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Original Research Article

Current Scenario of Antimicrobial Drug Resistance Pattern of Bacteria Isolated from Patients of Urinary Tract Infection Attending Tertiary Care Teaching Hospital, Vijayapur.

Leela Hugar[1], Daneshwari C. Kottalamath[2], Chandrashekhar B. Bhuyyar[3]

[1]MBBS, MD, Assistant Professor, Department of Pharmacology, BLDE(DU)'S Shri B. M. Patil Medical College Hospital and Research Centre, Vijayapur, Karnataka

[2]MBBS, PG Student, Department of Obstetrics and Gynaecology, Government Medical College

[3]MBBS and MD, Associate Professor, Department of Forensic Medicine and Toxicology, BLDE(DU)'S Shri. B.M.Patil Medical College Hospital And Research Centre, Vijayapur, Karnataka,

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Corresponding author: Dr. Daneshwari C. Kottalamath
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Abstract

Background: Detection of UTI causing pathogens and analysing resistance pattern of these pathogens to commonly prescribed antibiotics in the clinical practice is essential and helpful in improving the efficacy of empirical treatment.

Objectives: this study was conducted to analyse the current trend of antimicrobial drug resistance pattern of bacteria isolated from patients of urinary tract infection.

Methods: A total of 120 positive urine culture and sensitivity reports of either sex and all the age groups were analysed. Sensitivity/resistance of isolated microorganisms to commonly used antimicrobial agents was detected by Kirby-Bauer disc diffusion method in the laboratory.

Results: E coli (50%) was the most common organism isolated followed by Klebsiella (20%), Pseudomonas aeruginosa (10%), Enterobacter (7%), Staphycococcus aureus (5%), CONS (5%) and Citrobacter (3%). The overall antimicrobial sensitivity pattern to uropathogens was the highest to FOS (70%) and NFT (70%). Moderate susceptibility was seen with AMI (67%) and C+S (51%).Highest resistance was seen with C+C (92.5%) followed by AMP (91%), and other Penicillins, AZI, other Cephalosporins, Fluoroquinolones, COT.

Conclusion: This study provides valuable laboratory data to monitor the status of antimicrobial resistance among uropathogens and to improve treatment recommendations in a specific geographical region. From the study, it is clear that, E. coli is still the most common uropathogen. Sensitivity to nitrofurantoin, fosfomycin and amikacin are still retained and may be prescribed for complicated UTI, hence they should be used as a reserve antibiotics to prevent the development of resistance.

Keywords: Antimicrobial Resistance, Susceptibility, Uropathogens, *Urinary Tract* Infection (UTI)

Introduction

Urinary tract infection (UTI) is a common and painful human illness that, fortunately, is rapidly responsive to modern antibiotic therapy. UTI occurs far more commonly in females than in males between 1 year and ~50 years of age, UTI and recurrent UTI are predominantly diseases of females. The prevalence of asymptomatic bacteriuria is ~5% among women between ages 20 and 40 and may be as high as 40–50% among elderly women and men. The uropathogens causing UTI vary by clinical syndrome but are usually enteric gram-negative rods. [1]

UTI can be caused by Gram-negative bacteria such as *Escherichia coli (E coli)*, *Klebsiella* species, *Enterobacter* species , and *Proteus* species. *E. coli* is the most common organism causing both community as well as hospital-acquired UTI. [2]

Detection of UTI causing pathogens and analysing resistance pattern of these pathogens to commonly prescribed antibiotics in the clinical practice is essential and helpful in improving the efficacy of empirical treatment. [3]

With the inappropriate and inadvertent use of higher antibiotics, these bacterial isolates have acquired multidrug resistance and it has become much tougher than ever to treat these infections. UTI caused by multidrug-resistant (MDR) **E. coli** increases the cost of treatment, morbidity, and mortality, especially in developing countries like India. As the antibiotic pipeline is empty with only few alternatives available for treating these resistant infections, old antibiotics like Fosfomycin, Nitrofurantoin, Colistin have gained importance recently. [4,5]

In almost all cases of UTI, empirical antimicrobial treatment is initiated before the laboratory results of urine culture are available. Antibiotic resistance may develop in uropathogens due to misuse and overuse of antibiotics. Since resistance rates vary by local geographic region, with individual patient characteristics, and over time, it is important to use current and local data when choosing a treatment regimen. [6,7]

Hence, regular antimicrobial susceptibility surveillance is essential for regional level monitoring of resistance patterns and an antibiotic policy may help to preserve the effectiveness of antimicrobial agents and for better patient management. In this context, this study was conducted to analyse the current trend of antimicrobial drug resistance pattern of bacteria isolated from patients of urinary tract infection attending tertiary care teaching hospital, Vijayapur. Clinical laboratory records of cases of urinary tract infection were studied and antimicrobial susceptibility results was analysed for recommending suitable antimicrobial therapy.

Methodology

This cross sectional observational study was conducted in the department of Pharmacology in collaboration with the department of Microbiology, BLDE (Deemed to be University)'s Shri B.M. Patil Medical College Hospital and Research Centre, Vijayapur, Karnataka. Study was performed in 2 months, from 1st June 2017 to 31st July 2017. Data was collected from microbiology laboratory records for culture and sensitivity of uropathogens. Positive urine culture reports for uropathogens and its sensitivity pattern to antimicrobial agents was collected from Central Microbiology Laboratory of same institute. Institutional ethical clearance was obtained before starting the study.

A total of 120 positive urine culture and sensitivity reports of either sex and all the age groups were analysed. Sensitivity/resistance of isolated microorganisms to commonly used antimicrobial agents was detected by Kirby-Bauer disc diffusion method in the laboratory.

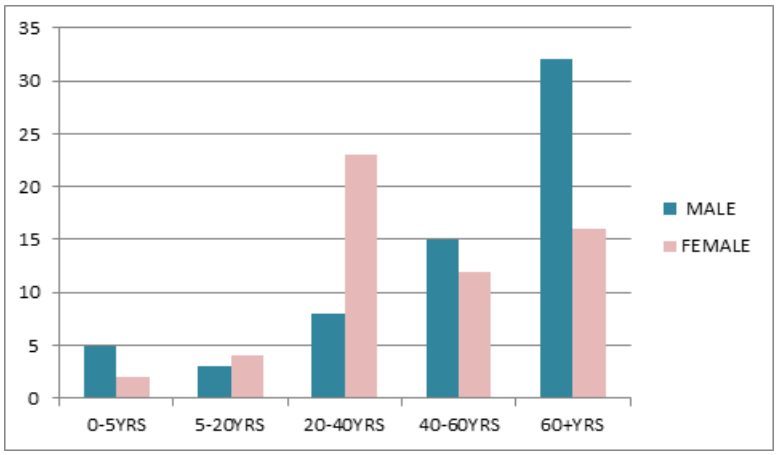
[8]

Antibiotics against which sensitivity was tested included Amoxicillin (AMO), Nitrofurantoin (NFT), Cotrimoxazole (COT), Norfloxacin (NOR), Ofloxacin (OFL), Ciprofloxacin (CIP), Levofloxacin (LEV), Azithromycin (AZI), Gentamicin (GEN), Ceftazidime + Clavulanic acid (C+C), Ceftazidime (CFT), Ceftriaxone + Sulbactam (C+S), Piperacillin+Tazobactam (P+T), Cefotaxime (CFO), Fosfomycin (FOS), Amikacin (AMI), Ampicillin (AMP).

The collected data were subjected to the statistical evaluation. Descriptive statistics were used for the analysis, and the results were expressed as frequency and percentage. Microsoft Excel 2010 software was used to analyse the data.

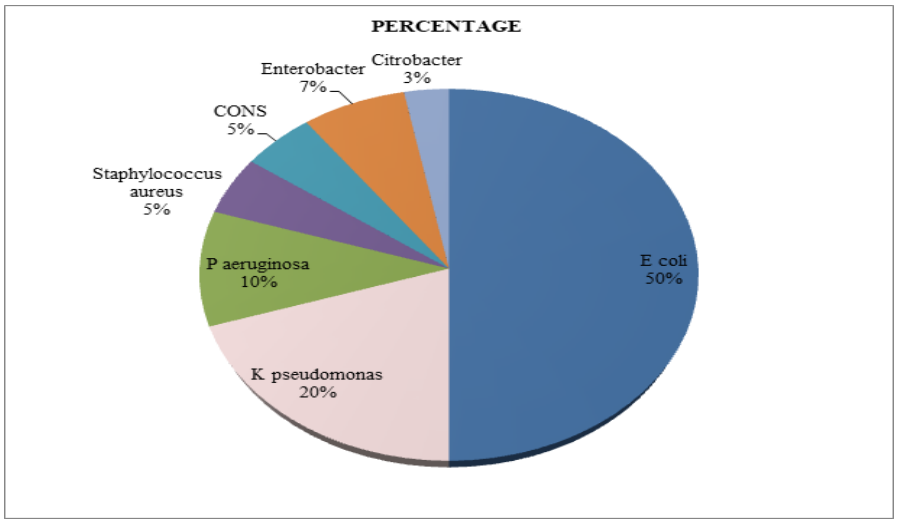
Results

120 culture sensitivity reports were analyzed, samples from male patients were 68 (57%) and that of females were 52 (43%). Males of age group 0-5 years and above 60 years and females of age group 20-40 years were mostly affected. [Table No.01 and Graph No.01]



Graph no.01: Percentage of age-sex ratio

E coli (50%) was the most common organism isolated followed by Klebsiella (20%), Pseudomonas aeruginosa (10%), Enterobacter(7%), Staphylococcus aureus (5%), CONS(5%) and Citobacter (3%).[Graph No.02]



Graph no.02: percentage of organisms isolated

E. coli was most sensitive to NFT (96.7%), FOS (91.7%) AMI (88.3%) and moderately sensitive to C+S(68%) , P+T(65%) and less sensitive to GEN (42%), Fluoroquinolones , COT (33%), CFT (18%), AMP (15%), AZI(15%), AMO (8%), CFO (8%), and C+C (3%).

Klebsiella species was most sensitive to Fosfomycin (91.6%), moderately sensitive to NFT (66.66%), C+S(62.5%), P+T(50%) and less sensitive to GEN, Fluoroquinolones, COT, CFT, AMP, AZI, AMO, CFO and C+C. [Table-2]

Table 1: Percentage Of Age-Sex Ratio

AGE GROUP	TOTAL NUMBER (%) n=120	MALE (%) n=63	FEMALE (%) n=57
0-5YRS	7 (6)	5 (71)	2 (29)
5-20YRS	7 (6)	3 (42)	4 (58)
20-40YRS	31 (27.5)	8 (24)	23 (76)
40-60YRS	27 (22.5)	15 (55)	12 (45)
60+YRS	48 (38)	32 (68)	16 (32)

Pseudomonas aeruginosa showed higher sensitivity to NOR (66.7%), LEV (66.7%) and least sensitivity to AMP, P+T, C+C (8.3%), Staphylococcus aureus showed highest sensitivity to AMO(100%), CFO (100%) and moderate sensitivity to GEN and COT, and 100% resistance to the remaining antibiotics. CONS showed highest sensitivity to CFO and C+C (66.7%) and least sensitivity to the remaining antibiotics. Citrobacter showed highest sensitivity to FOS and AMI(100%) followed by fluoroquinolones (50-75%), AZI, P+T, C+S,CFO (75%) and least sensitivity to NFT, AMO, AMP. Enterobacter showed higher sensitivity to NOR (62.5%) and GEN (50%) and least sensitivity to the remaining antibiotics. [Table-2]

Table 2: Antibiotic Susceptibility Pattern Of Individual Organisms

Antibiotic	Susceptibility pattern	Ecoli (n=60)	K pneumonia (n=24)	P aeruginosa (n=12)	S aureus (n=06)	CONS (n=06)	Enterobacter (n=8)	Citrobacter (n=4)
AMO	S	5 (8.3%)	5 (20.8%)	2 (16.7%)	6 (100%)	1 (16.7%)	0 (0%)	1 (25%)
	R	55 (91.7)	19 (79.2)	10 (83.3)	0 (0)	5 (83.3)	8 (100)	3 (75)
NFT	S	58 (96.7)	16 (66.7)	6 (50)	0 (0)	0 (0)	3 (37.5)	1 (25)
	R	2 (3.3)	8 (33.3)	6 (50)	6 (100)	6 (100)	5 (62.5)	3(75)
COT	S	20 (33.3)	7 (29.2)	3 (25)	3 (50)	2 (33.3)	0 (0)	2 (50)
	R	40 (66.7)	17 (70.8)	9 (75)	3 (50)	4 (66.7)	8 (100)	2 (50)
NOR	S	23 (38.3)	7 (29.2)	8 (66.7)	0 (0)	0 (0)	5 (62.5)	3 (75)
	R	37 (61.7)	17 (70.8)	4 (33.3)	6 (100)	6 (100)	3 (37.5)	1 (25)
OFL	S	11 (18.3)	3 (12.5)	3 (25)	0 (0)	0 (0)	0 (0)	2 (50)

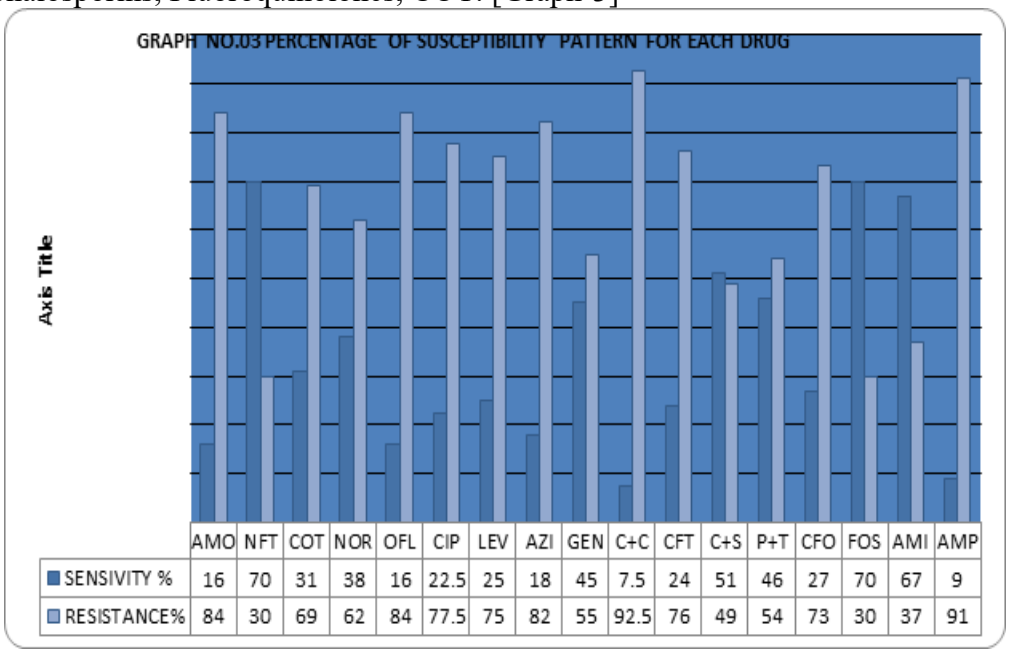
	R	49 (81.7)	21 (87.5)	9 (75)	6 (100)	6 (100)	8 (100)	2 (50)
CIP	S	14 (23.3)	3 (12.5)	7 (58.3)	0 (0)	0 (0)	0 (0)	3 (75)
	R	46 (76.7)	21 (87.5)	5 (41.7)	6 (100)	6 (100)	8 (100)	1 (25)
LEV	S	13 (21.7)	5 (20.8)	8 (66.7)	0 (0)	1 (16.7)	0 (0)	3 (75)
	R	47 (78.3)	19 (79.2)	4 (33.3)	6 (100)	5 (83.3)	8 (100)	1 (25)
AZI	S	9 (15)	9 (37.5)	1 (8.3)	0 (0)	0 (0)	0 (0)	3(75)
	R	51 (85)	15 (62.5)	11 (91.7)	6 (100)	6 (100)	8 (100)	1(25)
GEN	S	25 (41.7)	11 (45.8)	7 (58.3)	4 (66.7)	1 (16.7)	4 (50)	2 (50)
	R	35 (58.3)	13 (54.2)	5 (41.7)	2 (33.3)	5 (83.3)	4 (50)	2 (50)
C+C	S	2 (3.3)	0 (0)	1 (8.3)	0 (0)	4 (66.7)	2 (25)	0(0)
	R	58 (96.7)	24 (100)	11 (91.7)	6 (100)	2 (33.3)	6 (75)	4 (100)
CFT	S	11 (18.3)	7 (29.2)	5 (41.7)	0 (0)	1 (16.7)	2 (25)	2 (50)
	R	49 (81.7)	17 (70.8)	7 (58.3)	6 (100)	5 (83.3)	6 (75)	2 (50)
C+S	S	41 (68.3)	15 (62.5)	2 (16.7)	0 (0)	0 (0)	0 (0)	3 (75)
	R	19 (31.7)	9 (37.5)	10 (83.3)	6 (100)	6 (100)	8 (100)	1(25)
P+T	S	39 (65)	12 (50)	1 (8.3)	0 (0)	0 (0)	0 (0)	3(75)
	R	21 (35)	12 (50)	11 (91.7)	6 (100)	6 (100)	8 (100)	1(25)
CFO	S	5 (8.3)	7 (29.2)	4 (33.3)	6 (100)	4 (66.7)	3 (37.5)	3(75)
	R	55 (91.7)	17 (70.8)	8 (66.7)	0 (0)	2 (33. 3)	5 (62.5)	1 (25)
FOS	S	55 (91.7)	22 (91.7)	3 (25)	0 (0)	0 (0)	0 (0)	4 (100)
	R	5 (8.3)	2 (8.3)	9 (75)	6 (100)	6 (100)	8 (100)	0(0)
AMI	S	53 (88.3)	14 (58.3)	7 (58.3)	0 (0)	2 (33.3)	0 (0)	4 (100)
	R	7 (11.7)	10 (41.7)	5 (41.7)	6 (100)	4 (66.7)	8 (100)	0 (0)
AMP	S	9 (15)	1 (4.2)	1 (8.3)	0 (0)	0 (0)	0 (0)	0(0)
	R	51 (85)	23 (95.8)	11 (91.7)	6 (100)	6 (100)	8 (100)	4(100)

Table 3: Grade Of Susceptibility Of Each Causative Organism

E coli	NFT, FOS, AMI	C+S, P+T	GEN, Fluoroquinolones, COT, CFT, AMP, AZI, AMO, CFO, and C+C
K pneumoniae	FOS	NFT, C+S, P+T	C+C, COT, AMP, AMO, GEN, Fluoroquinolones, other Cephalosporins
P aeruginosa	NOR, LEV	GEN, CIP, NFT, AMI	FOS, COT, C+C, Penicillins, Cephalosporins
Enterobacter	NOR, GEN	NFT, FOS,	C+C, COT, AMP, AMO, Other

			Fluoroquinolones, Penicillins, Cephalosporins
Staphylococcus aureus	AMO, CFO	GEN, NOR	C+C, COT, AMP, Other Fluoroquinolones, Penicillins, Cephalosporins
CONS	CFO, C+C,	COT	FOS, GEN, AMP, Other Fluoroquinolones, Penicillins, Cephalosporins
Citrobater	FOS, AMI	CFT, P+T, CFO, C+S	NOR, NFT, GEN, AMO, Other Fluoroquinolones, Penicillins, Cephalosporins
Amoxicillin (AMO), Nitrofurantoin (NFT), Cotrimoxazole (COT), Norfloxacin (NOR), Ofloxacin (OFL), Ciprofloxacin (CIP), Levofloxacin (LEV), Azithromycin (AZI), Gentamicin (GEN), Ceftazidime + Clavulanic acid (C+C), Ceftazidime (CFT), Ceftriaxone + Sulbactam (C+S), Piperacillin + Tazobactam (P+T), Cefotaxime (CFO), Fosfomycin (FOS), Amikacin (AMI), Ampicillin (AMP).			

The overall antimicrobial sensitivity pattern to uropathogens was the highest to FOS (70%) and NFT (70%). Moderate susceptibility was seen with AMI (67%) and C+S (51%). Highest resistance was seen with C+C (92.5%) followed by AMP (91%), and other Penicillins, AZI, other Cephalosporins, Fluoroquinolones, COT. [Graph-3]



	AMO	NFT	COT	NOR	OFL	CIP	LEV	AZI	GEN	C+C	CFT	C+S	P+T	CFO	FOS	AMI	AMP
SENSIVITY %	16	70	31	38	16	22.5	25	18	45	7.5	24	51	46	27	70	67	9
RESISTANCE%	84	30	69	62	84	77.5	75	82	55	92.5	76	49	54	73	30	37	91

Amoxicillin (AMO), Nitrofurantoin (NFT), Cotrimoxazole (COT), Norfloxacin (NOR), Ofloxacin (OFL), Ciprofloxacin (CIP), Levofloxacin (LEV), Azithromycin (AZI), Gentamicin (GEN), Ceftazidime + Clavulanic acid (C+C), Ceftazidime (CFT), Ceftriaxone + Sulbactam (C+S), Piperacillin+ Tazobactam (P+T), Cefotaxime (CFO), Fosfomycin (FOS), Amikacin (AMI), Ampicillin (AMP).

Discussion

UTI is one of the commonly encountered diseases in developing countries with an

estimated annual global incidence of at least 250 million. [9] The resistance to the antimicrobials has increased over the years. Resistance rates vary from one region to another. Excessive and/or inappropriate use of antibiotics in treating UTIs is responsible for the emergence and spread of multi-drug resistant (MDR) urinary bacteria. [10-12]

Escherichia coli are the most common uropathogen accounting for 53% of cases. The incidence of *E. coli* as a causative pathogen in India varies from 48% to 65% as reported by various studies done earlier. [13,14]. In our study, E coli (50%) is the most common organism isolated.

In Our study E coli is most sensitive to NFT (97%) followed by FOS (92%), AMI (88%), P+T (65%) and less sensitive to GEN (42%), Fluoroquinolones, COT (33%), CFT (18%), AMP (15%), AMO (8%), CFO (8%), and C+C (3%). Similar findings were found in a study conducted by V Niranjan *et al*, where E coli were sensitive to NFT (82.1%), AMI (82.6%), P+T (78.2%) and the sensitivity to AMP, CFO, C+C, NOR CIP varied from 11-25 percent. [15] Similar results were also found in a Study conducted in Andhra Pradesh; *E coli* was least resistant to AMI (16%), moderate to ceftazidime (36%) and showed high resistance pattern to co-trimoxazole (69%), fluoroquinolones, and ampicillin (86%). [16] In Our study, Klebsiella species showed good sensitivity to NFT (66.66%) and least sensitivity to C+C (1%) and Fluoroquinolones (12-29%). In the study conducted by Prakash D *et al* , *K.* pneumoniae were less sensitive against CTZ (13.79%) similar to our study but NFT showed resistance of 62% and Fluoroquinolones LEV and OFL showed very good sensitivity of 89.6 and 82.76% respectively [17]. Reduced susceptibility to Fluoroquinolones in our study might be due to using these antibiotics without restriction.

In case of P aeruginosa, it showed highest sensitivity to NOR and LEV (67%) and less sensitivity to CIP (58.3%), OFL (25%), NFT (50%), Penicillins and Cephalosporins (0-1%). In study conducted by Prakash D *et al P. aeruginosa also* showed good sensitivity to LEV (60%) and resistance to penicillins and cephalosporins. In contrast to our study, this study showed highest sensitivity to CIP (95%) and OFL (85%). [17]

Enterobacter spp is most sensitive to NOR (62.5%) and less sensitive to other Fluoroquinolones (0%), penicillins and cephalosporins (0-1%) and NFT (37.5%), where as in conducted by Prakash D et al isolates showed similar results for NTF(18%); however, all 100% were sensitive to OFL, LEV in contrast to our study[17]. In our study staphylococcus aureus is sensitive to AMO, CFO (100%), and showed resistance to other penicillins, cephalosporins and fluoroquinolones, whereas study conducted by Prakash D *et al* all, S. *aureus* (100%) showed resistance against CFO. [17]

In our study, CONS shows maximum sensitivity to CFO, C+C (66.7%). Similar results were found in a study done in Andhra Pradesh where CONS was sensitive to Ceftazidime (76%) and CFO (68%). [15] Citrobacter showed highest sensitivity to AMI (100%) and least sensitivity to AMO, AMP.The above mentioned study showed similar susceptibility of Citrobacter to AMI, AMO and AMP. [15]

The overall antimicrobial sensitivity pattern to uropathogens was the highest to FOS (70%) and NFT (70%). Moderate susceptibility was seen with AMI (67%) and C+S (51%). Highest resistance was seen with C+C (92.5%) followed by AMP (91%), and other Penicillins, AZI, other Cephalosporins, Fluoroquinolones, and COT. The overall antimicrobial susceptibility was similar in study done by Prakash D *et al* [17] except for NFT (~50% sensitive) and Fluoroquinolones (highly sensitive to LEV and OFL >70%). In contrast to our study Somashekara SC *et al*

[16] showed overall good antimicrobial sensitivity to CFT and CEF (~65%).

The alarming finding in this study is the resistance to third generation cephalosporins and penicillins; This is an indication that many of the organisms are ESBL producers. [18] The other possible explanation behind this situation is that the III generation cephalosporin has been in use for a long period and must have been abused and over time organisms have developed resistant mechanisms due to changing their mode of action. The inappropriate usage of wide spectrum antibiotics, insufficient hygiene, immunosuppression, and a prolonged stay in the hospital are some other major etiological factors that elevate the chances of MDR infections. [19]

Reduced susceptibility of uropathogens to fluoroquinolones in the present study might be due to using antibiotics without restriction. In several studies it has been shown that the highly prescribing habits of the physicians are the driving factor for the antibiotic resistance for this group of antibiotic. [20–22] Recently, fosfomycin has been introduced for the treatment of infections with multidrug-resistant uropathogens for which there are limited treatment options. It has a unique mechanism of action, which may provide a synergistic effect with other antibiotics including β-lactams, aminoglycosides and fluoroquinolones. [23] Our study showed overall sensitivity of uropathogens to fosfomycin as 70%.

Overall, this study provides important data on antimicrobial resistance among uropathogens in this region of north Karnataka. Smaller sample size is a limitation of this study and it did not distinguish the distribution of organisms in the community acquired UTI and nosocomial UTI. As a consequence, the prevalence of microorganisms and their resistance pattern in both types of UTI could not be ascertained. [24]

Conclusion

This study provides valuable laboratory data to monitor the status of antimicrobial resistance among uropathogens and to improve treatment recommendations in a specific geographical region. From the study, it is clear that, E. coli is still the most common uropathogen. Antibiotics such as ampicillin, third generation cephalosporins, co-trimoxazole, fluoroquinolones (first-generation), azithromycin may not be appropriate choices for empirical treatment of UTI in our setting. Sensitivity to nitrofurantoin, fosfomycin and amikacin are still retained and may be prescribed for complicated UTI, hence they should be used as a reserve antibiotics to prevent the development of resistance. Hence, routine monitoring of antimicrobial susceptibility patterns is necessary. This will guide the clinicians in the empirical treatment of UTI and also for the preparation of antibiotic policy of the individual institute. This will avoid the indiscriminate use of antibiotics and prevent the further development of antimicrobial resistance.

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