Pattern of urinary tract infection in Kashmir and antimicrobial susceptibility

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Abstract

Antibiotic resistance of urinary tract pathogens has increased worldwide. The purpose of this study is to provide information regarding the causative agents of urinary tract infection in Kashmiri patients, identify the uropathogens responsible for the infection and study the antibiotic susceptibility patterns of the uropathogens. Clean voided mid-stream urine samples were collected from 2190 patients. The specimens were cultured and the isolates were identified using standard microbiological techniques. The antibiotic susceptibilities of the isolates were also determined. Of 2190 specimens, 591 (27%) showed significant growth upon culture. Approximately 84.1 % (497/591) of the 591 patients with UTI were females, most of which belonged to the 21-30 age group (206). The males accounted for 15.9% (94/591) UTI cases. Most of the male patients belonged to the 21-30 age group (34). The lowest incidence of urinary tract infections was seen among the 13-20 years age group. Throughout this study males accounted for only 16% of all UTI cases. *Esherichia coli* was the most predominant isolate, 53.8% followed by *Klebsiella pneumoniae* 22.4% and *Pseudomonas aeruginosa* 7.6%. All isolates were fully sensitive to ofloxacin, and more than 94% were sensitive to cefuroxime. Apart from group D Streptococcus , the overall response to ampicillin by all isolates was less than 15%. The prevalence of multi-resistant *Pseudomonas aeruginosa* in community-acquired urinary tract infections is increasing. All *Pseudomonas aeruginosa* isolates were fully susceptible to cefuroxime and ofloxacin. It is recommended that cefuroxime and ofloxacin or both are used in the blind treatment of urinary tract infection while awaiting the culture and sensitivity results. Concurrent with the necessary shift in the prescription pattern, attention should be paid to restriction of antibiotic abuse in the community to retard development of further drug resistance.

Introduction

Broadly speaking, urinary tract infections (UTI) refer to infections occurring anywhere along the urinary tract from the perinephric fascia to the urethral meatus. Urinary tract infections are common in general practice[1,2] and have important economic consequences[2]. UTI is one of the most common diseases encountered in clinical practice today. Urinary tract infection is not only common but the range of clinical effects varies from asymptomatic bacteriuria to acute pyelonephritis[3]. Bacterial infections of the urinary tract have been reported in hospital and community situations[4,5]. In the community the prevalence has been reported in all age groups and in both sexes. In women between the ages of 16-35 years, the prevalence of urinary tract infection is approximately 20%[6], and the major risk factors in this age group appear to be sexual intercourse and the use of the diaphragm and spermicide[7,8]. Among young men who develop uncomplicated UTI, homosexuality as a result of

exposure of the urethra to *Escherichia coli* (*E.coli*) during receptive rectal intercourse, lack of circumcision and human immuno-defiency virus (HIV) infection, are important risk factors[9,10]. The prevalence of bacteriuria is approximately 1% in schoolgirls, but rare in elementary school-age boys[11]. In the elderly the incidence of UTI increases sharply in both sexes, and rates of 17%, 55% and 15%-31% have been reported in women and men[12,13].

The disorders are generally treated empirically with antibiotics. It is useful for GPs to be aware of the locally prevalent strains of uropathogens and their sensitivity pattern in order to decide on their choice of antibiotics. This knowledge might help primary care physicians who were often guilty of excessive and inappropriate use of antibiotics[14]. The judicious use of antibiotics requires accurate data on antimicrobial susceptibility which may vary in time and place. Regular surveillance is therefore necessary.

Urinary pathogens, especially from community patients, have been known to include strains that are resistant to many of the commonly used antibiotics.[15] Data on the patterns of resistance in most developing countries is inadequate. In Kashmir little is known about the resistance patterns of urinary pathogens isolated from patients living in different communities. This study reviews the susceptibility profiles of urinary isolates from patients who were seen in a general practice in Srinagar, Kashmir over a period of 24 months.

Material and Methods

Study population: Urine samples were collected from a total of 2190 patients suspected of urinary tract infection at Al-Haram diagnostic, research and training center, Srinagar, Kashmir, India during the period of April 2007 - March, 2009. The subjects were made up of 1890 females and 300 males. All these persons were outpatients visiting different private practioners and private hospitals in Srinagar city. Patients who have been on antibiotics for at least three days were excluded from the study.

Sterilization of media and materials: The media used were cysteine lactose electrolyte deficient (CLED) media, Sheep Blood Agar (SBA) and Muller Hinton Agar supplied by Oxoid Limited. All glassware were washed with detergent and rinsed with water, then allowed to dry. The glassware were later wrapped in aluminum foil and sterilized in a hot air oven at 160°C for 3 hrs. Media were sterilized by autoclaving at 121°C for 15 mins.

Urine collection: Patients with suspected UTI were instructed in the method of midstream urine (MSU) collection with aseptic precaution (posters in the collection areas re-inforce the method). Specimens were collected in wide mouth screw-on-top containers and stored at 4°C until transported to our laboratory in Eight-quart Coleman coolers. Quantitative bacteriologic cultures were performed according to standard laboratory procedures[16].

Culturing of urine sample: All samples were processed within one hour after arriving at the laboratory. A standard calibrated platinum wire loop delivering 0.001 ml of uncentrifuged urine was used to inoculate sheep blood agar (SBA) and cysteine lactose electrolyte deficient (CLED) media. These plates were incubated aerobically at 35-37°C for 18-24 hours. Specimens of urine containing >10^5 organisms per ml of a single species were considered as having significant bacteriuria. Wet preparations were made from centrifuged samples and casts, leukocytes and erythrocytes per high power field were looked for. A rapid dipstick (Combur 10 test, Boehringer Manheim, Diagnostics and Biochemicals, East Sussex, United Kingdom) was also used to detect pyuria via leukocyte esterase activity[17].

Bacterial identification: Identification of organisms was based on gram reaction, morphology, and biochemical characteristics. In addition isolates were also identified by using commercially available API 20 E kit (BioMerieux, France).

Antibiotic sensitivity test: Antibiotic susceptibility testing was carried out using the Kirby-Bauer disc diffusion technique on Muller-Hinton agar and commercial antibiotic discs (Oxoid, United Kingdom) were used for antimicrobial testing[18]. The antibiotic discs used were: Ampicillin (10µg), Naldixic Acid (30µg), Nitrofurantoin (300mg), Norfloxacin (30µg), Gentamicin (10µg), Trimethoprim-Sulphamethoxazole (1.25/23.75 µg), Ceftazidime (30µg), Ciprofloxacin (5µg), Cefuroxime (30µg) and ofloxacin (5mg). The antibiotic disc impregnated culture plates were incubated at 37°C for overnight. The diameter of the zone of inhibition was measured and recorded as resistant or susceptible according to the National Committee for Clinical Laboratory Standards (NCCLS) interpretative criteria[19].

Results

A total of 2190 urine specimens were submitted for culture and sensitivity testing, of which 1890 (86.3%) were obtained from females and 300 (13.7%) were from males. Of 2190 specimens, 591 (27%) showed significant growth upon culture.

Table I Portrays the distribution of patients with UTI by age and gender. Approximately 84.1% (497/591) of the 591 patients with UTI were females, most of which belonged to the 21-30 years age group (206) followed by 31-40 years (106) and 41-50 years (95) respectively. The males accounted for 15.9% (94/591) UTI cases. Most of the male patients belonged to the 21-30 years age group (34) followed by 31-40 years (17) and 41-50 (15) respectively. The lowest incidence of urinary tract infections was seen among the 13-20 years age group closely followed by the 0-12 years old patients. Throughout this study males accounted for only 16% of all UTI cases seen in this general practice.

Table I: Distribution of Patients with UTI by age and sex

| Sex | Age group in years | | | | | | |
	0-12	13-20	21-30	31-40	41-50	>50	Total
Male	12	4	34	17	15	12	94
Female	19	21	206	106	95	50	497
Total	31	25	240	123	110	62	591

Table II depicts the distribution of Uropathogens and their resistance pattern to various antimicrobial agents. *E.coli* was the most frequent isolate, 53.8% (318/591), followed by *K.pneumoniae* 22.4% (132/591), *Pseudomonas aeruginosa* 7.6% (45/591), *Proteus mirabilis* 4.0% (24/591), *Enterobacter spp.* 3.0% (18/591), *Acinetobacter spp.* 2.7% (16/591) and group D Streptococcus 6.5% (38/591). None of the specimens yielded polymicrobial cultures. All isolates except two *E.coli* and one *Klebsiella pneumoniae* were fully sensitive to ofloxacin, and more than 94% were sensitive to cefuroxime. A part from group D *Streptococcus*, the overall response to ampicillin by all isolates was less than 15%. All *Klebsiella pneumoniae* isolates were resistant to Ampicillin. *P.aeruginosa* isolates were susceptible to cefuroxime, ceftazidime and ofloxacin.

Table II: Distribution of Uropathogens and their Resistance Pattern to various antimicrobial agents

Organism	No. & % of Isolates	Percent of resistant isolates against									
		AMP	Co-Tri	CXM	Ofl	CAZ	CIP	GM	NA	NOR	NIT
Escherichia coli	318(53.8)	75.2	62.2	1.3	0.6	48.1	15.2	58.5	67.2	42.1	36.2
Klebsiella pneumoniae	132(22.4)	100	44.4	2.5	0.7	37.1	22.1	17.4	55.5	34.4	NT
Pseudomonas aeruginosa	45 (7.6)	NT	NT	5.2	0	14.1	26.8	15.8	NT	58.2	NT
Proteus mirabilis	24 (4.0)	76.1	66.1	13.8	0	38.8	18.3	59.1	68.8	34.4	NT
Enterobacter spp.	18 (3.0)	88.1	69.0	6.6	0	48.6	17.7	55.0	66.9	33.3	49.9
Acinetobacter spp.	16 (2.7)	90.1	74.3	8.3	0	49.0	15.5	56.1	76.3	45.6	18.2
Group D *Streptococcus*	38 (6.5)	15.1	NT	2.6	0	NT	40.9	70.4	44.1	35.7	29.7

AMP=ampicillin, Co-Tri=Cotrimoxazole, CXM= Cefuroxime, Ofl=ofloxacin, CAZ=ceftazidime, CIP=ciprofloxacin, GM=gentamicin, NA=nalidixic acid, NOR=norfloxacin, NIT=nitofurantion, NT=not tested

Discussion

The study was undertaken in Srinagar city to determine the antimicrobial susceptibility pattern of urinary tract infection as well as to evaluate the bacterial agents involved in this UTI. The predominance of Escherichia coli among the causative agents of urinary tract infection in this report supports the view[20-23], that E. coli even now is the most frequent cause of the infection. However, the incidence of infection due to this organism in this series (54%) was much lower than that reported by Erwa[24] (70.9%) and Mahgoub et al[25], (75%). Nevertheless, its incidence compares well with that recorded in other reports[23,26,27]. However, our incidence was higher than that reported by Aiyegoro et al[28], (52%).

The results of this survey also showed both *E.coli* and *Klebsiella pneumoniae* as the main causes of urinary tract infection in Srinagar where they accounted for 76% of the isolates. It corroborated well with that of Shamweel and Mubaraki[23], 2011; Shamweel and Farooque[26], 1995; Ahmed and Ragaa[27], 1988, where *E. coli* and *Klebsiella pneumoniae* accounted for approximately 70% of the isolates respectively. It is therefore evident that the predominant organisms associated with UTI are gram-negative bacteria belonging to the family Enterobacteriaceae. These organisms are part of the normal flora of the gastrointestinal tract. The short female urethra and the proximity of the anus to the urethra make females more prone to bacterial infections, due to colonization of the anterior urethra and the vaginal introitus. This may then partly account for the higher prevalence and incidence of UTI in females. Also, other predisposing factors of UTI include clinical conditions as pregnancy, prostatic disease, hydronephrosis, urethro-pelvic stenosis and constipation[29,30].

Several reports have shown that the incidence rates for UTI vary with age and sex, with a higher incidence occurring in those over 20 years of age[8,30,31]. Our results indicate that the incidence in adult females was about 6 times higher than males of similar age. The great majority of males with UTI in this study, 96%, had indwelling urethral catheters due to prostatic disease and only came to this practice because the hospital was always overcrowded or little far away. These men were either unfit for surgery, refused surgery or there was a long waiting list for surgery[32].

International guidelines for treatment of acute uncomplicated urinary infection have updated the Infectious Diseases Society of America (IDSA) treatment guideline of 1999[33]. The updated guidelines consider empiric antimicrobial therapy for acute cystitis in the context of the increasing global resistance observed in E. coli[34]. The term "collateral damage" is used to describe the propensity of an antimicrobial to induce resistance in gut flora which may then compromise infection management beyond cystitis. For empiric treatment of acute uncomplicated cystitis recommended first line agents are TMP/SMX or TMP by itself for 3 days if the local prevalence of resistance is less than 20%, nitrofurantoin for 5 days, pivmecillinam

for 3–7 days, or fosfomycin as a single dose. Three of these agents like nitrofurantoin, pivmecillinam, and fosfomycin are currently indicated only for acute cystitis, and are unique classes of antimicrobials without cross-resistance with other agents. Fluoroquinolones given for three days may be 5% to 10% more effective in clinical trials than some of the recommended first line regimens, but are discouraged for use as first line therapy because of the propensity for "collateral damage." For oral treatment of acute nonobstructive pyelonephritis, ciprofloxacin, ofloxacin or levofloxacin are recommended[33]. TMP/SMX or TMP are effective alternate oral agents if the infecting organism is known to be susceptible. When TMP/SMX is used empirically, an initial parenteral dose of an aminoglycoside or ceftriaxone is suggested for coverage of potential TMP/SMX resistant organisms pending culture results. Empiric parenteral therapy for pyelonephritis is little changed from the 1999 guidelines. Suggested regimens include an aminoglycoside with or without ampicillin, a third generation cephalosporin, or a fluoroquinolone.

The antibiotic in-vitro susceptibility testing showed that co-trimoxazole and ampicillin are unlikely to be effective in treating patients with Urinary tract infection due to *E. coli*, *Klebsiella pneumoniae* and *Proteus mirabilis* in this community as these organisms showed relatively low sensitivity to these drugs. Improper use of antibiotics often facilitates the selection of resistant bacterial strains. The more antibiotics are used in the community the more likely it is that resistant strains will be selected and maintained in that environment[35]. In Srinagar self mediation with easy-to-obtain over the counter drugs such as co-trimoxazole and ampicillin, are very common. The inadequate dosage of these antibiotics used in self-medication, along with the wide spread use in animal feeds of antibiotics to improve livestock are important contributors to the development of resistant strains to these drugs in the community.

Srinagar city is heavily populated and majority of the hospitals are usually heavily attended and sometimes the doctor only spends a few hours there and leaves, thus putting tremendous financial pressure on patients who desperately need help to visit the general practitioners. The high resistance rate of uropathogens to some of the commonly used oral antimicrobial agents as seen in this study, has influenced the introduction of the use of relatively new antibiotics such as cefuroxime and ofloxacin into the country, which may produce higher cure rates as evidenced by in-vitro testing against more than 94% of urinary isolates in this study.

The high frequency of single and multiple antibiotic resistance in this community should cause alarm. The ease of procuring antibiotics in these areas without a prescription can result in uncontrolled self-medication. Also, the absence of antibiotic prescribing policies and in adequate information on patterns of bacterial resistance, may all contribute to the emergence of resistant strains. It can be concluded from this study that *E. coli* and *Klebsiella pneumoniae* were the main pathogens isolated and that the majority of pathogens were sensitive in vitro to ofloxacin and cefuroxime or both. It is recommended that ofloxacin or cefuroxime, or both, are used in the empirical treatment of UTIs, following the submission of MSU specimens for culture, while awaiting the culture and sensitivity results in view of high prevalence of UTI in Kashmir. It is also recommended to monitor continuously the pattern of urinary pathogens, from the community at large, and their resistance patterns to guide the empirical treatment of patients in the future.

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