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Original Article

Recent Trend in the Antimicrobial Resistance Pattern of Urinary Pathogens in a Tertiary Care Hospital

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Abstract

Introduction: Antibiotic resistance is a worldwide problem. Organisms are developing resistance not only to commonly used antibiotics but also to high end and less commonly used antibiotics. **Aim:** The present study has been designed to find out the recent trend of antibiotic resistance profile of uropathogens as urinary tract infection is one of the commonest infections among outdoor and indoor patients. This will help clinicians to select most appropriate antibiotics to treat their patients empirically. This will also help in not only preventing the development but also reducing the spread of antibiotic resistance. **Material and Methods:** The study was conducted in the Microbiology Department, F.H. Medical College, Etmadpur, Agra, India, from March 2019 to August 2019. Mid-stream urine samples were collected from patients and transported within an hour and were inoculated on blood agar and MacConkey agar. After incubation at 37°C for 24 h, organisms were identified and sensitivity test was done by Kirby Bauer's disc diffusion method using Mueller Hinton Agar. **Results:** Members of the *Enterobacteriaceae* family showed resistance to almost all groups of antibiotics except piperacillin-tazobactam, imipenem, and nitrofurantoin while gram-positive organisms were found to be sensitive only to vancomycin, teicoplanin, linezolid, and nitrofurantoin. Situation with nonfermenters (*Pseudomonas aeruginosa* and *Acinetobacter* spp.) was alarming as they were found resistant to ceftazidime, cefepime, piperacillin, gentamicin and ciprofloxacin, and also significant resistance with imipenem was seen. Only colistin, polymyxin B and piperacillin-tazobactam showed satisfactory results and could be considered for use in empirical treatment. **Conclusion:** Present study shows how serious the problem of increasing antibiotic resistance is and emphasizes the need of continuous surveillance of antibiotic susceptibility of uropathogens that will help to formulate an effective antibiotic policy to guide the clinicians.

Keywords: *Antibiotic resistance, urinary tract infection, uropathogens*

Submission: 27-08-2020,
Decision: 30-04-2021,
Acceptance: 28-04-2022,
Web Publication: 19-07-2022

Introduction

Urinary tract infection (UTI) is one of the most common conditions experienced by clinicians.[1] *Escherichia coli* is the most commonly isolated organism causing UTI while *Enterococcus*, *Klebsiella*, *Enterobacter*, *Citrobacter*, *Serratia*, *Pseudomonas aeruginosa*, *Providencia*, and *Staphylococcus epidermidis* are also implicated with UTI.[2] Any condition that affects the free flow of urine in the urinary tract such as stone, prostatic hypertrophy, tumor, external catheter, and neurogenic disorder increases the chances of UTI and symptoms of UTI depend upon the organ involved and type of organisms associated with the disease.[3] Incidence of UTI is more in diabetics due to compromised host defense

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Quick Response Code:

Website: www.mjdrdypv.org

DOI: 10.4103/mjdrdypu.mjdrdypu_476_20

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How to cite this article: Astha, Singh RP. Recent trend in the antimicrobial resistance pattern of urinary pathogens in a tertiary care hospital. Med J DY Patil Vidyapeeth 2022;15:707-12.

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mechanisms, diabetic cystopathy, and microvascular disease of the kidneys.[4]

UTI is generally treated by different groups of drugs such as cephalosporins, fluoroquinolones, and aminoglycosides depending upon the result of antibiotic sensitivity test. Organisms are becoming resistant not only to antibiotics of different groups but also to newer antibiotics developed in the recent past few years. Emergence of resistance to different antibiotics is not only a national problem but has spread all over the world. It has been experienced that resistance patterns of uropathogens have been changing, both in the community and hospitalized patients.[5] This has left a very limited choice of antibiotics for clinicians to treat their patients. This is also responsible for increasing number of cases of treatment failure leading to huge financial burden to patients.

Since treatment of UTI is generally started empirically, availability of data showing antimicrobial resistance pattern of commonly isolated organisms is mandatory to help clinicians in selecting most appropriate antibiotic for empirical therapy.[1]

Keeping in mind the seriousness of the resistance problem, present study has been aimed to find out the recent trend of antimicrobial resistance profile of prevailing uropathogens so that effective antibiotic policy can be formulated and patients can be treated empirically till the culture report becomes available.

Material and Methods

Study design

A cross-sectional retrospective study was conducted in the Department of Microbiology of F.H. Medical College, Etmadpur, Agra, India, from March 2019 to August 2019 after obtaining approval from Institutional Ethics Committee vide letter number FHMC/Eth. Com./2019/24. The culture-positive reports of the urine specimens received in the bacteriology laboratory from all the patients attending various OPDs (outpatient departments) and IPDs were included in the present study. The exclusion criteria for the present study were urine specimens showing more than one isolates and sample not received in the laboratory within an hour of collection.

Sample processing

The mid-stream urine (MSU) specimens received from the patients were processed within one hour and inoculated onto 5% blood agar and MacConkey agar and incubated aerobically overnight at 37°C. Any growth obtained was considered significant if the bacterial colony count was $>10^5$ cfu/ml except for *Staphylococcus aureus* for which a single colony was considered significant. The colony count was performed by using automated colony counter. They were further processed for identification following standard laboratory procedures.[6] Antimicrobial susceptibility test was performed by Kirby Bauer's disc diffusion method using Mueller Hinton agar as per Clinical Laboratory Standards Institute (CLSI) guidelines.[7] *E. coli* ATCC 25922, *Pseudomonas* ATCC 27853, and *S. aureus* ATCC 25923 were used as quality control strains according to the CLSI guidelines.

Results

A total of 341 (11.97%) samples showed significant growth, out of which 198 (58.06%) were obtained from female patients and 143 (41.94%) were from male patients. Sex-wise distribution of patients has been depicted in Figure 1.

It was also noticed that more isolates were recovered from outpatients, that is, 194 (56.89%) as compared to inpatients, that is, 147 (43.11%). Distribution of outpatient and inpatient is shown in Figure 2.

When data were analyzed on the basis of age of the patients, it was observed that maximum number of patients belonged to the age group of 21–40 years, that is, 38.71% followed by 41–60 years of age group, that is, 33.14%. Patients up to 20 years of age showed minimum incidence, that is, 13.49% [Table 1].

Distribution of bacterial isolates causing UTI has been shown in Table 2. Out of 341 isolates, *E. coli* isolates were maximum, that is, 58.94% followed by *Klebsiella pneumoniae* (17.30%), *Enterococcus* spp. (11.14%), *P. aeruginosa* (3.52%), *S. aureus* (2.64%), *Proteus* species (2.64%), *Acinetobacter* species (1.76%), *Coagulase-negative Staphylococci* [CoNS] (1.47%), and *Citrobacter* species (0.59%).

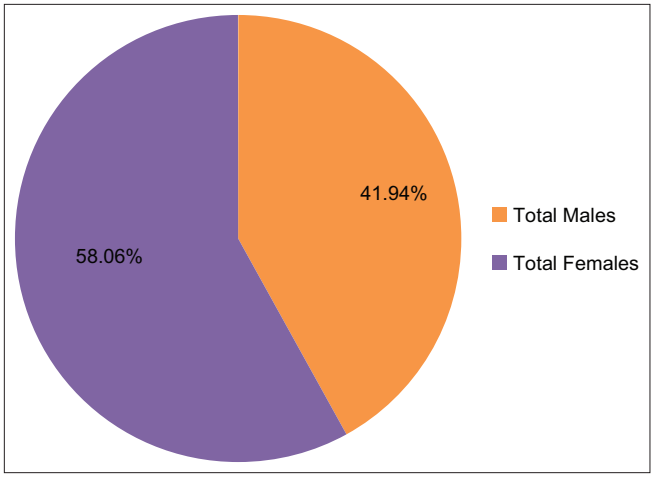


Figure 1: Sex-wise distribution of patients

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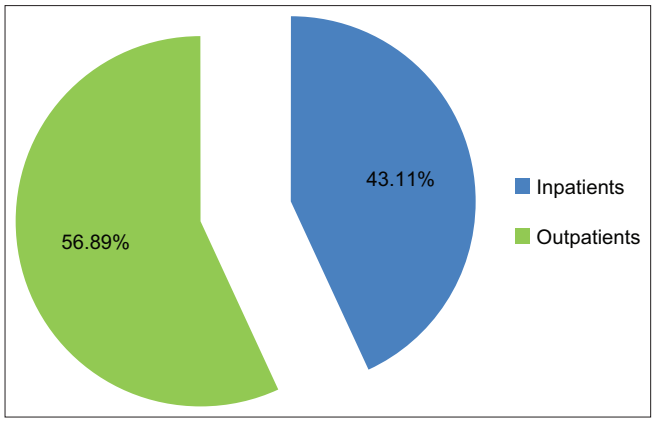


Figure 2: Inpatient/Outpatient distribution

The antibiotic resistance pattern of all the isolates was analyzed and the results are shown in Tables 3–6.

Resistance pattern of organisms of *Enterobacteriaceae* family was showing high degree of resistance to all groups of antibiotics except piperacillin-tazobactam, imipenem, and nitrofurantoin. Similarly, gram-positive cocci (*Enterococcus*, *S. aureus*, and CoNS) showed high degree of resistance to most of the drugs except vancomycin, teicoplanin, linezolid, and nitrofurantoin.

As far as the resistance pattern of nonfermenters, that is, *P. aeruginosa* and *Acinetobacter* spp., is concerned, problem appears to be more serious as they were showing resistance not only to ceftazidime, cefepime, piperacillin, gentamicin, and ciprofloxacin but also significant imipenem resistance was found which is quite frequently used against these organisms. Only colistin and polymyxin B were showing promising results while piperacillin-tazobactam can also be considered for empirical treatment.

Discussion

UTI has been challenging for clinicians due to alarming resistance profile of the uropathogens. The prevalence of UTI in the present study is 11.97% which is similar to the study of Thass *et al*.[8] (10.75%) and lower than Patel *et al*.[9] (46.48%). Present study shows higher prevalence of UTI in females (58.06%) as compared to males (41.94%). A study conducted by Mishra *et al*.[10] and Janifer *et al*.[11] showed similar results. Similar results have also been reported by another study conducted by Savas *et al*.[12] In another study of Hasan AS *et al*.,[13] prevalence rate in females was 70.5% and males was 29.5% which is in concordance with results of the present study. The difference in prevalence between females and males may be attributed to approximation of urethral, vaginal, and anal openings in females. This could also be due to shorter urethra in females

Table 1: Age-wise distribution of patients (*n*=341)

Age group	Total	%
Up to 20 years	46	13.49
21-40 years	132	38.71
41-60 years	113	33.14
More than 60 years	50	14.66

Table 2: Bacterial isolates from urine samples of patients with suspected UTI (*n*=341)

Bacteria isolated	Frequency	Percent (%)
E. coli	201	58.94
Klebsiella pneumoniae	59	17.30
Enterococcus species	38	11.14
Pseudomonas aeruginosa	12	3.52
Staphylococcus aureus	9	2.64
Proteus species	9	2.64
Acinetobacter species	6	1.76
CoNS	5	1.47
Citrobacter species	2	0.59

that leads to easy accessibility to microorganisms from perineum.[14] Antibacterial property of prostatic fluid is also responsible for less chances of infection in males.[15]

Present study revealed higher prevalence of UTI in reproductive age group of 21–40 years, that is, 38.71% with similar reports of Calvin *et al*.[16] This might be due to their initial exposure to sexual activity and independent movement in the environment without enough hygiene practices at this age.[3] More isolates were recovered from outpatients (56.89%) as compared to inpatients (43.11%). This is in contrast with the study of Yadav *et al*.[2] which shows higher prevalence in indoor patients than OPD patients. This difference may be due to the fact that most of the patients with UTI are treated in OPD and do not need hospitalization. Among gram-negative organisms, *E. coli* (58.94%) was the most common pathogen causing UTI followed by *K. pneumoniae* (17.30%), *P. aeruginosa* (3.52%), *Proteus* species (2.64%), *Acinetobacter* species (1.76%), and *Citrobacter* species (0.59%). Similarly, Mishra *et al*.,[11] Khan *et al*.,[17] Chaudhary *et al*.,[18] and Janifer *et al*.[12] in their studies have also reported *E. coli* as the most predominantly isolated organism, followed by *Klebsiella* spp. This is because gram-negative organisms of *Enterobacteriaceae* family have adhesins and pili which help them to colonize and attach to urogenital mucosa.[5] Higher isolation rate of *E. coli* might also be due to its presence in fecal matter, nature, and its ubiquity.

Among gram-positive organisms, *Enterococcus* spp. (11.14%) was predominant followed by *S. aureus* (2.64%) and CoNS (1.47%). In a study

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Table 3: Antimicrobial resistance pattern of *Enterobacteriaceae* family

Antimicrobial agents	*E. coli* (*n*=201)		*Klebsiella pneumoniae* (*n*=59)		*Proteus species* (*n*=9)		*Citrobacter species* (*n*=2)	
	No.	%	No.	%	No.	%	No.	%
Ampicillin	153	76	59	100	8	89	2	100
Piperacillin-tazobactam	33	16	15	25	2	22	0	0
Cefazolin	125	62	53	90	7	78	2	100
Ceftriaxone	67	33	33	56	4	44	1	50
Imipenem	29	14	9	15	1	11	0	0
Gentamicin	52	26	24	41	3	33	1	50
Tetracycline	157	78	48	81	7	78	2	100
Ciprofloxacin	107	53	43	73	6	67	1	50
Cotrimoxazole	120	59	41	69	6	67	1	50
Nitrofurantoin	44	21	15	25	2	22	0	0

Table 4: Antimicrobial resistance pattern of *Enterococcus* species (*n*=38)

Antimicrobial agents	No.	%
Penicillin	35	92
Ampicillin	31	82
Vancomycin	0	0
Teicoplanin	0	0
Erythromycin	20	53
Tetracycline	18	47
Ciprofloxacin	31	82
Nitrofurantoin	7	18
Linezolid	0	0
High-level gentamicin	14	37

Table 5: Antimicrobial resistance pattern of *Staphylococcus* species

Antimicrobial agents	*Staphylococcus aureus* (*n*=9)		CoNS (*n*=5)	
	No.	%	No.	%
Penicillin	9	100	5	100
Cefoxitin	3	33	2	40
Vancomycin	0	0	0	0
Teicoplanin	0	0	0	0
Gentamicin	4	44	1	20
Azithromycin	7	78	3	60
Tetracycline	8	89	4	80
Ciprofloxacin	7	78	4	80
Nitrofurantoin	1	11	0	0
Clindamycin	6	67	3	60
Linezolid	0	0	0	0

conducted by Mishra *et al*.,[11] *Enterococcus* spp. (15%) was found to be the predominant organism which was followed by CoNS (1.6%) while Akram *et al*.[19] found *S. aureus* as most frequently isolated pathogen among gram-positive organisms. This could be due to difference in demography and prevalence of different organisms in different environment.

Present study also determines the antibiotic resistance profile of different organisms. As far as members of *Enterobacteriaceae* family are concerned, it was observed that only piperacillin-tazobactam, imipenem, and nitrofurantoin were showing less resistance while all other groups of antibiotics were showing remarkable resistance. This is similar to a study conducted at northern part of country by Kumar D *et al*.[20] which has showed higher susceptibility to imipenem (100%), piperacillin-tazobactam (87.22%), cefoperazone/sulbactam (76.67%), amoxicillin/clavulanic acid (75.55%), and ceftazidime/clavulanate.

High degree of resistance in present study can be attributed to indiscriminate use of antibiotics in the hospitals and easy availability of these drugs over the counter. Resistance to ciprofloxacin, cotrimoxazole and third-generation cephalosporins are quite high due to this reason only. In studies conducted by Khan *et al*.[17] and Prakash *et al*.,[21] resistance to fluoroquinolones was found to be significantly high, which is very much similar to the results of the present study.

The resistance pattern of non-fermenters is very alarming [Table 6] where only colistin and polymyxin B have been found to be very effective and not even single isolate of *P. aeruginosa* and *Acinetobacter* spp. have been found to be resistant to these drugs. Even imipenem is showing high degree of resistance. Emergence of resistance to imipenem may be attributed to carbapenem-destroying β-lactamases and reduced uptake of β-lactam drugs by gram-negative organisms by altering their cell membrane porin channels associated with reduced outer membrane permeability, thus leaving narrow therapeutic options.[22] This is a very alarming sign for clinicians as thereafter there would be very limited choice of antibiotics in the form of polymyxin B and colistin which have serious side effects and toxicity as well.[23,24]

Among gram-positive organisms, only high-end antibiotics such as vancomycin, teicoplanin and linezolid have been found to be hundred percent sensitive and

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Table 6: Antimicrobial resistance pattern of non-fermenters

Antimicrobial agents	*Pseudomonas aeruginosa* (*n*=12)		*Acinetobacter* spp. (*n*=6)	
	No.	%	No.	%
Piperacillin	10	83	6	100
Piperacillin-tazobactam	2	17	2	33
Ceftazidime	10	83	6	100
Cefepime	9	75	5	83
Imipenem	5	42	4	67
Colistin	0	0	0	0
Polymyxin B	0	0	0	0
Gentamicin	7	58	5	83
Ciprofloxacin	9	75	5	83

are still effective in the management of UTI with multidrug-resistant organisms. Problems with these drugs are that they are available only in injectable form and are very expensive. The only drug available in oral form to treat OPD patients is nitrofurantoin which is also showing less resistance.

In the present study, nitrofurantoin has been found to be good choice for treating UTI. This finding is consistent with the studies conducted by Sasirekha[25] and Khameneh.[26] Low resistance for nitrofurantoin may be due to its localized action on urinary tract and not being exposed outside urinary tract.[2]

It is obvious that uropathogens are becoming more and more resistant not only to commonly used drugs but also to higher antibiotics. Since the pattern of resistance is everchanging and continuous process, there is always a need of a study that can provide reliable information for optimal empirical therapy for patients with UTI from time to time.

The alarming increase in resistance has reached at a level that a day is not far off when no antimicrobial agent would be available to treat infections and it appears that we are heading towards pre-antibiotic era. This is high time that all precautions and measures should be taken not only to minimize the development of resistance but also to prevent their spread. The need of the hour is to become very alert and understand the gravity of the situation and take necessary measures accordingly.

Conclusion

It may be concluded from the study that early diagnosis and appropriate treatment of UTI should be based on the current knowledge of recent trend of resistance profile which would be provided by microbiology laboratory periodically. It is also necessary that urine samples must be sent to the laboratory in all suspected cases of UTI for culture and sensitivity so that real-time data of resistance profile of organisms can be obtained for a given hospital. This study will help to formulate an effective antibiotic policy which will guide clinicians to select appropriate antibiotics to treat their patients. This will not only help to reduce misuse of antibiotics but also prevent development of resistance. Present study shows how serious the problem of increasing antibiotic resistance is. This emphasizes the need of continuous surveillance of antibiotic susceptibility of uropathogens.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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