

Spectrum of Bacterial Pathogens and their Antibiogram from Cases of Urinary Tract Infection at a Tertiary Care Centre of Nashik, Maharashtra

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Abstract

Background: Urinary tract infection and asymptomatic bacteriuria are one of the most common infections encountered in a routine clinical setting. These also forms one of the most common indications of antimicrobial therapy even before the laboratory results of the cultures becomes available. This mainly accelerates the rate of antibiotic resistance among these routinely isolated uropathogens.

Aims and Objectives: The study was designed with two main aims and objectives:

1. To study the prevalence of different organisms isolated from urine samples of urinary tract infection (UTI) suspected patients
2. To study the antibiotic sensitivity patterns of the bacterial isolates under study

Materials and Methods: This prospective observational study was conducted on 100 urine samples. A structured information of the patient was collected. The samples was examined microscopically and then cultures were inoculated according to the standard laboratory precautions on appropriate media. The cultures were later analysed for antibiotic sensitivity by Kirby Bauer Disk Diffusion Technique. Appropriate statistical method was used to analyse the data.

Results: The overall culture positivity in clinically suspected cases of UTI was 60%. The most common organism isolated was Escherichia coli (28.16%) followed by Klebsiella pneumonia (22.53%). All the gram negative organisms were found to be sensitive to Colistin. Sensitivity to carbapenems, beta lactam inhibitors, aminoglycosides and nitrofurantoin was also good. Among gram positive organisms sensitivity to glycopeptides, linezolid, nitrofurantoin, rifampicin and fluoroquinolones was found to be fairly good.

Conclusion: Regular monitoring is required to establish reliable information about susceptibility pattern of urinary pathogens for optimal empirical therapy of patients with UTI.

Keywords: UTI, bacteriuria, Escherichia coli.

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Introduction

Urinary tract infection (UTI) is one of the commonest bacterial infections in community as well as in the hospital settings. It also comes with a high rate of morbidity and economic burden. It has been estimated that 150 million people were infected with UTI per annum worldwide which costed global economy more than 6 billion US dollars[1]. A urinary tract infection, or UTI, is an infection in any part of the urinary system, which includes, bladder, ureters, and urethra. A simple UTI, or simple cystitis, is an infection of the lower Urinary tract and is characterized by symptoms such as dysuria, frequency, urgency, and suprapubic tenderness. The UTI is classified into two types that is uncomplicated and complicated UTI mainly for treatment purposes.

The normal female urinary tract has a comparatively short urethra, and therefore, carries an inherent predisposition to proximal seeding of bacteria. The other main factors which make females more prone to UTI are pregnancy and sexual activity [2]. In pregnancy, the physiological increase in plasma volume and decrease in urine concentration develop glycosuria in up to 70% women which ultimately leads to bacterial growth in urine [3]. Also in the nonpregnant state the uterus is situated over the bladder whereas in the pregnant state the enlarged uterus affects the urinary tract [4]. Sexual activity in females also increases the risk of urethra contamination as the bacteria could be pushed into the urethra during sexual intercourse as well as bacteria being massaged up the urethra into the bladder during child birth. Simple cystitis, a one-off episode of ascending pyelonephritis, and occasionally even recurrent cystitis in the right context can be considered as uncomplicated UTI, provided

there is a prompt response to first-line antibiotics without any long-term sequela.

Any urinary tract infection that does not conform to the above description or clinical trajectory is considered a complicated UTI[5,6,7]. Examples of a complicated UTI include:

- Infections occurring due to anatomical abnormalities, for example, an obstruction, hydronephrosis, renal tract calculi, or colovesical fistula
- Infections occurring due to an immune compromised state, for example, steroid use, post chemotherapy, diabetes, elderly population, HIV)
- Atypical organisms causing UTI
- Recurrent infections despite adequate treatment (multi-drug resistant organisms)
- Infections are occurring in pregnancy (including asymptomatic bacteriuria)
- Infections are occurring after instrumentation, nephrostomy tubes, ureteric stents, suprapubic tubes or Foley catheters

The spectrum of bacteria causing complicated UTI is much broader than of those causing uncomplicated UTI. However, the most commonly encountered microorganisms are Gram negative bacteria including *Escherichia coli*, *Klebsiella pneumoniae*, *Citrobacter* spp., *Enterobacter aerogenes*, *Pseudomonas aeruginosa*, and *Proteus vulgaris* and gram positive cocci including *Staphylococcus aureus*, and *Enterococcus* spp. [8]

Mostly in a clinical setting a symptomatic case of UTI is treated with a broad spectrum antibiotics before the culture results becomes available which usually takes around 48 hours of time. This inappropriate

and non-judicious usage of antibiotics has resulted in the development of worldwide antibiotic resistance in bacteria, leading to the emergence of multi resistant strains of bacterial uropathogens. Hence, it is necessary to circumvent non-judicious use of antibiotics that lead to the emergence of antimicrobial resistance and most appropriate antibiotics should be opted for first-choice empiric treatment of UTI. The antimicrobial susceptibility pattern among bacteria varies from country to country[9]. The Infectious Diseases Society of America recommends that regional surveillance should be conducted to monitor changes in susceptibility of uropathogens in specific regions.[10]

In present scenario where the antimicrobial resistance pattern is changing at an alarming rate our study highlights the importance of selection of antimicrobial agents on the basis of the most likely pathogen and its expected resistance pattern in a geographic area. Therefore there is a need for periodic monitoring of etiologic agents of UTI and their resistance pattern in the community. This study was undertaken in view of paucity of data of the most common causative agents causing UTI and their resistant patterns in this geographical area.

Material and Methods

Type of study: Prospective Study

Place of study: Department of Microbiology at a tertiary care hospital in Maharashtra

Duration of study: Three months

Study Population: Urine samples were collected from outpatients and inpatients who had signs and symptoms of urinary tract infection(UTI). Patients who had two or more episodes of UTI due to prolonged hospitalization or any other cause were considered as a separate case of UTI. A total of 100 urine samples were collected out of which 60 were females and 40 were males. The age of patients included in the study ranged from 0 to 80 years

Sample Collection: Clean catch midstream urine was collected from each patient into a 20mL calibrated sterile screw-capped universal container. The specimens were labelled, transported to the laboratory, and analyzed within 4 hours. All patients were well instructed on how to collect sample aseptically prior to sample collection to avoid contaminations from urethra. Institutional ethics committee approval was taken before starting the study.

Collection of mid-stream urine:

Appropriate instructions were given to patient regarding collection of mid-stream urine collection as follows:

1. Read the instructions carefully and follow each of the steps to ensure you collect the correct specimen for the test. Early morning urine specimens are preferred, although urine collected at other times of the day are acceptable.
 2. Use the sterile screw-capped urine container provided to you for collection.
 3. Wash and dry your hands thoroughly.
 4. Remove the cap on the container and set it aside. You should not touch the inner surface of the cap or the container.
 5. For women, keep the legs apart and hold the skin folds apart while voiding. For men, retract the foreskin (if uncircumcised) while voiding.
 6. Pass a small amount of urine into the toilet.
 7. Midway through urination, fill the container to half full
 8. You may finish voiding into the toilet until the bladder is empty
 9. Replace the cap and tighten firmly
- For sanitary reasons, it is recommended that the container be enclosed in a plastic bag.
10. Wash your hands thoroughly
 11. Deliver the container to the laboratory as soon as possible after completion of the collection with proper labelling of the sample and duly filled requisition form.

Sample Processing

Physical parameters: The collected urine specimens was first examined for physical parameters such as volume, pH, color, appearance was analyzed and recoded

Microscopy: To examine the urine specimens, microscopically wet preparation was made by taking a drop of urine sample and transferring to a slide and covering it with a glass slide. Finally it was examined under 10x and 40x objective. Pus cells, crystals, casts, were recorded.

Culture: A calibrated loop method was used for the isolation of bacterial pathogens from urinary samples. A sterile 4.0mm platinum wired calibrated loop was used which delivered 0.001mL of urine. A loopful urine sample was plated on Cystine-Lactose-Electrolyte Deficient (CLED) agar. The inoculated plates were incubated aerobically at 37°C for 24 hours. The number of isolated bacterial colonies was multiplied by 1000 for the estimation of bacterial load/mL of the urine sample. A specimen was considered positive for UTI if an organism was cultured at a concentration of $\geq 10^5$ cfu/mL .(11)

Identification: Identification of bacterial isolates was done on the basis of their cultural and biochemical characteristics. Gram negative bacteria were identified by a battery of standard biochemical tests which included Indole test, Citrate test, Triple sugar iron agar test, Urease test and Sugars and others wherever required. The gram positive microorganisms were identified with the corresponding laboratory tests: catalase, coagulase, mannitol test for *Staphylococcus aureus* and *Enterococcus spp.* Identified and pure isolates were maintained in nutrient agar slants and were subcultured periodically.

Antibiotic Susceptibility Testing: Isolates were tested for antimicrobial susceptibility testing by the standard Kirby Bauer's disc diffusion method [12]. Standard inoculums adjusted to 0.5 McFarland was swabbed on Mueller Hinton agar and was allowed to soak for 2 to 5 minutes. After that antibiotic disks were placed on the surface of media

and pressed gently. Mueller Hinton agar plates were then incubated at 37°C for 24 h. After 24 h the inhibition zones were measured and interpreted by the recommendations of clinical and laboratory standards 2020.[13] Organisms resistant to more than three classes of drugs were considered as Multi Drug Resistant.(14)

The following standard antibiotic discs were used for the isolates Amikacin(AK), Amoxicillin-clavulanic acid(AC), Ampicillin,(AM), Cefazolin(CZ), Clindamycin(CD), Ceftazidime(CAZ), Cefipime(CPM), Ciprofloxacin(CIP), Colistin(CL), Co-trimoxazole(COT), Cefoperazone(CPZ), Cefoperazone-sulbactam(CFS), Ceftriaxone(CTR), Cefotaxim(CTX), Erythromycin(E), Gentamicin(GEN), Tobramycin(TOB), Imipenem(IPM), Linezolid(LZ), Netilmicin(NET), Nitrofurantoin(NIT), Norfloxacin(NX), Piperacillin(PI), Piperacillin-tazobactam(PT), Rifampicin(RIF), Tetracycline(T), Vancomycin(VA).

All the isolates which showed resistance to third generation cephalosporins were further tested for confirmation of **Extended Spectrum Beta Lactamase (ESBL)** production by phenotypic methods.

Criteria for Performance of ESBL Test: (CLSI 2021)

- Disk diffusion: For *K. pneumonia* and *E. coli*
 - ✓ Cefpodoxime 10µg or
 - ✓ Ceftazidime 30µg or
 - ✓ Aztreonam 30µg or
 - ✓ Cefotaxime 30µg or
 - ✓ Ceftriaxone 30
- Results:
 - ✓ Cefpodoxime zone: ≤ 17 mm
 - ✓ Ceftazidime zone: ≤ 22 mm
 - ✓ Aztreonam zone: ≤ 27 mm
 - ✓ Cefotaxime zone: ≤ 27 mm
 - ✓ Ceftriaxone zone: ≤ 25 mm
 - Zones above may indicate ESBL production.

ESBL Test:

- **Disk diffusion:**

Ceftazidime 30 μ g

Ceftazidime-clavulanate 30/10 μ g

and

Cefotaxime 30 μ g

Cefotaxime-clavulanate 30/10 μ g

A \geq 5-mm increase in a zone diameter for either antimicrobial agent tested in

combination with clavulanate vs the zone diameter of the agent when tested alone = ESBL (eg, ceftazidime zone = 16; ceftazidime-clavulanate zone = 21)

- Confirmation of ESBL production was done by using E-test (Hi-Media Laboratory, Mumbai)

Results

Table 1: Age and sex distribution among study participants

Age group	Sex		Total
	Female	Male	
0-10 yrs	13	10	23
10-20 yrs	2	1	3
20-30 yrs	10	5	15
30-40 yrs	8	9	17
40-50 yrs	14	4	18
50-60 yrs	5	9	14
60-70 yrs	6	2	8
70-80 yrs	2	0	2
Total	60	40	100

Out of total 100 symptomatic UTI patients, 60 were females (60%) while 40 were males (40%). Among Female participants maximum (%) belongs to 0 – 10 year age group that is paediatric age group while amongst male, maximum belongs to 30 – 40 year age group that is middle age group.

Prevalence:

Out of the 100 urine samples collected 60 samples showed positive growth on

cultures (\geq 105cfu/ml) .Among these 60 positive cultures 40 (66.6%) cultures were from female patients and 20 (33.3%) from males. Thus, the overall prevalence of urinary tract infection in the study population was found to be 60%. *Escherichia coli* was the most common organism isolated from the urine culture followed by *Klebshiella pneumoniae* and *Pseudomonas aeruginosa*.

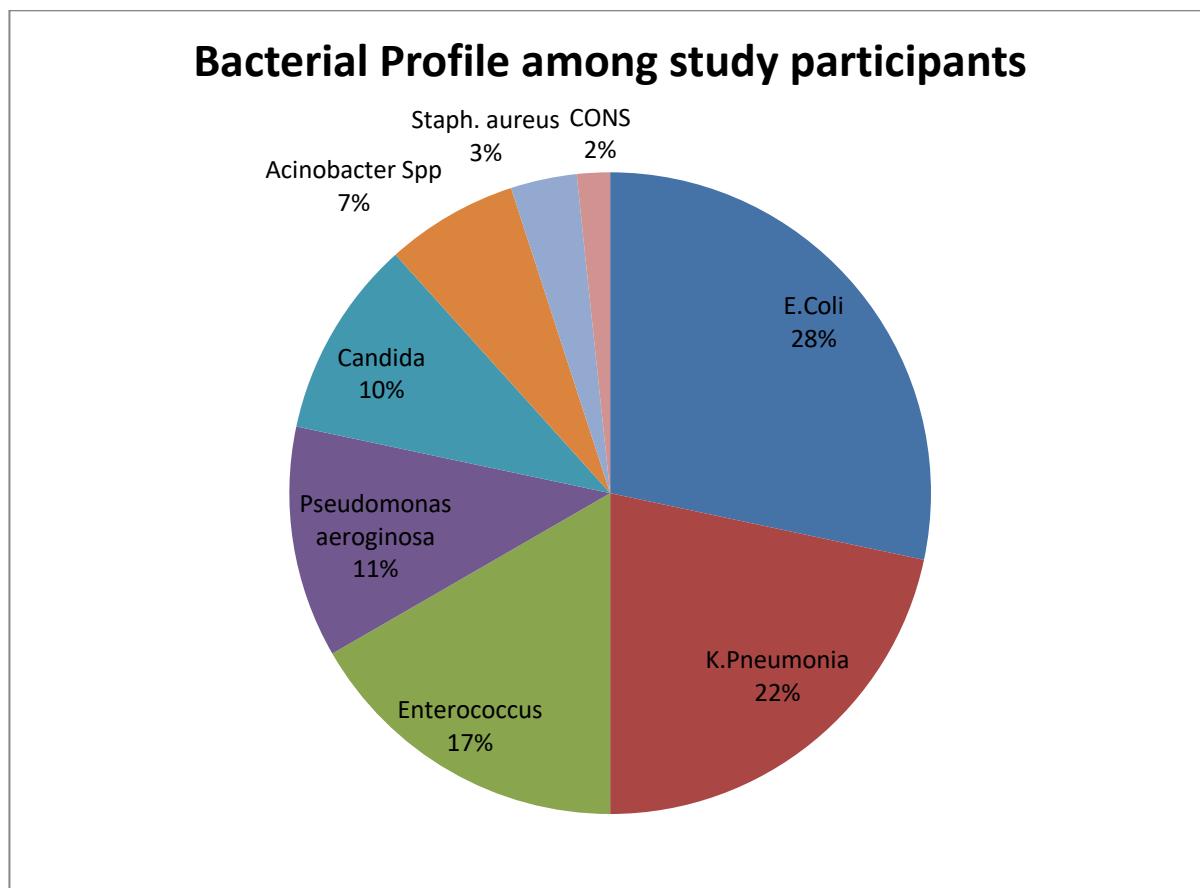


Figure 1 : Bacterial profile detected in urine culture among study participants

Table 2 : Age and sex profile among study participants in whom bacterial growth was detected.

Age group	Sex		Total
	Female	Male	
0-10 yrs	10	4	14
10-20 yrs	1	0	01
20-30 yrs	8	2	10
30-40 yrs	4	4	08
40-50 yrs	10	2	12
50-60 yrs	3	6	09
60-70 yrs	3	2	05
70-80 yrs	1	0	01
Total	40	20	60

Table 3: Antibiotic sensitivity pattern among Gram negative urinary pathogens

Resistant Antibiotic	<i>Escherichia coli</i>	<i>Klebsiella pneumoniae</i>	<i>Pseudomonas aeruginosa</i>	<i>Acinetobacter Baumanii</i>
Amoxycillin	15(88.23%)	12(92.30%)	IR	IR
Amoxycillin clavulanic acid	10(58.82%)	08(61.53%)	IR	IR
Ampicillin sulbactam	NT	NT	NT	03(75%)
Cefazolin	12(70.50%)	10(76.92%)	IR	IR

Ceftazidime	11(64.70%)	09(69.23%)	05(71.42%)	04(100%)
Cefoperazone	12(70.50%)	10(76.92%)	05(71.42%)	04(100%)
Cefoperazone-sulbactam	06(35.29%)	06(46.15%)	03(42.85%)	03(75%)
Ceftriaxone	13(76.47%)	11(84.61%)	IR	04(100%)
Cefotaxime	12(70.50%)	09(69.23%)	IR	04(100%)
Cefipime	09(52.94%)	07(53.84%)	05(71.42%)	04(100%)
Piperacillin	13(76.47%)	11(84.61%)	04(57.14%)	03(75%)
Piperacillin-tazobactam	07(41.17%)	07(53.84%)	02(28.57%)	02(50%)
Imipenem	01(5.88%)	02(15.38%)	02(28.57%)	01(25%)
Ciprofloxacin	12 (70.50%)	11(84.61%)	05(71.42%)	03(75%)
Norfloxacin	11(64.70%)	10(76.92%)	NT	NT
Co-trimoxazole	13(76.47)	10(76.92%)	IR	03(75%)
Colistin	0 (0%)	0 (0%)	0(0%)	0(0%)
Amikacin	03(17.64)	04(30.76%)	03(42.85%)	01(25%)
Gentamicin	04(23.52%)	05(38.46%)	04(57.14%)	01(25%)
Tetracycline	NT	NT	NT	03(75%)
Nitrofurantoin	01(5.88%)	04(30.76%)	NT	NT

Table 4 : Antibiotic sensitivity pattern among Gram Positive urinary pathogens

Resistant Antibiotic	<i>Staphylococcus aureus</i>		Coagulase negative <i>Staphylococcus aureus</i> (MR)	<i>Enterococcus spp</i>	
	MRSA (no:1)	MSSA (no:1)		<i>E.faecalis</i> (no:7)	<i>E.faecium</i> (no:3)
Penicillin	01(100%)	01(100%)	01(100%)	05(71.42%)	03(100%)
Ampicillin	01(100%)	01(100%)	01(100%)	02(28.57%)	02(66.66%)
Erythromycin	0(0%)	0(0%)	0(0%)	04(57.14%)	02(66.66%)
Clindamycin	0(0%)	0(0%)	0(0%)	NT	NT
Cefoxitin	01(100%)	0(0%)	01(100%)	NT	NT
Ceftazidime	NT	NT	NT	NT	NT
Cefoperazone	NT	NT	NT	NT	NT
Ceftriaxone	01(100%)	0(0%)	01(100%)	NT	NT
Co-trimoxazole	0(0%)	0(0%)	0(0%)	NT	NT
Linezolid	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
Vancomycin	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
Tetracycline	0(0%)	0(0%)	0(0%)	02(28.57%)	01(33.33%)
Rifampicin	0(0%)	0(0%)	0(0%)	NT	NT
Nitrofurantoin	0(0%)	0(0%)	0(0%)	01(14.28%)	01(33.33%)
Ciprofloxacin	01(100%)	0(0%)	01(100%)	03(42.85%)	02(66.66%)
Gentamicin (Enterococcus 120µg)	NT	NT	NT	04(57.14%)	02(66.66%)

IR: Intrinsic Resistance, NT: Not tested

Table 5: ESBL Producing Organisms

Name of Organism (n)	Number of ESBL Producers (n)	% of ESBL Producers
<i>Escherichia coli</i>	8	72.72%
<i>Klebsiella pneumoniae</i>	5	55.55%
<i>Pseudomonas aeruginosa</i>	2	50.00%

Discussion:

Urinary tract infection is one of leading cause of morbidity in both out patients and inpatients and an important cause for seeking medical care. In the present study the overall prevalence of urinary tract infection was found to be 60%. This was in corroboration with other studies done in India by Singh *et al* [14] and Prakash *et al* [15]. The prevalence of urinary tract infection was higher in females (66.66) than in males (33.33). This finding was also similar to other studies done in India [15,16].

Among the 40 urine samples which were culture positive in females 10 (25%) samples each were from age groups 0-10 years and 40-50 years respectively, 12 (30%) samples were from age group 20-40 years and the rest 7 samples (17.50%) were from age group 50 to 80 years. These findings also is similar to a study done by Christy VR *et al* [17]. According to Pulipati *et al* [18] UTI prevalence in female child in the age group 0-15 was because of anatomic or abnormalities in urologic functions, congenital defects, and vesico-ureteral reflux in females. It is also important for the clinician to enquire about toilet habits and hygiene condition of the child with their parents during their medical consultation. Often it is found that unhygienic napkins or diapers, overcrowding leading to poor toilet habits, poor housing conditions and parents hygiene play an important role in paediatric UTI. Women in the age group of 20 to 40 years are most prone to develop UTI because of various reasons. Firstly, they are sexually active during this age group and various factors like frequent sexual intercourse, multiple sexual partners, voiding habits pre and post coitus, vaginal douching, tight undergarments predisposes them to recurrent UTI. Secondly, most of these women have pregnancies during this age group. Pregnancy predisposes a women to UTI due to ureteric and renal pelvis dilation; increased urinary pH; decreased muscle tone of the ureters, and glycosuria, which promotes bacterial growth. Prevalence of UTI is also high in women of

postmenopausal age group. Harjustsalo *et al*. [19] demonstrated that there is a link between diabetes and UTI in women. The prime reason why women with diabetes is more prone to UTI is that the lower portion of genitourinary tract has glucose rich urine due to glycosuria. This gives nutritional growth for the microflora to flourish. The prevalence of UTI appears to be more in postmenopausal age group as reported by Murugan *et al* [20].

Among the 20 urine samples which were positive in males 04 (20%) samples were obtained each from age group 0 to 10 years and 30-40 years and 06 samples (30%) was obtained from age group 50 to 60 years. In the male child in addition to the risk factors mentioned for the female child for UTI uncircumcised penis is one of additional cause . Among 50 to 60 years in males diabetes, enlarged prostate, urinary catheterization and any urological surgery are the main risk factors.

In the present study, the most common isolated microorganism from culture positive urine samples was *Escherichia coli* (28.33%), followed by *Klebsiella pneumonia* (21.66%) and *Enterococcus spp* (16.66%). These findings also corroborated well with other studies done by Chooramani *et al* [13] and Ahmed *et al* [21].

All the gram negative organisms were found to be sensitive to Colistin (100%). Among the isolates of *Escherichia coli* high level of resistance was seen with beta lactams (Amoxycillin=88.23%, Piperacillin=76.47%), Cephalosporins (Cefazolin=70.50%, Ceftriaxone=64.70%, Cefoperazone=70.50%, Ceftriaxone=76.47%) and Fluoroquinolones (Ciprofloxacin=70.50%, Norfloxacin=64.70%). These findings also corroborated with the findings of other studies (16,14). Among *Klebsiella pneumonia* isolates higher level of resistance was seen with beta lactams (Amoxycillin=92.30%, Piperacillin=84.61%), Cephalosporins

(Cefazolin=76.92%, Ceftazidime=69.23%, Cefoperazone=76.92%, Ceftriaxone=84.61%) and Fluoroquinolones (Ciprofloxacin=84.61%, Norfloxacin=76.92%). These findings also corroborated well with the findings of a study done by Ahmed *et al* [21]. Interesting finding to note here is that 70% of isolates of *Escherichia coli* and 75% of isolates of *Klebsiella pneumonia* were found to be resistant to more than three classes of drugs. As, organisms resistant to more than three classes of drugs were considered as Multi Drug Resistant(14). This shows high levels of Multi Drug Resistance among these isolates which is of great concern. 72.72% (n=8) of *Escherichia coli* isolates showed ESBL production. All of these isolates were also resistant to other three or more classes of drugs. Thus, all of the ESBL producing *Escherichia coli* were multidrug resistant.

Major finding in our study was increasing resistance of gram negative uropathogens to beta lactam, beta lactam inhibitors and cephalosporins. Also, resistance to carbapenems was found to be higher in *Escherichia coli*, *Klebsiella pneumonia*, *Acinetobacter spp* and *Pseudomonas aeruginosa*. Resistance to two or more antibiotics leads to the development of multi drug resistant strains of uropathogens, rendering treatment difficult. Assessment of prevalence and identification of the major uropathogens with the local antibiotic susceptibility trends is of paramount importance in today's scenario. The increasing resistance patterns in the present study might be due to inappropriate prescription of drugs, and lack of knowledge about drug resistance in the study area. To reduce non-judicious use and risk of resistance development, antibiotic sensitivity must be made compulsory for the management of UTI.

Similar surveillance was conducted in the same centre in the year 2017 which also showed most common uropathogens as *Escherichia coli* followed by *Klebsiella pneumonia*. The major finding to note here

is that the percentage of ESBL production in *Escherichia coli*, *Klebsiella pneumonia* and *Pseudomonas spp* was only 45.5%, 30.4% and 25.45% respectively in the previous study and in the present study it has increased to 72.72%, 55.55% and 50.00% respectively.[22]

Conclusion:

Continuous surveillance of the most causative uropathogens and their antibiotic sensitivity patterns of drug resistance are needed in order to know the changing trends of bacterial resistance in prevalent bacterial isolates and changing antimicrobial resistance pattern to reduce selective pressure. The need for revision to the existing antibiotic policy and the use of commonly used antibiotics like nitrofurantoin, fluoroquinolones, ceftriaxone and cefuroxime should be assessed by each Healthcare Institute periodically as the trends of the endemic bacterial isolates keep changing over the period of years. This will help to ensure clinician confidence in empiric therapy. The current high rate of multidrug-resistant bacterial infections among hospitalised patients with UTIs is alarming. Due to selection pressure, drug resistance amongst the endemic bacterial isolates keep changing. Based upon this, strategies like Formulary restrictions, Antibiotic cycling and Antibiotic mixing can be implemented and antibiotic policy can be revised periodically accordingly. Periodic surveillance is the key tool to monitor and keep a check on this

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