

Changing Patterns in Antimicrobial Drug Resistance among Uropathogens Isolated From Hospital and Community Patients with Urinary Tract Infections in Rajahmundry

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Abstract

Background: Urinary tract infection (UTI) is one of the most common bacterial infections encountered in clinical practice. The increasing prevalence of antimicrobial resistance (AMR) among uropathogens has significantly limited therapeutic options, emphasizing the need for continuous surveillance to guide empirical therapy.

Aim: To compare the bacteriological profile and antimicrobial resistance patterns of uropathogens isolated from urine cultures during two study periods (January–March 2016 and January–March 2022) at a tertiary care teaching hospital.

Materials and Methods: A retrospective comparative study was conducted on urine culture isolates conventionally during January–March 2016 and January–March 2022. Midstream clean-catch urine samples were processed by semi-quantitative culture on cysteine lactose electrolyte-deficient (CLED) agar. Significant bacteriuria ($\geq 10^5$ CFU/mL) isolates were identified using Gram staining and conventional biochemical methods. Antimicrobial susceptibility testing was performed by the Kirby–Bauer disk diffusion method on Mueller–Hinton agar and interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines.

Results: A total of 1,421 urine culture isolates were analysed, comprising 445 isolates from 2016 and 976 isolates from 2022. Gram-negative bacilli predominated in both periods (86% in 2016 and 82% in 2022). *Escherichia coli* remained the most frequently isolated pathogen (44.5% in 2016 and 34.2% in 2022), followed by *Klebsiella* spp., *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Proteus* spp., *Citrobacter* spp., *Enterobacter* spp., and *Acinetobacter* spp. A significant increase in resistance was observed for ampicillin, amoxicillin–clavulanate, piperacillin–tazobactam, cephalosporins, fluoroquinolones, nitrofurantoin, aminoglycosides, and carbapenems between the two study periods ($p < 0.05$ for most agents). Resistance to carbapenems increased markedly, with imipenem resistance rising from 4.9% to 31.6% and meropenem resistance from 4.2% to 27.0%. Fosfomycin demonstrated excellent activity against tested isolates in 2022, while vancomycin retained 100% susceptibility among Gram-positive isolates.

Conclusion: *Escherichia coli* continues to be the predominant pathogen. A substantial increase in antimicrobial resistance, particularly to carbapenems, cephalosporins, and fluoroquinolones, was observed. These findings highlight the urgent need for sustained antimicrobial resistance surveillance, timely revision of institutional antibiotic policies, and implementation of strict antimicrobial stewardship programmes to optimize empirical therapy and lessen the emergence of multidrug-resistant pathogens.

Keywords: Urinary tract infection, Uropathogens, Antimicrobial resistance, Antibigram, *Escherichia coli*, Antimicrobial stewardship, CLSI.

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Introduction

Urinary tract infection (UTI'S) is one of the most frequently occurring bacterial infection, where in an abnormal bacterial growth causes inflammation

of the urinary tract [1]. In a healthy person the UTI generally lacks any bacterial growth; however, in conditions when the bacteria arise from the rectal

reservoir, they may give rise to UTI [1]. UTI is most common in patients with diabetes and those with structural and neurological abnormalities which interfere with urinary flow. Nosocomial UTI is also common following catheterization and cystoscopy. The manifestation of UTI may vary from mild asymptomatic cystitis to pyelonephritis and septicemia and gram-negative organisms are the most common pathogens involved in UTI, but almost all known pathogens have been incriminated as possible causative agents for UTI [3]

Approximately 150 million cases related to UTI's are reported annually. Women, as compared to men, are more susceptible to UTI and close to 50% of them encounter UTI once in their lifetime. Inappropriate and empirical usage of wide spectrum antibiotics, insufficient hygiene, immunosuppression and prolonged hospitalization are some of the major etiological factors that elevate the chances of infection [2]. the usage of low standards antimicrobials further adds to the emerging drug resistance which could turn to be one of the biggest factors for mortality in developing and underdeveloped countries [4].

Mathematically, an appropriate increase or decrease in testing and reporting rates for antibiotics might cause an error in estimation of prevalence in resistance rates. This factor has not been considered in antimicrobial surveillance protocols to large extent till now [3]. Evidence supports that empirical treatment guidelines based on local bacterial spectrum and AMR surveillance provide best clinical results and prevent the emergence of resistance strains [3].

Thus, AMR surveillance forms the link between testing and treatment guidelines which are often provided by different kinds of agencies. It is very much evident that AMR has been increasing at an alarming rate throughout the world with appearance of more extended ESBL infection [3]. WHO's global plan of action on AMR has stressed AMR surveillance across nations as an important strategy for reducing AMR [3].

This warrants continuous reporting and surveillance of the emergence of AMR among the uropathogens across regions and nations [3]. There are many studies conducted in the past in different geographical regions of the world, to assess the antimicrobial resistance in uropathies. Most of the studies closed the argument to a panicking situation. Hence, the present study has performed to identify the changing etiological trends of UTI and the AMR.

Materials and Methods

Specimen Type: Midstream clean catch urine samples were collected in wide mouthed sterile containers.

Inclusion and Exclusion Criteria: Inclusion criteria: both in-patient and outpatient individuals of age groups in between 9-80 years attending our institution during the period.

Exclusion Criteria: patients who are already on the antibiotic treatment.

Bacterial Culture: Semi quantitative culture of urine sample on CLED (cysteine lactose electrolyte deficient) media. Bacteria with significant bacteriuria (CFU > 10⁵ /ml) for fortnight incubated.

Bacterial Identification and Ast: The isolates were identified by Gram staining and conventional biochemical methods. Antimicrobial susceptibility was done by Kirby Bauer diffusion method on muller Hilton Agar and the interpretation were carried out according to the CLSI guidelines (CLSI).

Study Area:

Type of study: Retrospective study.

Study: January 2016 to March 2016 AND January 2022 to March 2022.

Sample size:

2016-445

2022 -976

Data Analysis: All the data were tabulated and analysed. Descriptive statistics were used for analysis and the results were expressed as frequency and percentage [1]

Data analysis was performed using IBM Statistical package for social sciences version 22.0 (IBM SPSS Inc USA). The significance of the antibiotics resistance was analysed using the Chai framework P value less than 0.05 were considered statistically significant [6]

Ethical Approval: Approval from the institutional ethical committee was obtained.

Limitations: There are several limitations of our study. Cultures from paediatric population were not included in the study. Data on patient's demography risk factors and clinical characters were not collected and analysed. The data were not separately analysed for hospitalized and non-hospitalized patients, which might influence the prevalence of the resistance.

Results

Antibiogram of urine culture samples in the month of Jan 2016 and urine culture samples in the month of Jan 2022 were analysed in the study.

The most common organism isolated during both studies was E.Coli. The other common organism were S.aureus, Pseudomonas aeruginosa, Klebsiella

species. The prevalence of the other organisms was less than 10% in both study periods in *Proteus* species, *Citrobacter*, *Enterobacter* and

Acinetobacter species were seen in the causative spectrum.

Table 1: Bacteriological profile of urinary tract infection isolates obtained during the study periods. 2016 (N= 445)

Gpc 63 (14%)	Gnb 382 (86%)
s.aureus 27 (6%)	e.coli 198 (44.5%)
Cons 19 (4.2%)	k.pneumoniae 56 (12 %)
Entero 9 (2%)	k.oxytoca 40 (8.9%)
Strep 8 (1.7%)	Pseudo 19 (19%)
	Prot.mirabilis 21 (4.7%)
	p.vulgaris 18 (4%)
	Citrobacter 11 (2.5%)
	Enterobacter 8 (1.8%)
	Acinetobacter 11 (1.5%)
	Providentia 0

2022 (N= 976)

Gpc 175 (18%)	Gnb 801 (82%)
s.aureus 69 (7%)	e.coli 334 (34.2%)
Cons 81 (8.3%)	k.pneumoniae 82 (8.4 %)
Entero 16 (1.6%)	k.oxytoca 186 (19%)
Strep 9 (0.1%)	Pseudo 42(4.3%)
	Prot.mirabilis 45 (4.6%)
	p.vulgaris 22 (2.26%)
	Citrobacter 27 (2.8%)
	Enterobacter 17 (1.7%)
	Acinetobacter 35 (3.6%)
	Providentia 11 (1.1%)

The most frequently tested antibiotic were Ampicillin, nitrofurantoin, cephalosporin, and norfloxacin.

There was a significant increase in testing for piperacillin tazobactam, cepheperazone sulbactam cefotaxime, cefepime, ciprofloxacin, levofloxacin and tobramycin during 2022 compare to 2016

Fosfomycin was present in the testing panel during 2022 and was not compared to 2016.

There was a significant increase in resistance proportion noted for imipenem, meropenem, ertapenem, ciprofloxacin nitrofurantoin, amikacin, cefotaxime in 2022 as compared. There was marginal increase in resistance percentage

levofloxacin, linezolid, norfloxacin, ceftazidime and cefuroxime in 2022 as compare to 2016.

Among these in resistance for Amoxycylav achieved statistical significance.

A significant increase in susceptibility was seen for tobramycin, cefepime, polymyxin in table 3. There was a marginal decrease in resistance for ampicillin, gentamicin continues cephalixin, cepheperazone sulbactam, and piper-tazobactam.

The decrease in resistance for tobramycin and statistical significance in the comp ($p=0.000$) table 3. Vancomycin susceptibility was 100 during both study period. Fosfomycin susceptibility for tested isolates was 100% in 2022.

Table 2: Antibiotic Panels Used During Different Study Intervals For Sensitivity Testing.

ANTI BIOTIC	2016	2022
AMP	440 (98.8)	876(89.7)
PIT	341(76.6)	932(95.5)
AMC	372 (83.5)	843(86.4)
CFX	168(37.7)	442(45.3)
CXM	243(54.6)	567(58)
CTX	364(81.7)	942(96.4)
CAZ	385(86.5)	679(69.6)
FEP	157(35.2)	507(51.9)
CFS	276(62)	835(85)

IMP	282(63.3)	846(86.6)
MRP	282(63.3)	839(85.9)
COT	53(11.9)	92(9.4)
NIT	417(93.7)	875(89.6)
NOR	378(84.9)	826(84.6)
CIP	29(6.5)	211(21.6)
LE	16(3.5)	187(19.1)
GEN	319(71.6)	892(91.3)
AK	315(70.7)	895(91.7)
TOB	37(8.3)	264(27)
FO	0()	67(6.9)
PB	15(3.3)	53(5.4)
VA	16(3.6)	77(7.9)
LZ	15(3.3)	63(6.4)

Table 3: Comparison of Bacteriological Resistance Rates with the 2 Study Intervals.

Anti-Biotic	2016	Total	%	2022	Total	%	P Value
AMP	392	440	89	852	876	97.2	<0.0001
PIT	91	341	26.7	396	932	42.4	<0.0001
AMC	89	372	24	408	843	48.3	<0.0001
CFX	122	168	72.6	378	442	85.5	0.0004
CXM	119	243	49	393	567	69.3	<0.0001
CTX	172	364	47.2	687	942	73	<0.0001
CAZ	198	385	51.4	483	679	71	<0.0001
FEP	69	157	44	312	507	61.5	=0.0001
CFS	79	276	28.6	419	835	50	<0.0001
IMP	14	282	4.9	268	846	31.6	<0.0001
MRP	12	282	4.2	227	839	27	<0.0001
COT	28	53	52.83	34	92	37	NS
NIT	119	417	28.5	471	875	54	<0.0001
NOR	186	378	49.2	702	826	85	<0.0001
CIP	11	29	29	137	211	65	<0.0074
LE	3	16	16	82	187	44	NS
GEN	157	319	319	577	892	64.6	<0.0001
AK	124	315	315	589	895	66	<0.0001
TOB	21	37	37	139	264	52.6	NS
FO		0	0	3	67	4.4	-
PB	-	15	15	9	53	17	NS
VA	-	16	16	16	77	21	NS
LZ	-	15	15	2	63	3.1	NS

Table 4: Bacteriological Profile of Uti Isolates Reported By Different Authors from Different Regions.

Ravishankar Et All	Dash Et All	Muhammad Et All	Deepak Et All	Manjunath Et All	Jan Herbeck Et All	Our Study
E.Coli(52)	E.Coli(68.8)	E.Coli (68)	E.Coli (37)	E.Coli (59.2)	E.Coli (26)	E.Coli (34.5)
Kleb Sp(17)	Cons (60.2)	Kleb Sp (9.1)	Kleb Sp (11)	Kleb Sp(12.1)	Kleb Sp (11.3)	Kleb Sp (27.4)
E. Faecalis(12)	E. Faecalis(9.7)	Staph (5.1)	Gbs (31)	E. Faecalis (10.1)	E. Faecalis (22.4)	Staph Sp (15.3)
Others(19)	Others (18)	Others (18)	Others (21)	Others (29)	Others (41)	Others (23)

Table 2: Antibiotic Resistance Reported Among Different Studies And Study Settings.

Anti-Biotic	Ravi shankar et al All uropath	Dash et al e.coli	Muhammad et al All uropath	Elk. S. sokhn et al e.coli	k.pnuem	Jan herback et al e.coli	Entero.sp	Manjunath et al 2011	Our study all uro pathogens
AMP	81	94.7	86	-	-	55.8	10.6	80.4	97.2
PIT	18	-		14	21	14	-	4.4	42.4
AMC	-	63.7		-	-	14.3	-	70.4	48.3
CFX	77			-	-	-	-	49.4	81.5
CXM	68			54	44	12.5	-	47.4	69.3
CTX	70			-	-	9.5	-	-	73
CAZ	62			27	25	8.8	-	46.5	71.1
FEP	-			24	21	23.4	-	14.4	61.5
CFS	-			-	-	-	-	-	50
IMP	32			-	-	-	-	7.5	31.6
MRP	38.3			-	-	-	-	-	27
COT	60	51.9		45	39	34.6	-	47.9	37
NIT	30	9.8		-		4.8	48	5.3	54
NOR	62			30	36	-	-	53.3	85
CIP	63	53.4		30	34	42.1	-	73	65
LE	80			-	-	-	-	-	44
GEN	47	38.3		17	18	7.1	-	40.2	64.6
AK	18	5.3		20	22	1.3	-	6.9	66
TOB	-			-	--	-	-	5.6	52.6
FO	0			4	3	-	-		4.4
PB	-			-	-	-	-		17
VA	-			-	-	-	1		21
LZ	-			-	-	-	-	0.1	3.1

Discussion

The spectrum of Europe pathogens causing both hospital acquired urinary tract infection and community acquired urinary tract infection has been more or less similar and constant over periods throughout the world in our analysis in both the periods the most common organisms were e coli 56.6% versus 51.6%, Klebsiella pneumonia 14.7% versus 16.5% Enterococcus 11.6% versus 12% and pseudomonas aeruginosa 4.5% versus 5%. This spectrum is similar to the previous studies. Most authors have reported Escherichia coli and Klebsiella pneumonia among the top 3 causative organisms for UTI which is similar in our study. The causative spectrum is very much similar with the top 6 organism more or less of same prevalence in both the periods of our study table. In this aids in doing a fair comparison between the 2 study groups in our institution the antimicrobial susceptibility testing and reporting have been based on CLSI guidelines. About 88% of the reporting in 2016 and 86% of the reporting in 2022 where for the 3 groups of pathogens namely enterobacterial Enterococcus species and pseudomonas species. Hence the pattern of antimicrobial susceptibility testing and reporting would be largely influenced by these organisms during the study periods. Antimicrobial resistance has been reported

worldwide for the prevalence has been waiting across geographical regions and study settings. Study for monitoring antimicrobial resistance trends data had found that the prevalence of ESBL producers among the Enterobacteriaceae was highest in Asia and middle east countries while it was much less in North America.

Our study showed a higher prevalence of resistance to most antibiotics tested. Among the tested antibiotics only Amikacin, Piperacillin-tazobactam, Vancomycin, Fosfomycin and acceptable sensitivity. This prevalence pattern is similar to the compliance of review of various other particles referred to for comparison and all had recently reported a much higher prevalence of assistance for all antibiotics as compared to our study with even carbapenem resistance reaching 40%. The increased prevalence of carbapenem resistance in our study and similar geographical regions could be due to the higher prevalence of gene among the ESBL isolates. On the other hand another article had reported a much lesser prevalence from resistance of various antibiotics in their recent analysis. In the starting from the United states 2022 across both Community and Hospital e isolates AMR prevalence was very low with maximum resistance observed from cotrimoxazole while carbapenems hand 100 percent sensitivity. Our

analysis shows the prevalence of AMR is alarmingly high in the developing countries as compared to developed nations in concurrence with other authors. Several others have reported increasing trends in AMR from various regions by comparing 2 or more periods. Many others had earlier reported a significant increase in AMR in north India over a period of 5 years.

In a study from another part of South India over 5 years on *Escherichia coli* infections there was a significant increase in resistance from quinolones and piperacillin tazobactam. The study also showed a significant increase in the prevalence of ESBL producers over the study. The above discussion shows that there has been an increasing trend in the resistance in general across the world though the rates and patterns of increased varied widely.

The trend of increase is at an alarmingly higher in middle and low income countries with carbapenem resistance rates approaching nearly 35% this calls for urgent strengthening of AMR surveillance and implementation of strong alms programs in these regions. On the positive side our study showed increased susceptibility for many antibiotics among which the increase for tobramycin and cephalexin in 2022 compared to 2016 was statistically significant however there has been a lack of consistent reporting on the increasing susceptibility for the antibiotics over the time period. Reporting of this might be useful and revisiting the guidelines for the treatment of UTI periodically.

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