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Original Research Article

Bacteriological profile and sensitivity pattern of microorganisms causing Urinary Tract Infection at a tertiary care center in eastern Uttar Pradesh

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Abstract

Introduction: Urinary tract infection (UTI) is one of the most common infections worldwide and the pattern of antimicrobial susceptibility varies widely in different geographical regions depending on the antibiotic policies.
Aim: To know the bacteriological profile of UTIs and the antibiogram of uropathogens in eastern Uttar Pradesh.
Material and Methods: This study was prospective and conducted at tertiary care center in one year study duration (2015). All the patients clinically suspected of having UTI were enrolled, culture and sensitivity was performed as per standard protocol, irrespective of age, sex, indoor/outdoor and associated illnesses.
Results: In a total of 2217 patients, 967 (43.61 %) were positive for uropathogen by culture, and positivity in female was high (46.48%) as compared to male (38.46%). *Escherichia coli* was the most common 346 (35.80 %) uropathogen followed by *Klebsiella pneumoniae* 183 (18.92%) and *Enterococcus species* 125 (12.92%). Gram negative isolates were most sensitive to imipenem (92%), ceftazidime-clavulanic acid (71%), piperacillin-tazobactam (68%), amikacin (60%), followed by nitrofurantoin (56%). Gram positive isolates were most sensitive to vancomycin (91%) followed by linezolid (80%) and amoxycillin-clavulanic acid (45 %).
Conclusion: UTI is a very common problem and rate of antibiotic resistance is relatively high. Imipenem, ceftazidime-clavulanic acid, piperacillin-tazobactam, amikacin, vancomycin and linezolid, were found sensitive against isolated uropathogens.
Keywords: Urinary Tract Infections (UTI), uropathogens, Antimicrobial susceptibility pattern.

1. Introduction

Urinary tract infections (UTIs) are the most common bacterial infection encountered in tertiary care settings.[1] Urine samples are the largest single category of specimens received by most microbiology laboratories, but the majority of the urine culture yield clinically insignificant results.[2] The diagnosis of UTI is primarily based on signs and symptoms rather than isolated laboratory findings; importantly, bacteriuria is not a disease thus, the collection and interpretation of urine cultures should be based on the clinical scenario.[3] Generally, women with acute uncomplicated cystitis culture are not recommended. However, for individuals with acute pyelonephritis or complicated UTI it is important to obtain a urine culture in order to find the appropriate antimicrobial regimen, prior to start empiric therapy.[4] Antimicrobial prescription should be prudent and rational. The choice of antimicrobial agents should be preferably based on the patient's allergy history, antibiogram pattern, availability, cost and compliance.[5] Overuse of antimicrobial in clinical situations where they are not necessary or in prolonged courses of therapy when shorter durations are effective, are responsible for causing antibiotic resistance and it renders a major public health problem worldwide.[6] Thus, the purpose of this study is to know the antibiogram of uropathogens and to guide the patients for appropriate antibiotics.

2. Material and Methods

The present study was undertaken to find out the prevalence of common micro-organisms causing UTI and to determine the antimicrobial sensitivity pattern among the patients attending Baba Raghav Das Medical College and associated Nehru Hospital, Gorakhpur, Uttar Pradesh, India.

2.1 Duration

Prospectively designed one year study duration i.e. from January 2015 to December 2015

2.2 Specimen

Clean-Catch midstream urine of the patients were collected in a sterile container and immediately transported to

the bacteriology laboratory. Guidelines for proper specimen collection were given to all patients on a printed card.[7]

2.3 Inclusion criteria

All patients clinically suspected of having UTI were subjected to semi-quantitative culture and sensitivity; all culture positive micro-organisms among any age group irrespective of sex distribution were included, except candiduria.

2.4 Specimen Processing:

Urine specimens were cultured semi-quantitatively for isolation of the microbial agents of UTI on blood agar and MacConkey agar media (Himedia, India & Merck, Germany). All the bacteria isolated from urine in this study were identified using conventional biochemical tests. [8]

2.5 Bacterial identification

Semi-quantitative culture of urine samples was done by calibrated loop method on 5% sheep blood agar and MacConkey agar plates and incubated in aerobic conditions at 37℃ for 24-48 hours. The urine cultures of colony count $>10^5$ colony forming units (CFU)/mL with no more than two species of microorganisms were considered as positive for UTI and cultures showing growth of more than two types of bacteria were considered contaminated. Positive cultures were further subjected to battery of various biochemical reactions for identification up to species level.[9]

2.5.1 Antimicrobial susceptibility testing

Antimicrobial susceptibility testing was done on Mueller-Hinton agar (Merck, Germany) using standard disk diffusion (Kirby Bauer's) technique. This test and interpretation of result was done according to Clinical and Laboratory Standards Institute (CLSI) guidelines to determine susceptibility of agents causing UTIs. [10]

The antimicrobial agents tested were amikacin (30 µg), gentamicin (10µg), cefotaxime (30 µg), ceftriaxone (30 µg), ceftazidime (30 µg), ceftazidime-clavulanic acid (30/10 µg), amoxycillin (10 µg), amoxycillin-clavulanic acid (20/10 µg), trimethoprim-sulfamethoxazole (25 µg), norfloxacin (10 µg), ciprofloxacin (5 µg), imipenem (10 µg), nitrofurantoin (300 µg), linezolid (30 µg), vancomycin (30 µg), teicoplanin (30 µg), tetracycline (30 µg), cefoxitin (30 µg), piperacillin-tazobactam (100/10 µg), (Himedia, India). [10]

2.5.2 Criteria for the selection of the ESBL producing strains

The isolates were tested for their susceptibility to the third generation cephalosporins e.g. ceftazidime (30 µg), cefotaxime (30 µg) and ceftriaxone (30 µg) by using the standard disc diffusion method, as per CLSI guidelines. If a zone diameter of < 22 mm for ceftazidime, < 27 mm for cefotaxime and < 25 mm for ceftriaxone were found, the strain was considered to be "suspicious for ESBL production". Simultaneously, the ESBL status was further confirmed by disk using beta-lactam antibiotic plus beta-lactamase inhibitor combination by phenotypic disk diffusion test. [10]

2.6 Statistical analysis

The statistical analysis was performed by using the Chi-square test and p- value of less than 0.05 was considered as statistically significant.

3. Result

A total of 2217 samples were collected in the study period of one year, of which 1424 (64.23%) were from female and 793 (35.77%) were from male. Culture positivity was 43.61% (967/2217) for significant bacteriuria irrespective of all age groups and sex. Among male patients maximum number of positivity were from age group less than one year, while in female patients the maximum number of positivity were found in age group 1-30 years as shown in table 1. In this study, out of 967 total culture positive samples, 648 (67.01%) Gram-negative bacilli and 319 (32.99%) Gram-positive cocci were isolated.

Table1: Age and sex wise distribution of UTI patients

Age (Years)	Total number of samples		Number of positive samples		Prevalence in %	
	Male	Female	Male	Female	Male	Female
<1 year	58	21	36	12	62.06	57.14
1-10	385	399	160	163	41.55	40.85
11-20	186	248	62	100	33.33	40.33
21-30	62	496	11	280	17.74	56.45
31-40	22	125	5	48	22.72	38.40
41-50	17	70	01	23	05.88	32.85
51-60	33	35	16	13	48.48	37.14
>60 year	30	30	14	23	46.66	76.66
	793	**1424**	**305**	**662**		
Total	**2217**		**967**		**43.61%**	

The most common isolated uropathogen was *E. coli* (35.80%) followed by *Klebsiella pneumoniae* (18.92%), *Enterococcus* species (12.91%), *Coagulase Negative Staphylococcus* (CoNS) (12.10%), *Staphylococcus aureus* (7.96%), *Acinetobacter species* (5.27%), *Citrobacter species* (3.42%), *Pseudomonas aeruginosa* (2.69%), and *Proteus species* (0.93%). The prevalence of UTI was 46.48% (662/1424) in female, 38.46% (305/793) in male as shown in table 2.

Table 2: Frequency and distribution of uropathogens

Isolated Bacteria	Total no. of positive isolates	Total %	No. of male	No. of female
Escherichia coli	346	35.80	83	263
Klebsiella pneumoniae	183	18.92	69	114
Enterococcus faecalis	90	9.30	34	56
Enterococcus faecium	35	3.61	17	18
Staphylococcus epidermidis	27	2.80	04	23
Staphylococcus saprophyticus	90	9.30	23	67
Staphylococcus aureus	77	7.96	30	47
Acinetobacter baumannii	38	3.93	15	23
Acinetobacter lwoffi	13	1.34	04	09
Citrobacter fruendii	30	3.10	08	22
Citrobacter koseri	03	0.32	01	02
Pseudomonas aeruginosa	26	2.69	14	12
Proteus vulgaris	06	0.62	02	04
Proteus mirabilis	03	0.31	01	02
Total	**967**	**100%**	**305**	**662**

The antimicrobial sensitivity of selected and recommended antimicrobial agents against Gram negative and Gram positive uropathogens are summarized in table 3 and 4 respectively.

Nearly all the isolates (Gram negative and Gram positive) were found to be resistant against most of the commonly used oral antibiotics. Overall Gram negative pathogens showed more resistance as compared to Gram positive organisms for empirical antibiotics commonly used to treat UTI.

Table 3: Antibiogram pattern of Gram negative urinary pathogens

Antimicrobial agents	*E. coli* (346)			*Klebsiella pneumoniae* (183)			*Acinetobacter spp.* (51)			*Citrobacter spp.* (33)			*Pseudomonas aeruginosa* (26)			*Proteus spp.* (09)		
	*S	IS	R	S	IS	R	S	IS	R	S	IS	R	S	IS	R	S	IS	R
Amikacin	225	69	52	115	00	68	20	00	31	11	00	22	12	01	13	07	00	02
Gentamicin	69	64	213	73	15	95	09	00	42	05	01	27	05	02	19	03	00	06
Ofloxacin	49	00	297	19	15	149	07	03	41	03	00	30	05	01	20	01	00	08
Ciprofloxacin	54	02	290	32	04	147	09	00	42	04	00	29	06	01	19	05	01	03
Levofloxacin	52	00	294	33	00	150	04	04	43	03	00	30	04	02	20	01	00	08
Ceftriaxone	72	00	274	24	00	159	05	00	46	04	00	29	03	00	23	02	00	07
Cefotaxime	73	00	273	23	00	160	03	00	48	04	00	29	03	00	23	01	00	08
Ceftazidime	73	00	273	25	00	158	05	00	46	05	00	28	05	00	21	02	00	07
Nitrofurantoin	218	00	128	112	00	71	24	00	27	07	01	25	01	01	24	02	02	05
Imipenem	321	00	25	166	00	17	49	00	02	31	02	00	21	04	01	08	01	00
Piperacillin-tazobactam	245	15	86	120	12	51	32	06	13	21	00	12	19	00	07	06	00	03
Ceftazidime-clavulanic acid	228	00	118	130	00	53	38	00	13	33	00	00	19	00	07	09	00	00

* S- Sensitive, IS- Intermediate sensitive, R-Resistant

Table 4: Antibiogram pattern of Gram positive urinary pathogens

Antimicrobial agents	*Enterococcus spp.* (125)			*S. aureus* (77)			CoNS† (117)		
	S	IS	R	S	IS	R	S	IS	R
Amoxycillin	26	00	99	16	02	59	27	03	87
Amoxycillin-clavulanic acid	39	00	86	42	00	35	63	00	54
Azithromycin	22	00	103	14	00	63	12	00	105
Cefazolin	20	00	105	32	00	45	53	00	64
Ciprofloxacin	09	02	114	19	00	58	22	00	95
Norfloxacin	10	00	115	13	00	64	18	00	99
Tetracycline	38	00	87	35	02	40	50	00	67
trimethoprim-sulfamethoxazole	11	00	114	22	00	55	19	00	98
Linezolid	98	00	27	69	00	08	87	00	30
Teicoplanin	62	00	63	51	00	26	23	6	88
Vancomycin	125	00	00	77	00	00	88	00	29

†CoNS –Coagulase Negative *Staphylococcus*, *S. aureus- Staphylococcus aureus*

In our study, antibiotic sensitivity pattern of Gram-negative isolates are imipenem (92%), ceftazidime-clavulanic acid (71%), pieracillin-tazobactam (68%), amikacin (60%), nitrofurantoin (56%), high level gentamicin (25%), ceftazidime (18%), ceftriaxone (17%), cefotaxime (17%), ciprofloxacin (17%), levofloxacin (15%) and ofloxacin (13%) as shown in table 5.

Table 5: Antibiogram pattern of Gram negative UTI isolates in percentage

Antimicrobial Agents	Antibiogram of total 648 Gram negative uropathogens (percentage)		
	S	IS	R
Amikacin	390 (60%)	70 (11%)	188 (29%)
Gentamicin	164 (25%)	82 (13%)	402 (62%)
Ciprofloxacin	110 (17%)	08 (01%)	530 (82%)
Ofloxacin	84 (13%)	19 (03%)	545 (84%)
Norfloxacin	97 (15%)	06 (01%)	545 (84%)
Ceftriaxone	110 (17%)	00	538 (83%)
Cefotaxime	107 (17%)	00	541 (83%)
Ceftazidime	115 (18%)	00	533 (82%)
Nitrofurantoin	364 (56%)	04 (01%)	280 (43%)
Imipenem	596 (92%)	07 (01%)	45 (07%)
Pipercillin-tazobactam	443 (68%)	33 (05%)	172 (27%)
Ceftazidime-clavulanic acid	457 (71%)	00	191 (29%)

In this study, Gram-positive organisms showed the following sensitivity pattern vancomycin (91%), linezolid (80%), amoxycillin-clavulanic acid (45%), tetracycline (39%), piperacillin (36%), teicoplanin (43%), cefazolin (33%), amoxycillin (21%), ciprofloxacin (16%), trimethoprim-sulfamethoxazole (16%), and azithromycin (15%) as displayed in table 6.

Table 6: Antibiogram pattern of Gram positive UTI isolates in Percentage

Antimicrobial agents	Antibiogram of total 319 Gram positive uropathogens (percentage)		
	S	IS	R
Amoxycillin	69 (21%)	05(02%)	245 (77%)
Amoxycillin-clavulanic acid	144 (45%)	00	175(55%)
Azithromycin	48(15%)	00	271(85%)
Cefazolin	105 (33%)	00	214 (67%)
Ciprofloxacin	50 (16%)	02 (01%)	267 (83%)
Ofloxacin	41 (13%)	00	278 (87%)
Tetracycline	123 (39%)	02(01%)	194 (60%)
trimethoprim-sulfamethoxazole	52 (16%)	00	267 (84%)
Linezolid	254 (80%)	00	65 (20%)
Teicoplanin	136 (43%)	06 (02%)	177 (55%)
Piperacillin	116 (36%)	18 (6%)	185 (58%)
Vancomycin	290 (91%)	00	29 (9%)

It has found that Gram negative isolates were mostly resistant to all third generation cephalosporins ceftazidime (82%), ceftriaxone (83%) and cefotaxime (83%) and among these most of them were sensitive against beta lactam plus beta lactamase inhibitor combination i.e, ceftazidime-clavulanic acid (69%) and showed 69.13 % overall prevalence of ESBL.

Table 7: Prevalence of ESBL among Gram negative isolates

Isolated bacteria	Culture positive	ESBL positive	% of ESBL	p-value
Acinetobacter spp.	51	43	84.31%	<0.05
Pseudomonas aeruginosa	26	19	73.07%	>0.05
Klebsiella pneumoniae	183	130	71.03 %	<0.05
Escherichia coli	346	228	65.89 %	<0.05
Citrobacter spp.	33	22	66.67 %	>0.05
Proteus spp.	09	06	66.67%	>0.05
Total % of ESBL	**648**	**448**	**69.13 %**	

In this study, *Acinetobacter species* found most common ESBL producer 43 out of 51 (84.31%), followed by 19 out of 26 (73.07%) of *Pseudomonas aeruginosa*, 130 out of 183 (71.03%) of *Klebsiella pneumoniae* and 228 out of 346 (65.89%) of *E. coli*, most of these isolates confirmed as ESBL producing strains by phenotypic confirmatory disc diffusion test using beta lactam plus beta lactamase inhibitor combination as shown in table 7.

4. Discussion

Early detection and selection of an appropriate effective antimicrobial agent is highly essential for effective management of patients suffering from UTIs. In our study, male children (<1 year) have higher incidence of UTI than female children of the same age group. This was in accordance with a similar study in which during the first year of life, the incidence of UTI in female child was low as compared to male. [11] In this study, it has been found that during reproductive age group (18-40 years) the prevalence of UTI in female was high as compared to male as similar with other study.[12] Female are more prone to UTI because of anatomic reasons; short and straight urethra and short distance between the ostium of the urethra and the anus contribute to easy colonization of the peri-urethral region with enteric bacteria.[13] High prevalence rate of UTI found in elderly female in this study with age group of more than 60 years, several factors importantly influence the occurrence of UTI among postmenopausal women. The reason for high prevalence of UTI include, a recurrent history of UTIs, nonsecretor status, and possibly other inherited predispositions, as well as urodynamic factors, especially incontinence, residual urine volume, and presence of a cystocele.[14] In the present study, overall prevalence is also high in female (46.48%) as compared to male (38.46%), which is consistent with other study. [15]

Among Gram negative uropathogens, *Escherichia coli* was the most common isolated organism (35.80%) followed by *Klebsiella pneumoniae* (18.92%), which is similar with other studies. [15,16] Several factors are responsible for attachment of Enterobacteriaceae to the uroepithelium like, they colonize the urogenital mucosa with adhesin and pili. [17]

In our study, among higher antibiotics imipenem (92%), ceftazidime-clavulanic acid (71%), piperacillin-tazobactam (68%) followed by amikacin (60%) and nitrofurantoin (56%) were found to be the most effective antibiotics against commonly isolated Gram negative uropathogens whereas flouroquinolones(13-17%) and oral cephalosporins (17%) found to be least sensitive, as observed in similar other study where, antibiotic sensitivity test performed for *Escherichia coli*, *Klebsiella pneumoniae* showed lowest sensitivity to cephalosporins (28%) and highest sensitivity to imipenem(100%). [18] Although all of these are parenteral antibiotics and is difficult to use in outdoor patients setting except nitrofurantoin, which is oral antibacterial agent, cheap and easily available in developing countries. *E. coli* was most frequently isolated uropathogen (35.80%) and consistently sensitive (63%) to nitrofurantoin as shown by other similar study.[19] The consistent and high-level susceptibility of *E. coli* to nitrofurantoin may be influenced by its narrow spectrum of activity, limited indication, narrow tissue distribution, and limited contact with bacteria outside the urinary tract. [20] Thus, nitrofurantoin has become an important oral agent in the treatment of uncomplicated urinary tract infections. [21]

Among Gram positive isolates, *Enterococcus species* were the most common isolated organism (12.92%) followed by coagulase negative *Staphylococcus* (12.10%), in contrast with other study where *Enterococcus species* was found as the most frequent organism (15%), followed by *Staphylococcus aureus* (1%).[22]

Our results indicated that only (32.99%) 319/967 of the UTI cases were caused by Gram-positive microorganisms. *Enterococcus spp.* was detected as a more resistant uropathogen than *Staphylococcus aureus* Moreover, *Enterococcus spp*. showed a high rate of resistance to norfloxacin (92%), ciprofloxacin (91%) and trimethoprim-sulfamethoxazole (91%) but showed highest sensitivity to vancomycin (100%) and linezolid (78%), these findings are in agreement with other study.[22] Similarly, *Staphylococcus aureus* showed highest sensitivity to vancomycin and linezolid (100%) and (90%) respectively. Overall vancomycin and linezolid had strong antimicrobial activity against Gram positive isolates similar with other studies[22,23] whereas, trimethoprim-sulfamethoxazole are recommended as a first-line therapy for the management of uncomplicated UTIs, but our study revealed high rate of resistance (84%) against this antimicrobial agents. [24]

Our study, demonstrated the highest frequency of ESBL production by *Acinetobacter spp.* (84%) whereas, Alyamani *et al.*, reported (94%). [25] The second higher producer of ESBL was *Pseudomonas aeruginosa* (73.07%), in contrast Shaikh *et al.*, reported 25.13% ESBL prevalence, which is much lower than our finding. [26] This shows a rising trends of ESBL in these days and the reason may be indiscriminate and rampant use of cephalosporins for the treatment of common infections, as well as horizontal transmission of resistant genes among hospital acquired bacterial strains. The prevalence of ESBL was 71% in *Klebsiella species* and 66% in *E.coli*, which is much higher as compared to other study; where 35% *E. coli* and 23.6 – 41% *Klebsiella pneumoniae* were found to ESBL producers. [18, 27] Most of these isolates were confirmed by combination of beta lactam and beta lactamase inhibitor and showed overall 69.13 % of ESBL producing strains.

In developing countries, the frequent prescriptions of antibiotics for the treatment of UTI and community level poor hygiene are the reasons for the ever-growing antimicrobial resistance in uropathogens. Urinary pathogens showed resistance to commonly used antibiotics like flouroquinolones but good sensitivity was observed with nitrofurantoin. The susceptibility and resistance patterns as observed in the defined geographical area should be considered before starting empirical treatment for UTI. As susceptibility pattern is changing with the change in use of type of antibiotics, a regular monitoring of antibiotic resistance pattern is very helpful in ensuring proper therapy

for patient with urinary tract infections.

We conclude that clinicians should encourage accurate bacteriological diagnosis of each symptomatic patient as far as possible and refer to the record of local microbial isolation and their antibiogram in cases of emergency or in areas where the culture facility is not available and to minimize the antimicrobial resistance. The microbiology laboratory could play an important role in record keeping of UTI isolates and their antibiogram, may succour clinicians for better and efficient management of these cases.

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