Antibacterial Resistance and Trend of Urinary Tract Pathogens to Commonly Used Antibiotics in Kashmir Valley

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ABSTRACT

Objective: Increase in resistance pattern of urinary tract pathogens to conventional antimicrobial agents used for urinary tract infections (UTIs) are gaining the attention of many microbiologists worldwide in respect to treatment of UTIs. The aim of the present study was to obtain data on resistance patterns of pathogens responsible for UTIs in Sher-I-Kashmir Institute of Medical Sciences (tertiary healthcare hospital) to currently used antimicrobial agents.

Method: A total of 2842 samples were collected from both outpatient and inpatient departments. The majority of samples in this study were midstream urine specimens, others included catheterized urine samples. Standard parameters were followed for isolation and identification of clinical isolates and further antimicrobial susceptibility test was done by Kirby Bauer disk diffusion method.

Keywords: Antibiotic sensitivity, drug resistance, *E coli*, urinary tract infection (UTI)

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Results: Out of 2842 samples, 1980 (67%) were culture positive. *Escherichia coli* (*E coli*) was the most prevalent isolate (OP 63%, IP 45.5%) followed by *Klebsiella pneumonia* (*K pneumonia*) as the second commonest UTI-causing agent (OP 15.9%, IP 21.7%). High percentage of isolates showed resistance to sulfa drugs such as cotrimoxazole. First generation cephalosporins were ineffective, while aminoglycosides and third generation cephalosporins were effective against *E coli, K pneumoniae, Pseudomonas aeruginosa* (*P aeruginosa*)*, Enterococcus faecalis* and *Staphyococcus aureus* (*Staph aureus*). Furthermore, this study noticed that glycopeptide drugs such as vancomycin are highly effective against *E faecalis* and *Staph aureus* UTIs.

Conclusion: This study reveals the increased trend in resistance pattern of uropathogens in the valley region. These data may aid health professionals in choosing the appropriate treatment for patients with UTI in the region and hopefully will prevent the misuse of antibiotics.

INTRODUCTION

The most common human bacterial infections in the community as well as in hospital settings are urinary tract infections [UTIs] (1–2). Every year about 150 million people worldwide are affected by UTIs at a cost of about US$ 6 billion (3). Urinary tract infections may involve only the lower urinary tract or may involve both the upper and lower tract. Previous studies indicated that more than 80% of uncomplicated UTIs are solely due to *Escherichia coli* [*E coli*] (4). The manifestations of UTIs are due to an interplay of the predisposing host factors and the virulence factors released by the pathogens. Congenital anomalies of the urinary tract, urinary tract obstruction, pregnancy, catheterization, instrumentation and diabetes mellitus are considered some of the predisposing factors for UTI (5), whereas virulence factors include neutrophil activation, haemolysin, adhesions and capsular polysaccharide (6). Frequently, broad-spectrum antibiotics are used to treat UTIs, however, narrow spectrum antibiotics may be suitable because of resistance concerns (7, 8). Fluroquinolones are preferred as initial antimicrobial agents because of their low rate of resistance and high clinical cure rates (9, 10). The exhaustive use of antibiotics leads to development of antibiotic resistance which becomes the major problem in treatment of UTIs globally (11).

The resistance pattern of community acquired UTI pathogens has not been studied extensively (9). Over the past years, the aetiology and antibiotic resistance pattern of uropathogens in UTIs has been changing in both community and in healthcare centres (12, 13).

However, in India, the data on aetiology and antibiotic resistance pattern were not enough to treat community acquired UTIs. Hence the aim of the current study is to investigate the relative role of uropathogens and their antibacterial resistance patterns among both inpatient and

outpatient departments of Sher-I-Kashmir Institute of Medical Sciences (tertiary healthcare hospital), India, to antimicrobial agents currently used in the treatment of UTI.

SUBJECTS AND METHODS

The study was conducted during February 2007 to November 2007 on patients attending the outpatient and inpatient departments of Sher-I-Kashmir Institute of Medical Sciences, Soura, Srinagar, India. A total of 2842 samples were collected from both outpatients and inpatients. The patients were provided with a sterile and dry wide mouth container and were asked to collect 10−20 ml urine. The majority of samples were first early morning midstream urine specimens, a few inpatient samples were from urinary catheters.

Blood agar and MacConkey agar plates were inoculated with semiquantitative urine culture using a calibrated loop (14). Distinguishing between the genuine infection from contamination was done as per Kass recommendations (15). Culture of a single bacterial species from the urine sample at a concentration of > 105 cfu/ml was considered as significant monomicrobic bacteriuria. Out of a total of 2842 samples, 1980 samples (750 males and 1230 females) were identified as culture proven urine isolates. Only a single positive culture per patient was included in the analysis. Standard biochemical procedures were followed to identify the significant pathogens (16).

Antibiotic susceptibility test of clinical isolates was done by the Kirby Bauer disk diffusion method (17). Antimicrobial agents tested were gentamycin 10 mcgm per disk, cephalexin 30 mcgm, cefixime 30 mcgm, nitrofurantoin 30 mcgm, amikacin 30 mcgm, ciprofloxacin 5 mcgm, vancomicin 30 mcgm (only for *E faecalis* and *Staph aureus*) and cotrimoxazole 1.25 mcgm (Hi Media, India).

SPSS (Windows Version 17.0) software was used for descriptive analysis.

RESULTS

A total of 2842 urine samples were analysed as per standard bacterial isolation and identification methods, of which 1980 (67%) samples were culture positive; 1100 (56%) were from inpatients (IPs) [530 males and 570 females] and 880 (44%) samples were from outpatients (OPs) [220 males and 660 females].

The overall species distribution is shown in the Figure. The current study reveals that the most frequently isolated species were *E coli* (OP 63%, IP 45.5%) followed by *K pneumoniae* (OP 15.9%, IP 21.7%), In contrast, *P mirabilis* showed less frequency in prevalence (OP 1.2%, IP 2.7%).

A total of eight antibiotics were tested against all isolated uropathogens in the study, among which amikacin, cefixime, ciprofloxacin and nitrofurantoin were found to be the most effective. The antibiotic resistance pattern test of isolates to a routinely used antibiotic panel to treat UTI infections is shown in the Table. Results showed that *E coli* was the predominant cause of UTI, and had a higher percentage of resistance to cotrimoxazole (OP 76%, IP 79%) followed by cephalexin (OP 72%, IP 81%) and the lowest resistance to amikacin (OP 11%, IP 13%) and cefixime (OP 16%, IP 19%).

Klebsiella spp was the next most prevalent aetiologic aspect of UTI in this study and displayed a slightly different resistance pattern to *E coli*. *E faecalis* and *Staph aureus* isolates showed the highest antibiotic susceptibility rate (100%) to vancomycin, followed by cefixime (Table). In this study, *P mirabilis* was responsible for only about 3.9% of UTI cases (both OP and IP) and exhibited highest resistance to cotrimoxazole, cephalexin and lower resistance to cefixime (OP 13%, IP 19%).

DISCUSSION

Urinary tract infections are one of the most common infectious diseases worldwide (18−20). Due to lack of reliable indicators of UTI, early diagnosis and appropriate treatment with antibiotics are considered the most effective key factors to eliminate the uropathogens and to prevent further complications such as urosepsis and renal scaring. Urinary tract infection can be either asymptomatic or symptomatic (21). Bacteriuria with classical symptoms such as frequent urination, burning micturition and fever is referred as symptomatic UTI (22), whereas bacteriuria without classical symptoms is called asymptomatic UTI (23).

The present study shows that *E coli* is the predominant cause of UTI amongst the outpatients as well as inpatients, *K pneumoniae* being the next UTI-causing agent followed by *Staph aureus, P aeuruginosa, E faecalis* and *P mirabilis*. The frequency of *E coli* in urine samples varies in different studies from 32% (9) to 86% (24), with intermediate values in other cases: 40% (25), 65% (26) and 68% (24). Our results (OP 63% and IP 45.5%) fit with these.

Our study indicates that *E coli* is still the most predominant cause of UTI among in-and outpatients. This corresponds with the data obtained by other investigators (1, 27, 28). Some have shown, however, that the percentage of *E coli* is slowly declining, being replaced by other members of the Enterobacteriaceae and *Enterococci* (29).

The resistance pattern of *E coli* data are similar to those obtained in other countries indicating that *E coli* is still resistant to many antimicrobial agents (30, 31). Other species of the Enterobacteriaceae were more resistant when isolated from the hospital setting (31, 32).

In the current study, among inpatients, a high percentage of isolates showed resistance to sulfa drugs such as cotrimoxazole. First generation cephalosporins were ineffective in our study, while aminoglycosides such as amakicin and third generation cephalosporins were found to be

effective against *E coli, K pneumoniae, P aeruginosa, E faecalis* and *Staph aureus* (Table). Furthermore, this study noticed that glycopeptide drugs such as vancomycin are highly effective against *E faecalis* and *Staph aureus* UTIs.

Despite the abundant availability of antimicrobial agents against UTIs, it still remains one of the most common human infectious diseases (33). Antibiotic drug resistance in uropathogen may be due to overuse, abuse and at times misuse, due to wrong diagnosis and empirical prescription without urine culture (34, 35). Increased globalization could contribute to the spread of drug resistance. Appropriate knowledge on uropathogens and their antibiotic susceptibility is mandatory to ensure proper treatment of UTIs (36). Multidrug resistant pathogens spread locally as well as globally as a part of rapid globalization (9).

Initial treatment for UTIs can be started before the availability of diagnostic test results such as urine culture and antibiotic sensitivity test. This may give an idea on the trend of antibiotic drug resistance pattern among the uropathogens and also aid in the selection of accurate drug for the appropriate treatment of UTIs.

This study reveals the increased trend of resistance pattern of uropathogens in this region, which may be due to variation in geography, misuse of drugs or wrong diagnosis. These data may also aid health professionals to choose appropriate treatment for UTI patients in the region and limit the misuse of antibiotics in the valley. Continued surveillance at both local and national levels is necessary to maintaining the efficacy and safety of empirical therapy for UTIs.

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Table: Antibiotic resistance pattern (%) of clinically isolated uropathogens

Microorganism	n	Antimicrobial agent	% Resistance (OP)	% Resistance (IP)
E coli	1054	Gentamycin	36	42
		Cephalexin	72	81
		Cefixime	16	19
		Nitrofurantoin	46	53
		Amikacin	11	13
		Ciprofloxacin	34	46
		Cotrimoxazole	76	79
K pneumoniae	379	Gentamycin	41	53
		Cephalexin	68	72
		Cefixime	21	25
		Nitrofurantoin	39	41
		Amikacin	17	21
		Ciprofloxacin	41	37
		Cotrimoxazole	71	78
P aeruginosa	171	Gentamycin	37	45
		Cephalexin	72	79
		Cefixime	14	19
		Nitrofurantoin	47	53
		Amikacin	23	27
		Ciprofloxacin	51	59
		Cotrimoxazole	73	81
E faecalis	106	Gentamycin	47	52
		Cephalexin	77	78
		Cefixime	23	31
		Nitrofurantoin	61	74
		Amikacin	21	33
		Ciprofloxacin	37	45
		Vancomicin	00	00
		Cotrimoxazole	82	87
P mirabilis	90	Gentamycin	29	30
		Cephalexin	79	81
		Cefixime	13	19
		Nitrofurantoin	33	36
		Amikacin	29	37
		Ciprofloxacin	42	51
		Cotrimoxazole	78	82
Staph aureus	180	Gentamycin	49	57
		Cephalexin	87	92
		Cefixime	11	17
		Nitrofurantoin	62	69
		Amikacin	33	38
		Ciprofloxacin	31	38
		Vancomicin	00	00
		Cotrimoxazole	76	82

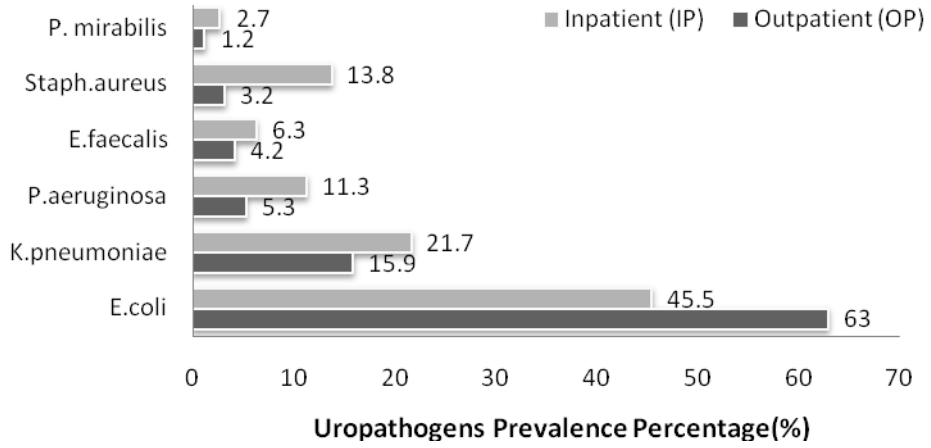

Figure: Prevalence of uropathogens among outpatients and inpatients.