN demonstrated strong efficacy against *Citrobacter freundii*, while amikacin significantly improved its sensitivity by 34% over five years. This is supported by Samonis G et al., who also highlighted the sustained effectiveness of aminoglycosides against multidrug-resistant organisms [15]. In the case of isolated GPC, CD and COT exhibited progressively increasing effectiveness against *Staphylococcus aureus*. In 2021, Montravers P and Eckmann C reported that these antibiotics demonstrated strong efficacy in treating bacterial infections caused by *Staphylococcus aureus* [16]. Several studies have shown this finding, with JA Karlowsky initiating a retrospective study on the Enterobacteriaceae family in 2017, which presented similar results in their report [17].

The implications of this study's findings are clinically significant. The observed shifts in antimicrobial resistance patterns highlight the need for routine surveillance of local pathogens to guide empirical treatment. A notable decline in the efficacy of key antibiotics, such as amikacin, underscores the urgency of implementing antimicrobial stewardship programs to promote rational antibiotic use and mitigate resistance.

Looking ahead, future research should focus on exploring alternative therapeutic options, including combination therapies, bacteriophage therapy, or novel antimicrobial agents, to combat multidrug-resistant organisms. Furthermore, educational initiatives aimed at both the general public and healthcare professionals are necessary to minimise the inappropriate use of antibiotics. By addressing these challenges, we can improve treatment outcomes and curb the spread of resistant pathogens in both community and healthcare settings.

Limitation(s)

There are several limitations to this study. First, the data for these findings were collected from a single centre, which may restrict the ability to generalise the results to other regions. Second, while the study spans five years, variations in patient demographics and sample sizes across the years could have influenced the trends observed. Third, the study primarily relied on conventional phenotypic methods for bacterial identification and antimicrobial susceptibility testing, which might lack the precision offered by advanced molecular techniques. Lastly, the focus was restricted to specific Gram-positive and GNB, potentially overlooking other significant pathogens that contribute to UTIs.

CONCLUSION(S)

This study highlights a notable decrease in the efficacy of amikacin against *Escherichia coli* and *Pseudomonas aeruginosa*, as well as a decrease in the efficacy of penicillin against *Staphylococcus aureus* over the five years from 2019 to 2023. In contrast, IMP, MRP and GEN demonstrated sustained effectiveness against GNB, underscoring their critical role in managing GNB-related infections. Similarly, GPC

exhibited high sensitivity to the Oxazolidinone, Glycopeptide and Sulphonamide classes of antibiotics, reaffirming the reliability of these agents in treating GPC infections. These findings emphasise the importance of periodic surveillance of antimicrobial susceptibility patterns to guide appropriate therapeutic strategies.

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