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The prevalence of Community Acquired Multi-resistance organisms, Urinary Tract Infection in Kashmir, India: a Pilot Study

Mohammad Amin Simbli, MD, MRCP (UK) and Imtiyaz Ahmed Wani, MD; DM

Abstract:

Background: Recurrent urinary tract infection in the community is the second most common infectious presentation in medical practice. The extensive use of antimicrobial agents has invariably resulted in the development of antibiotic resistance, which in recent years, has, become a major problem worldwide. *Material and methods:* A prospective multicenter study conducted in patients of all age groups and in both sexes suffering from recurrent urinary tract infections. A total of 125 cases diagnosed clinically and suspected as having MRO recurrent UTI were submitted to microbiological examination. *Results:* 80% out of 125 patients showed significant growth of uropathogens and the remaining cases 20% showed either insignificant bacteriuria or no growth. Gram-negative organisms were isolated in 90% of positive urine culture. *Conclusion:* Those patients who received multiple courses of antibiotics, and persisted with symptomatic UTI were included with assumption of multiresistant organism UTI in such patients. The choice of antibiotic should be meropenem alone or in combination with aminoglycoside which is the most effective treatment until the results of culture and sensitivity are available.

Keywords: Urinary tract infection (UTI), multi-resistant organism (MRO), antimicrobial.

Introduction:

Urinary tract infection (UTI) is the second most common infection presenting in community medical practice. Among both outpatients and inpatients, *Escherichia coli* is the primary clinically relevant organism, accounting for 75% to 90% of uncomplicated UTI isolates^(1,2). *Staphylococcus saprophyticus*, *Klebsiella* spp., *Proteus* spp., *Enterococcus* spp., and *Enterobacter* spp. are organisms less commonly isolated from outpatients. *Aerococcus viridans* is a rare organism causing UTI and very rare to show resistance to common antibacterial agents. The sparse documentation of this organism from human clinical infections may be due to its microbiologic similarity to alpha-hemolytic streptococci and enterococci and potential misinterpretation of aerococci in culture specimens⁽³⁾. The Infectious Diseases Society of America (IDSA) guidelines currently recommend empirically treating acute, uncomplicated bacterial cystitis in healthy adult, non-pregnant females with a 3-day course of double-strength trimethoprim-sulfamethoxazole (SXT) in settings where the prevalence of SXT resistance is <10-20%^(4,5). Alternative therapy for uncomplicated UTI include a fluoroquinolone, nitrofurantoin or fosfomycin, wherever SXT resistance is >10-20%⁽⁵⁾.

Recurrent infection can have a huge impact on quality of life. Although recurrence may suggest that these infections are complicated, in the majority of patients no predisposing factor can be identified. These patients are often extensively investigated because of the misery caused by recurrent infection.

The resistance pattern of community acquired uropathogens has not been extensively studied in the Indian subcontinent⁽⁶⁾. This study was planned to identify the most common

pathogens associated with community acquired recurrent urinary tract infections (CA-RUTI) in Kashmir valley, and to determine their antibiotic sensitivities.

This epidemiological data is essential to help formulate guidelines for physicians to choose empirically antibiotics for treatment of recurrent CA-UTI in Kashmir.

Material and methods:

Design and setting.

This was a prospective multicenter study conducted in patients of all age groups and in both sexes suffering from recurrent urinary tract infections. Patients with one or more of the following symptoms were evaluated by midstream morning clean catch urine culture for possible multiresistant organism UTI (MRO UTI): Frequency, dysuria, urgency, hematuria, suprapubic pain, and flank pain. The exclusion criteria were patients who were hospitalized or received antibiotics during the previous two weeks or patients on indwelling catheters. Patients who could not afford cost of the urine culture or refused for the urine culture were not included in the study. Patients included were from various parts of Kashmir valley, and registered from Government as well as Private outpatient clinics.

Collection of urine specimens and urine cultures.

Once a clinical diagnosis of recurrent UTI was established, the patient was informed about the study and urine sample was obtained. Each patient was carefully instructed regarding the collection of a first morning clean-catch mid-stream specimen of urine sample. Urine specimens were studied by reputed private as well as Government based microbiology laboratories.

Results:

A total of 125 cases diagnosed clinically and suspected as having MRO recurrent UTI were submitted to microbiological examination. Hundred (80%) out of 125 patients showed significant growth of uropathogens and the remaining cases twenty five (20%) showed either insignificant bacteriuria or no growth. See Table 1.

Name of Organism	Number	Percentage
<i>E. Coli</i>	70	70%
<i>Klebsiella pneumonia</i>	10	10%
<i>Klebsiella oxytoca</i>	5	5%
<i>Klebsiella aerogens</i>	5	5%
<i>Aerococcus viridians</i>	5	5%
<i>Enterococcus fecalis</i>	5	5%

Table 1. Causative microorganisms for CA-MRO UTI

Gram-negative organisms were isolated in ninety cases (90%) of positive urine culture. The commonest organisms isolated were *E. coli*, which comprised seventy cases (70%). Ten cases of *Klebsiella pneumonia* were the second most common pathogens isolated (10 %). *Klebsiella oxytoca*, *Klebsiella aerogens*, were isolated among five cases from each pathogen (5%). *Enterococcus fecalis* and *Aerococcus viridans*, Gram-positive organisms were isolated from five patients each.

Age and gender data of prevalence of uropathogens revealed that *E. coli*, were isolated in seventy patients. Five cases were isolated in female patients in age group below nineteen years, and none patient grew *E.coli* among males below nineteen years of age. Thirty five cases were isolated between age group twenty to forty nine years of age. Twenty cases were female patients and fifteen were male. Thirty patients with *E. coli* were isolated in age group fifty to seventy nine. Fifteen cases were among both sexes. *K. pneumonia* was the second most common uropathogens isolated (10%) and found in age group above twenty years. Female patients outnumbered males in all age groups growing Gram-negative organisms. *Enterococcus fecalis* and *Aerococcus viridans*, both Gram-positive organisms

were isolated in age group above twenty years. Gram-positive organisms were isolated more commonly in male patients. See Table 2.

Age Group	Various Organisms producing UTI												Percent age
	<i>E. coli</i>		<i>K. oxytoca</i>		<i>K. pneumonia</i>		<i>K. aerogens</i>		<i>Aerococcus viridans</i>		<i>Enterococcus fecalis</i>		
	M	F	M	F	M	F	M	F	M	F	M	F	
	30	40	0	5	3	7	1	4	4	1	0	0	
NB-19	0	5	0	1	0	0	0	0	0	0	0	0	10.52 %
20-49	15	20	0	2	0	4	0	1	4	1	0	1	49.12 %
50-79	15	15	0	2	3	3	1	3	0	0	4	0	40.35 %

NB: Newborn; M: Male; F: Female

Table 2. Age and gender wise distribution and frequency of MRO uropathogens isolated from community acquired infection.

Among the Gram-negative MRO pathogens causing community acquired recurrent UTI, aminoglycosides and meropenem susceptibility was highest and was at 89.47%. Piperacillin plus Tazobactam susceptibility was second highest at 78.94%. Nitrofurantoin susceptibility of MRO, UTI was 73.68%. Quinolones and co-trimoxazole susceptibility was less than 50%. See Table 3.

Antimicrobial	Percentage isolates susceptible
Aminoglycosides	89.47
Carbapenem (Imipenem, Meropenem)	89.47
Piperacillin-Tazobactam	78.94
Nitrofurantoin	73.68
Quinolones(Ciprofloxacin,Ofloxacin,Levofloxacin)	47.36
Co-trimoxazole	42.10

Table 3. Antibiotic susceptibility for all Gram-negative MRO isolates.

Among Gram-positive organisms, *Enterococcus fecalis* and *Aerococcus viridans*, drug susceptibility of 100% was seen for Linezolid, Vancomycin, Nitrofurantoin, and Teicoplanin. See Table 4. They manifested high resistance to penicillin, cephalosporin, and the Quinolones.

Antimicrobial	Percentage of isolates susceptible
Linezolid	100%
Vancomycin	100%
Nitrofurantoin	100%
Teicoplanin	100%

Table 4. Antibiotic susceptibility of Gram-positive organism.

The commonest Gram-negative uropathogens *E. coli* showed similar susceptibility to aminoglycosides and Carbapenems accounting for 85.71%. Nitrofurantoin susceptibility was

of 78.57%, followed by Piperacillin plus Tazobactam 71.42%. *E. coli* was least susceptible to Quinolones 35.71% and Co-trimoxazole 35.71%. See Table 5.

Antimicrobial	Percentage isolates susceptible
Amino glycosides	85.71 (n=60)
Carbapenem (Imipenem, Meropenem)	85.71 (n=60)
Nitrofurantoin	78.57 (n=55)
Piperacillin plus Tazobactam	71.42 (n=50)
Quinolones(Ciprofloxacin,Ofloxacin,Levofloxacin)	35 .71 (n=25)
Co-trimoxazole	35.71 (n= 35)

Table 5. Antibiotic susceptibility for MRO *E. coli* isolates (n=70).

Discussion:

Identification of the uropathogens and their susceptibility pattern is very important in treating the cases of UTIs⁽⁷⁾. In the present study, urine specimens from patients suffering from community acquired recurrent UTIs were cultured to detect type of uropathogens and their drug susceptibility pattern. Significant growth of bacteria was detected in hundred, 100 (80%), of the urine samples while the remaining cases of twenty five, 25 (20%) showed either insignificant bacteriuria or no growth.

In the current study, Gram-negative bacilli were the predominant uropathogens and Gram-positive cocci, *Enterococcus fecalis* and *Aerococcus viridians* were cultured in five cases each. None of the patients grew *Candida* species. On analyzing positive urine cultures as regards to uropathogens *E. coli* was the commonest pathogen isolated among the patients with recurrent UTI followed by *Klebsiella pneumonia*, *K. oxytoca*, *K. aerogens*, *Enterococcus fecalis* and *Aerococcus viridans* and this confirms the previous several studies of Akram et al⁽⁶⁾, Kothari and Sagar⁽⁸⁾, and Pilijic et al⁽⁹⁾. These isolated urinary pathogens are similar to that of the studies published elsewhere recently^(6,8,9). *E. coli* and *Klebsiella* were the commonest pathogens isolated in both studies. *Klebsiella spp* are rarely encountered in cases of community acquired UTI in studies done by Kumar et al⁽¹⁰⁾ and Manges et al⁽¹¹⁾. *Enterococcus fecalis* is a Gram-positive, commensal bacterium found in gastrointestinal tract. *Aerococcus viridans* are Gram-positive cocci, usually airborne that are widely distributed in the hospital environment. *A. viridans* is not a common source of recurrent UTI, and rarely shows resistance to Penicillins, and Cephalosporin. *A. viridans* is uniformly sensitive to vancomycin⁽¹²⁾. Susceptibility to penicillin has been variable in clinical cases and resistance is reported^(13,14). In the present study, *Enterococcus* and *A. viridans* strains were sensitive to vancomycin, Linezolid, Nitrofurantoin, and Teicoplanin.

Age related prevalence of uropathogens in the present study revealed that *E. coli*, and *Klebsiella* were more prevalent among middle aged patients. None of the uropathogens were isolated from males in age group below nineteen years. All the cases of *Aerococcus viridans* were isolated in age group 20-49 years. *Enterococcus fecalis* was common in elderly patients in age group of 50-79 years and Gram-positive cocci were commonest in male patients. Akram et al⁽⁶⁾ reported the same age distribution of the pathogens in their study.

On analyzing positive urine cultures as regards to sex distribution, there was a predominance of infection in females. This finding is consistent with reports published by other authors^(15,6) and explained by Kumar et al⁽¹⁶⁾ that adult women have a higher prevalence of UTI than men, owing to anatomic and physical factors. Farajinia et al⁽¹⁷⁾ added that males are less prone to UTI, possibly because of their longer urethra and presence of antimicrobial fluid in their prostatic fluid.

In the present work, *E. coli* are slightly less susceptible to aminoglycoside (85.71%), Meropenem (85.71%) and Piperacillin plus Tazobactam (71.42%), and SXT (35.71%). This is in contrast to 100% sensitivity of *E. coli* to imipenem as detected by Akram et al⁽⁵⁾ and Mashouf et al⁽¹⁸⁾ which might point to disturbing trend of growing higher resistance by *E.*

coli to these antibiotics. There is slightly higher sensitivity shown by *E. coli* to Nitrofurantoin (78.57%) in our study compared to other studies^(19, 20, 6). In the present work, *E. coli* and *Klebsiella* isolates were equally resistant to SXT. While in study of Akram et al⁽⁶⁾ *E. coli* is more resistant to it than *Klebsiella*.

In present study those patients who received multiple courses of antibiotics, either prescribed by physicians, by self-medication, or by quacks, and persisted with symptomatic UTI were included with assumption of MRO UTI in such patients. Our study showed high percentage of such patients has MRO UTI which includes both Gram-negative and Gram-positive organisms. The choice of antibiotic should be meropenem singly or in combination with aminoglycoside which is the most effective treatment until the results of culture and sensitivity are available. Patients suffering from MRO UTI should receive ten days to two weeks course of intravenous antibiotics, followed by repeat urine culture, to confirm the eradication of the infection. Prolonged prophylaxis with oral antibiotics, with nitrofurantoin or according to sensitivity pattern is recommended. In addition all patients should be stressed upon the importance of hand hygiene and sanitary measures.

Conclusion:

Recurrent UTI should be treated as per urine culture and sensitivity report only. One can start empirical antibiotic in vitally unstable patients only. This study should be followed by a community study at regular intervals on antimicrobial resistance in Kashmir, to determine whether the resistance patterns and the increase in resistance of uropathogens are similar. People should also be discouraged from self-medication, particularly in recurrent UTI, and there should be lesser threshold for asking a urine culture.

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Conflict of Interest: None declared.

Author Information: Dr. Mohammad Amin Simbli, MD; MRCP (UK) is Consultant, Department of Nephrology, SMHS Hospital, Srinagar, Kashmir 190008. Dr. Imtiyaz Ahmed Wani, MD; DM is Additional Professor, Department of Nephrology, SKIMS, Soura, Srinagar, Kashmir.

Email for Correspondence: dramin2004@rediffmail.com