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BACTERIA CAUSING COMMUNITY - ACQUIRED URINARY TRACT INFECTIONS AND THEIR ANTIMICROBIAL SUSCEPTIBILITY PATTERN IN PATIENTS ATTENDING OUTPATIENT DEPARTMENT IN TERTIARY CARE HOSPITAL

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ABSTRACT: Introduction: Community acquired urinary tract infection is defined as urinary tract infection occurring in outpatient setting, or in < 48 hrs after hospitalization, with no recent past history of urological procedure or catheter insertion. However, in almost all cases of community acquired urinary tract infection, antibiotic therapy is prescribed empirically before urine culture. Further there is increase in resistance to fluoroquinolones, ampicillin, and cephalosporin in bacteria causing community acquired UTI. Clinicians should be aware of sensitivity pattern of organisms causing community to acquire UTI. **Material and Method:** This retrospective study was conducted from 1/5/2024 to 15/9/2024 after obtaining approval from IEC committee. Patients who visited outpatient department and diagnosed themselves as UTI are included in this study. Hospitalized patient (> 48 hrs. admission), patient with catheter associated infection, patients recently undergone urological procedure were excluded from the study Urine cultures were done in our laboratory according to standard techniques. Antimicrobial susceptibility tests were performed using Kirby-Bauer's disk diffusion method. **Result:** Out of 115 urine specimens, 80 samples were positive for bacterial growth with significant bacteriuria. Total 64-gram negative pathogens and 16-gram positive pathogens identified. The predominant uropathogen isolated among gram negative bacteria was *E. coli* 47(73.43%), *Klebsiella pneumoniae* 13(20.31%), *P. aeruginosa* 3(4.68%) and *Proteus mirabilis* 1(1.5%). The predominant bacterial isolates among gram positive pathogens were *Coagulase negative Staphylococci* 8(50%), *E. faecium* 7(43.75%), MRSA 1(6.25%). In our study, *E. coli* strains showed highest susceptibility to fosfomycin 80.85%, Amikacin 78.72%, gentamicin 72.34%, and ertapenem 70.21% respectively. In our study, predominant gram-positive organism identified was *Coagulase negative staphylococci* with 50% susceptibility to Teicoplanin, Tigecycline, Nitrofurantoin. **Conclusion:** Community acquired infection remains most common bacterial infection occurring in community setting affecting individuals across all age groups for which empirical antibiotic administration is initiated. The increasing resistance to antibiotics such as ampicillin, cephalosporin, and quinolones have limited the use of these drugs in the treatment. Early diagnosis, appropriate antimicrobial therapy and implementation of preventive measures are crucial to reduce the burden of community acquired urinary tract infection. Periodic surveillance studies are recommended to guide empirical therapy and support antibiotic stewardship program in clinical settings.

INTRODUCTION: Urinary tract infections (UTI) are among the most common bacterial infections encountered in the community [1, 2]. UTI is defined as coexistence of urinary tract symptoms such as burning micturition, pain in lower abdomen or flank region, increased frequency and urgency of urine with significant bacteriuria (more than $1x10^5$ CFU/ml of urine) [3, 4].

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Community acquired UTI is urinary tract infection occurring in outpatient setting, or in < 48 hrs after hospitalization, with no recent past history of urological procedure or catheter insertion. UTI are estimated to affect 405 million people globally and nearly 0.23 million people died of UTIs contributing to 5.2 million disability adjusted life

years in 2019 [5]. However, in almost all cases of community acquired UTI, antibiotic therapy is prescribed empirically before final urine culture, or other laboratory results are obtained [2]. Over the years, the frequency of fluoroquinolones resistant pathogens has increased owing to the increased empirical use of fluoroquinolones. Also, gram negative bacteria such as *E. coli* and *Klebsiella pneumoniae*, and *Enterobacteriaceae* with multiple resistant mechanisms are influencing the decision regarding the empirical treatment of UTI [2, 6, 7]. Inappropriate use of antimicrobials is very common in management of UTI. In developing countries, the scenario is debilitating as a significant proportion of UTI patients purchase antibiotics directly from community pharmacies without prescription or any patient consultation [8, 9]. Therefore, clinicians should know the frequency and resistance pattern of uropathogens to provide appropriate treatment and antibiotic management [10].

MATERIAL & METHODS: This retrospective study was conducted from 1/5/2024 to 15/9/2024 after obtaining approval from IEC committee. Retrospective data was collected from microbiology laboratory register containing information about urine specimens obtained from patients attending OPD with UTI symptoms (burning micturition, urgency, increased frequency, pain lower abdomen or flank region). Patients of all age groups and both sexes were included. Pregnant women, diabetic individuals and patients with chronic kidney disease were excluded. Midstream clean- catch urine samples were collected in sterile containers. Patients were instructed for proper sample collection such as cleaning of perineal area with soap and water to avoid contamination. Samples were transported to the laboratory within 1 hr. Urine samples were inoculated using a calibrated loop technique (0.01ml) on culture media such as blood agar, MacConkey agar. Plates were incubated at 37° C for 18 to 24 hrs. Significant bacteriuria was defined as > $1x10^5$ CFU/ml. The organisms were identified by colony morphology and conventional biochemical tests. For *Enterococcus*, bile esculin hydrolysis test, 6.5% NaCl tolerance test performed. For Non fermenters, triple sugar iron test which shows k/k reaction used. CoNS were identified with negative coagulase test for *Staphylococci* species. MRSA identified with Cefoxitin disc diffusion test.

Antimicrobial susceptibility test was performed using Kirby-Bauer disk diffusion method on Muller Hinton agar. Pure colonies were emulsified in sterile saline to match 0.5 McFarland turbidity standard. Isolated strain was lawn cultured on Muller Hinton agar using a sterile swab. The plates were incubated at 37° c for 18-24 hrs. The zone of inhibition was measured using ruler. Results were interpreted as sensitive, intermediate, or resistant according to CLSI standard provided in CLSIM100:2024 guideline in 34th edition. Quality control was maintained using standard reference strain *E. coli* ATCC25922, *S. aureus* ATCC 25923, *P. aeruginosa* ATCC 27853.

Antimicrobial disk used for gram positive pathogens – Vancomycin (30µg) ciprofloxacin (5 µg), levofloxacin (5 µg), erythromycin (15 µg), teicoplanin (30µg), Tigecycline (15 µg).

Antimicrobial disk used for gram negative pathogens- Ampicillin (10µg), Amox+clav (20/10 µg), Piperacilline + Tazobactum (100/10µg), cefixime (5 µg), ceftriaxone (30 µg), Ceftazidime (30 µg), Cefoxitin, (30 µg) erythromycin (15 µg), norfloxacin (10 µg), gentamicin (10 µg), amikacin (30µg), fosfomycin (200µg).

RESULT: During the study period, Total 115 urine specimens were collected from the patient who visited outpatient department with urinary tract symptoms. 35 urine specimens were sterile and 80 samples were positive for bacterial growth with significant bacteriuria. Sterile samples excluded from analysis.

TABLE 1: SHOWING DEMOGRAPHIC SUMMARY ABOUT CULTURE POSITIVITY, ORGANISM DISTRIBUTION, SEX WISE DISTRIBUTION

Culture positivity rate	Culture positive samples (80)	Samples with no growth (35)	Total sample (115)	
Organism wise distribution	Gram positive pathogens (16/80)	Gram negative pathogens (64/80)	No growth (35)	Total sample (115)
Sex wise distribution	Female (57/80)	Male (23/80)	No growth (35)	Total sample (115)

Demographic profile study shows preponderance of UTI among Female patients (57) compared to male patients (23). Total 64-gram negative pathogens were isolated. The predominant uropathogen isolated among gram negative bacteria was *E. coli* 47(73.43%), *Klebsiella pneumoniae* 13(20.31%), *P. aeruginosa* 3(4.68%) and *Proteus* mirabilis 1(1.5%). Total 16-gram positive pathogens were isolated. The predominant bacterial isolates among gram positive pathogens were *Coagulase negative Staphylococci* 8(50%), *E. faecium* 7(43.75%), MRSA 1(6.25%).

TABLE 2: ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF PREDOMINANT GRAM-NEGATIVE PATHOGENS

Sr. no.	Antimicrobial drug	*E. coli (n=47)*	*Klebsiella pneumoniae (n=13)*	*Pseudomonas aeruginosa (n=3)*	*Proteus mirabilis (n=1)*
1	Ampicillin	12.76%	NA	0	0
2	Amox+clav	38.29%	46.15%	0	0
3	PIP+TAZ	19.14%	23.07%	33.33%	0
4	Cefixime	6.38%	15.38%	0	0
5	Ceftriaxone	14.89%	15.38%	0	0
6	Ceftazidime	29.78%	38.46%	0	0
7	Cefoxitin	40.42%	30.76%	0	0
8	Ertapenem	70.21%	61.53%	33.33%	0
9	Norfoloxacin	31.91%	38.46%	33.33%	0
10	Gentamycin	72.34%	69.23%	0	0
11	Amikacin	78.72%	84.61%	33.33%	0
12	Fosfomycin	80.85%	46.15%	0	0

For *Klebsiella pneumoniae*, there is intrinsic resistance to ampicillin. So, it is not applicable. For *Proteus species*, there is intrinsic resistance to Polymyxin, tetracycline, tigecycline, nitrofurantion, whereas acquired resistance to fluoroquinolones and aminoglycosides.

TABLE 3: ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF PREDOMINANT GRAM-POSITIVE PATHOGENS

Sr. no.	Antimicrobial drug	*Enterococcus faecium (n=7)*	*Coagulase negative Staphylococci (n=8)*	MRSA (n=1)
1	Ciprofloxacin	28.57%	0	0
2	Levofloxacin	28.57%	25%	0
3	Erythromicin	0	0	100%
4	Teicoplanin	28.57%	50%	100%
5	Vancomycin	71.42%	37.5%	100%
6	Tetracycline	0	37.5%	100%
7	Tigecycline	85.71%	50%	100%
8	Nitrofurantoin	100%	50%	100%

DISCUSSION: In the case of community acquired UTI, antibiotic therapy is often prescribed before culture and susceptibility studies. To prescribe antibiotic therapy for patients and reduce the development of antibiotic resistance, clinicians must determine the culture results and antibiotic resistance pattern of agents grown in culture locally. In this study, we aimed to determine the frequency and current antimicrobial resistance profile of agents causing community acquired UTI in outpatients attending our hospital. In our study, *E. coli* & *Klebsiella pneumoniae* were the most common organisms detected. *E. coli* is reported to be the most common cause of UTI in literature similar to our study. The second most common pathological agent differed between studies. Agca [11] reported that the second most common urine growth after *E. coli* were *P. aeruginosa* (6%), *Klebsiella* (5%), *Enterococcus* (5%), *S. aureus* (4%). In another study conducted in Kosovo [12]the second most common isolated pathogen was the *Proteus.* In two studies from Turkey, *Klebsiella* species were reported as the second most common pathogen similar to our study [13, 14] Kidwal *et.al* [15] reported *S. aureus* and *Klebsiella* species as the second most common growth after *E. coli* in patients in low socio-economic strata. Female sex has been reported as a risk factor of UTI in the literature. UTI occurs twice more frequently in women than in men [1, 15]. Short urethra and proximity to the anus have been reported to among the factors that increase of UTI [16]. In our study, *E. coli* strains showed highest susceptibility to fosfomycin 80.85%, Amikacin 78.72%, gentamicin

72.34%, and ertapenem 70.21% respectively. This was similar to the study conducted by Rehyan Ozturk, Gokhan Tazegul [17] who reported highest susceptibility to fosfomycin (95.2%), nitrofurantoin (95.3%) and gentamicin 90.3% respectively. Our study demonstrated less susceptibility to fluoroquinolones, 31.91 % for *E.coli* and 38.46% for *Klebsiella pneumoniae* among gram negative pathogens. Fluoroquinolones resistance among uropathogens especially *E. coli* has been dramatically increased over the past two decades with rates extending to 70 to 80% in many Indian settings. The rise is driven by antibiotic misuse, genetic mutation and plasmid mediated resistance, limiting the role of fluoroquinolones as empirical therapy for UTI. Current local practice and antimicrobial stewardship principles recommend limiting norfloxacin routine use because of increasing prevalence of fluoroquinolones resistance among community uropathogens Consequently, empirical therapy with norfloxacin is generally not preferred unless culture and sensitivity testing confirms sensitivity.

Our literature reported highest susceptibility of *Klebsiella pneumoniae* to amikacin (84.61%), gentamicin 69.23%, and ertapenem 61.53%. Aminoglycosides showed relatively good activity against uropathogens in the present study. Among them, amikacin demonstrated the highest susceptibility, followed by Gentamicin. This finding is consistent with several recent studies reporting preserved efficacy of aminoglycosides against common uropathogens such as *E. coli* and *Klebsiella pneumoniae*. However, emerging resistance to gentamicin highlights the need for continuous antimicrobial surveillance and rational antibiotic use. Overall, aminoglycosides remain important therapeutic options for the management of severe urinary tract infections, caused by gram negative pathogens. In studies that evaluated antibiotic susceptibility of *Klebsiella* strain, Shaifali [18] *et.al*, reported an ampicillin susceptibility rate of 54.54%. In our study, predominant gram-positive organism identified was Coagulase negative *Staphylococcus* with 50% susceptibility to Teicoplanin, Tigecycline, and Nitrofurantoin. *E. faecium* was 100% susceptible to nitrofurantoin and 85.71% susceptible to tigecycline. The difference in study results can be attributed to geographical variation in susceptibility pattern of uropathogens and local antibiotic policy guidelines.

CONCLUSION: Community acquired urinary tract infection remains one of the most common bacterial infections encountered in clinical practice, affecting individuals across all the age groups, particularly women.

The present study highlights the prevalence of bacterial pathogens responsible for community acquired urinary tract infection and their antimicrobial susceptibility pattern. The findings indicate that *E. coli* is the predominant uropathogen followed by organisms such as *Klebsiella pneumoniae*, *Proteus mirabilis*. The study also demonstrates increasing resistance to commonly used antimicrobials emphasizing the importance continuous monitoring of antimicrobial susceptibility pattern.

Early diagnosis, appropriate antimicrobial therapy and implementation of preventive measures are crucial to reduce the burden of community acquired urinary tract infection. Periodic surveillance studies are recommended to guide the empirical therapy and support antibiotic stewardship programme in clinical setting

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