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New insight into antibiotic resistance in urinary tract infections: Interplay between community and hospital acquired UTI

Hina Rahangdale [1] , Tejaswini Olambe [1] , Priyanka Klabhor [1] , Sangita Bhalavi [1]* , Varsha Wanjare [1], Sunanda Shrikhande [1]

1. Government Medical College and Hospital, Nagpur, India
* Correspondence: Sangita Bhalavi. Government Medical College and Hospital, Nagpur, India. Tel: +918698960383; Email: skhedikar09@gmail.com

Abstract

Background: Urinary tract infections (UTIs) are among the most common types of infections affecting people in community and hospital settings. Bacteria are the leading cause of UTIs, followed by fungi. 39% of all healthcare-associated infections (HAIs) affecting all age groups are UTIs, causing high morbidity and mortality rates. The antibiotic susceptibility pattern of causative organisms is changing due to improper antibiotic use. The study was conducted to determine the microbiological profile of both community and HAIs and their antimicrobial susceptibility pattern.

Methods: Clean-catch, mid-stream urine samples collected in the universal wide-mouthed sterile containers were transported to the laboratory. Samples were processed by standard conventional microbiological procedures. Antimicrobial susceptibility was done using the Kirby-Bauer disc diffusion method on Mueller-Hinton agar plates.

Results: The most common causative organisms among gram-negative bacteria were *E. coli* (26.05%), followed by *Klebsiella* spp (20.37%), and *Enterococcus* spp (12.81%) was more common among the gram-positive bacteria. Non-albicans *Candida* (64.10%) were more commonly isolated than *Candida albicans* (35.90%). *E. coli* was highly susceptible to nitrofurantoin and fosfomycin, and *Klebsiella* spp and *Enterococcus* spp were similarly highly susceptible. Antibiotic resistance was more common among bacteria isolated in HAIs.

Conclusion: In both settings, *E. coli* was the most common causative organism. The incidence of non-albicans Candida species has increased in comparison to Candida albicans. Antimicrobial susceptibility to empirical 3rd-generation cephalosporins and fluoroquinolones has drastically decreased. Hospital-acquired UTIs are a rising threat to the healthcare system and community. Based on hospitals' antimicrobial policy formulated by studying antimicrobial susceptibility patterns, empirical treatment should be chosen.

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Introduction

The urinary tract is divided into the upper urinary tract, composed of kidneys, renal pelvis, and ureters, and the lower urinary tract, which consists of the bladder and urethra. Lower urinary tract infections are more common, whereas upper urinary tract infections are most commonly ascending or less commonly result from the hematogenous spread of bacteria into the renal cortex in septicemia patients (1). According to a recent study carried out in January 2023 (2), the prevalence of UTIs worldwide is 16%.

Urinary tract infections (UTI) are the third most common type of infection, causing morbidity and mortality worldwide. More than 60 percent of women experience UTI once in their lifetime, as UTI is more common in females because of the shorter urethra (3). Different micro-organisms can cause UTIs, including protozoan parasites, fungi, and viruses; bacterial pathogens are the most common etiological agents that cause UTIs (4). UTI is particularly responsible for discomfort in elderly patients, representing a risk of bacteremia, septic shock, respiratory distress syndrome, and death. UTI is also the leading type of HAIs, accounting for up to 39% of all HAIs (5). UTIs are an important cause of septicemia, resulting in high mortality rates, prolonged hospital stays, and increased healthcare costs (4). Pathogens causing community-acquired UTI can be the members of intestinal microbial flora. From the perineal area through the urethra, they ascend to the bladder and migrate to the kidney or prostate. The result of host-pathogen complex interactions ultimately determines whether uropathies are successful in colonization or eliminated (6). In community-acquired urinary tract infection, *E. coli* and *S saprophyticus* account for 80% and around 10% of outpatients, respectively worldwide, and the remaining 5% to 10% of cases are due to *Klebsiella spp*, *Proteus spp*, and other gram-negative bacilli (7,8,9).

National Healthcare Safety Network (NHSN) reported catheter-associated UTI (CAUTI) as one of the most common types of healthcare-associated infection caused by prolonged use of the urinary catheter. For this reason, catheters should not be used without appropriate indications and should be removed as soon as they are no longer needed (10). Urinary tract infections are an important cause of septicemia, causing high mortality rates, hospital stays for a long duration, and increased healthcare costs (11). The deaths of hospitalized patients among the victims of hospital-acquired urinary tract infections are 2 to 3 times higher than those among nonbacteremic patients (12). Clinicians tend to prescribe broad-spectrum antibiotics instead of a specific antibiotic during empirical treatment in view of the resistance of the causative organism against the antibiotic. Antibiotic misuse and patients who are non-compliant or who do not complete the course of antibiotic therapy cause an increase in antibiotic-resistant bacteria (13). Increasing antimicrobial resistance complicates uncomplicated UTI treatment by increasing patient morbidity, costs of reassessment and retreatment, and use of broader-spectrum antibiotics (14). For effective treatment and control of UTI, a good knowledge of the antibiotic susceptibility pattern of the causative agents is of utmost importance.

This study was carried out to determine the prevalent uropathogens in our area and their antibiotic susceptibility pattern in community and hospital settings to commonly used antibiotics to provide a database for reference. The community patients were from the outpatient department (OPD), and all admitted patients in the hospital (IPD) were taken as patients with hospital-acquired UTI. In the present scenario, where the antibiotic resistance pattern is changing, our study aims to outline the recommendations for empirical treatment of UTI.

Methods

The present cross-sectional study was conducted at the Department of Microbiology in a tertiary care hospital in central India from January 2022 to October 2022. It was approved by the institutional ethics committee and complied with all regulations.

After obtaining consent from patients and giving proper instructions, clean catch, mid-stream urine samples from 4604 patients (723 from OPD and 3881 from IPD) were collected in sterile universal containers and were processed without delay. The microscopical examination of uncentrifuged urine was done by wet mount for screening by the number of polymorphs indicative of infection in the urinary tract. A total of 577 samples were screened positive, 226 from male patients and 351 from female patients. The samples were plated on CLED agar using the semi-quantitative plating method and the calibrated loop technique (0.001 mL). Plates were incubated aerobically overnight at 370C (15). Standard microbiological techniques were used to identify the isolates. Antimicrobial susceptibility test (AST) was done by the Kirby-Bauer disk diffusion technique according to the CLSI guidelines, and the percentage of resistance was compared between HAUTIs and CAUTIs (16).

Results

A total of 133 out of 723 OPD samples and 444 out of 3881 IPD samples were significant by screening. Of 96 inoculated OPD samples, 74 showed pure isolates, while 22 showed polymicrobial growth. Among the 444 inoculated IPD samples, 440 were culture-positive, and 62 were polymicrobial growths (3 or more types of colonies). Thus, out of 378 samples with pure isolates, 354 showed single isolates, and 24 samples showed two types of colonies. Thus, out of 402 isolates grown, 326 were bacterial, and 76 were candida isolates. Out of 577 screen-positive samples from OPD and IPD, 226 were males, and 351 were females. Most of the patients with UTI were 30-60 years old.

E. coli was the most common organism isolated in both community and hospital settings and showed higher susceptibility to nitrofurantoin and fosfomycin. *Enterococcus* spp was the most common isolate among Gram-positive bacteria, showing the highest sensitivity to fosfomycin and nitrofurantoin. A total of 78 isolates were of *Candida* spp, two isolates were from OPD, 76 were from IPD, 18 were *C. albicans*, and 50 were non-albicans *Candida* isolates. (Tables 1 and 2).

Discussion

Urinary tract infection is a common infection that affects people of all ages worldwide, both in community and hospital settings (17). The prevalence of community-acquired urinary tract infections (UTIs) was higher at 13.28% compared to hospital-acquired UTIs (9.74%).

In this study, 38% of the patients were male, and 62% were female, resulting in a male-to-female ratio of 0.6:1. This is consistent with the findings of other recent studies (18). The close proximity of the female urethral meatus to the anus and short urethra are the factors that influence the higher prevalence in women. Females predominantly presented in the age group of 30-60 years, whereas the majority of males were above 60 years. This finding is similar to studies conducted by Rafeek et al. and Sood et al (19,20). This is probably because, with advancing age, the incidence of UTI increases among males due to prostate enlargement and neurogenic bladder.

The prevalence of gram-negative bacteria was 93% and 64%, respectively, and that of Gram-positive organisms was 7% and 36% in OPD and IPD. As intestinal flora is a common source of pathogens causing UTIs, gram-negative isolates are the most prominent uropathogens. Also, fecal contamination of the urinary tract can be a contributing factor.

E. coli is the most common organism grown in both OPD and IPD samples, followed by Klebsiella spp, which is comparable to various studies, including those by Rafeek et al., Mancini A. et al., and Singhal A. et al. (20-22). Among gram-positive organisms, *Enterococcus* spp was the most common, as seen in the Rafeek et al. study (20).

Candida spp was isolated in 3% of OPD and 19% of IPD samples; 23% of Candida isolates were C. albicans, and 77% were nonalbicans candida. Fungal infections resulting from *Candida albicans* and non-albicans candida species have increased significantly in the last few years and are a serious public health concern (23). The reasons may be the excessive use of broad-spectrum antimicrobial agents, immune-suppressive agents, corticosteroids, neutropenia, elderly age, diabetes mellitus, structural or functional abnormalities of the urinary tract with an indwelling urinary catheter, or nephrostomy (24). In a study conducted by Goyal RK et. Al (25). prevalence of non-albicans *Candida* was more than *C. albicans* in accordance with the present study.

In the present study, *E. coli* showed maximum susceptibility to fosfomycin and nitrofurantoin and least to ampicillin. A similar pattern was seen in *Klebsiella* spp, and both organisms showed increased resistance to cephalosporins, as reported by Singhal et al. This might be due to injudicious use of these antibiotics. Similar to other studies, *Enterococcus* spp was also highly susceptible to fosfomycin and nitrofurantoin and least susceptible to penicillin (22). Most of the Staphylococcal isolates were MRSA found in hospital settings. The isolates from OPD samples were more sensitive than IPD sample isolates to the commonly used antibiotics, it may be due to the acquired resistance because of greater exposure of the bacteria to the antibiotics in hospitals.

The antibiotic susceptibility or resistance pattern of uropathogens has been changing over the years. One important factor contributing to the high resistance rates may be the increasing use of antibiotics without knowing the causative organism and its susceptibility pattern to antibiotics.

Table 1. Distribution and comparison of organisms grown in OPD and IPD patients

Organisms	OPD (%)	IPD (%)	Total (%)
E. coli	29 (40.27)	95 (23.57)	124 (26.05)
Klebsiella spp	14 (18.05)	83 (20.59)	97 (20.37)
Candida spp	2 (2.77)	76 (18.85)	78 (16.38)
Enterococcus spp	3 (4.16)	58 (14.39)	61 (12.81)
Acinetobacter spp	11 (15.27)	33 (8.18)	44 (9.24)
Pseudomonas spp	7 (8.33)	31 (7.69)	38 (7.98)
Citrobacter spp	8 (11.11)	15 (3.72)	23 (4.83)
Staphylococcus aureus	0 (0)	10 (2.48)	10 (2.10)
Proteus spp	0 (0)	1 (0.02)	1 (0.2)
Total	74	402	476

Table 2. Antimicrobial susceptibility in organisms grown in OPD and IPD patients

Antibiotic / *Bacteria*	*Staphylococcus spp. (%)*		*Enterococcus spp. (%)*		*E. coli (%)*		*Klebsiella spp. (%)*		*Pseudomonas spp. (%)*		*Acinetobacter spp. (%)*		*Citrobacter spp. (%)*	
	OPD	IPD	OPD	IPD	OPD	IPD	OPD	IPD	OPD	IPD	OPD	IPD	OPD	IPD
P	-	87	83	93	-	-	-	-	-	-	-	-	-	-
AMP	-	-	67	74	65	88	100	100	-	-	-	-	100	100
CZ	-	-	-	-	100	89	56	78	0	57	-	-	25	50
CXM	-	-	-	-	38	77	67	87	-	-	-	-	75	100
CX	-	70	-	-	43	44	54	95	-	-	-	-	24	50
CTX	-	-	-	-	42	66	63	82	-	-	-	-	100	100
CAZ	-	-	-	-	-	-	-	-	17	60	50	86	-	-
CPM	-	-	-	-	29	71	45	77	0	17	11	73	33	55
PIT	-	-	-	-	-	62	43	68	3	14	12	40	4	10
AMC	-	-	-	-	33	75	67	82	-	-	-	-	54	75
A/S	-	-	-	-	-	-	-	-	-	-	30	62	-	-
ETP	-	-	-	-	12	41	20	45	-	-	-	-	10	20
MRP	-	-	-	-	10	25	34	73	33	60	11	71	15	23
AT	-	-	-	-	-	-	-	-	20	67	-	-	-	-
VA	-	-	6	19	-	-	-	-	-	-	-	-	-	-
TEI	-	-	9	19	-	-	-	-	-	-	-	-	-	-
FO	-	-	0	11	4	8	0	9	0	0	-	-	0	0
GEN	-	25	-	-	0	13	12	42	23	75	5	50	0	0
TOB	-	-	-	-	27	27	33	55	-	-	23	60	13	20
NET	-	-	-	-	-	-	-	-	43	86	-	-	-	-
AK	-	-	-	-	13	18	18	39	4	57	50	46	5	10
HLG	-	-	13	39	-	-	-	-	-	-	-	-	-	-
HLS	-	-	11	29	-	-	-	-	-	-	-	-	-	-
T	-	-	100	100	-	-	-	-	-	-	-	-	-	-
DO	-	33	-	-	-	-	-	-	-	-	-	-	-	-
MI	-	-	-	-	-	-	-	-	-	-	53	67	-	-
LZ	-	0	0	9	-	-	-	-	-	-	-	-	-	-
NX	-	-	60	84	44	75	55	69	-	-	-	-	67	97
CIP	-	-	37	67	-	-	-	-	-	-	-	-	-	-
LE	-	-	-	-	73	90	74	83	40	75	20	25	0	0
NIT	-	10	0	13	8	16	15	30	-	-	-	-	13	20
COT	-	-	-	-	60	79	24	63	-	-	12	57	22	33

Note: P-Penicillin, AMP-Ampicillin, CZ-Cefazolin, CXM-Cefuroxime, CX-Cefoxitin, CTX-Cefotaxime, CAZ-Ceftazidime, CPM-Cefepime, PIT-Piperacillin-Tazobactam, AMC-Amoxicillin-Clavulanate, A/S-Ampicillin-Sulbactam, ETP-Ertapenem, MRP-Meropenem AT-Aztreonam, VA-Vancomycin, TEI-Teicoplanin, FO-Fosfomycin, GEN-Gentamycin, TOB-Tobramycin, NET-Netilmicin, AK-Amikacin, HLG-High Level Gentamicin, HLS-High Level Streptomycin, T-Tetracycline, DO-Doxycycline, MI-Minocycline, LZ-Linezolid, NX-Norfloxacin, CIP-Ciprofloxacin, LE-Levofloxacin, NIT-Nitrofurantoin, COT-Cotrimoxazole.

Conclusion

The present study underlines the role of different microorganisms as etiologic agents of UTIs. Also, it provides insight into the prevalence and antibiotic resistance pattern between hospital- and community-acquired UTIs. As there is markedly decreased susceptibility to 3rd generation cephalosporins, fluoroquinolones, currently used as empirical antibiotics, nitrofurantoin, and fosfomycin can be a promising option. Hospital-acquired UTIs are a rising threat to the healthcare system and community. Empirical treatment should be chosen based on the hospital's antimicrobial policy formulated by studying antimicrobial susceptibility patterns. It is critical to prioritize the control of bacterial resistance in hospital settings.

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Ethical statement

The research study has been approved by the institutional ethics committee and is compliant with all necessary regulationst.

Conflicts of interest

We declare that we do not have any conflicts of interest.

Author contributions

All authors contributed equally in writing this article.

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