CHANGES IN URINARY ISOLATES AND THEIR ANTIBIOTIC RESISTANCE PATTERN

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ABSTRACT

A total of 338 urinary isolates were studied at AFMC, Pune during 1998 for species identification and antibiotic resistance. Out of 145 community isolates *E coli* were 67% followed by *Staph aureus* (11%). The hospital isolates of *E coli* and *Proteus spp* showed higher resistance to ampicillin (81% and 89% respectively) than to cefotaxime (23% and 22% respectively). *K pneumoniae* showed relatively higher resistance to cefotaxime i.e. 54% for community strains and 75% for hospital strains. *Proteus spp* showed higher resistance to fluoroquinolones i.e. 78% for norfloxacin and 82% for ofloxacin as compared to other coliforms and *Pseudomonas aeruginosa*. Among aminoglycosides bacterial resistance to amikacin is less than to commonly used netilmicin and gentamicin. Hospital isolates of *K pneumoniae* are 100% resistant to sulphamethoxazole and to trimethoprim. Susceptibility testing is emphasized as a must both for hospital and community isolates, but when empirical treatment is contemplated for community isolates nitrofurantoin, nalidixic acid, amikacin, cefotaxime, gentamicin and piperacillin are recommended as first line choices and for hospital isolates amikacin, cefotaxime and netilmicin are recommended until susceptibility report is available.

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KEY WORDS: Antibiotic resistance;UTI.

Introduction

Urinary tract infections (UTI) are extremely common in both in and out patient settings [1]. There is a great difference between the bacterial flora of the urine in patients with an initial episode of UTI as compared with the flora from those with hospital infection [2]. *Escherichia coli* (*E coli*) is by far the most frequent infecting organism in acute infections [3]. The hospital environment is an important determinant of the nature of bacterial flora in UTI. *Proteus spp*, *Klebsiella spp*, *Enterobacter spp* and *Pseudomonas aeruginosa*, *Staphylococci* and *Enterococci* are most often isolated from inpatients as compared to a greater preponderance of *E coli* in an out patient population. Cross infection are important in the pathogenesis of hospital related UTI, especially with indwelling catheters [4].

Selection of appropriate antimicrobial agents has been complex because of the increasing number of compounds available, each with its characteristic spectrum and toxic properties. Ampicillin and amoxicillin have been the mainstay of therapy for uncomplicated lower UTI in the past, but they should no longer be considered first line of agents. Some 30-40% community acquired *E coli* strains produce β -lactamase and are resistant to the β -lactam drugs. These agents as compared to fluoroquinolones and co-trimoxazole

have poor ability to eradicate uropathogens [1]. The data available are mostly from studies abroad and may not be necessarily true for our community and hospital environment. There are very few Indian studies in this context. A constant review from various corners of our country of prevalence of organisms and their antibiotic resistant pattern is required for patient management, as these are dynamic areas where the pathogen and the antibiotic resistance change constantly. In view of the above, a study in this field is carried out and the data presented. [2]

Material and Methods

The bacterial isolates during the period 1995-96 at the Dept of Microbiology, AFMC, Pune formed the material of the study. The midstream urine and catheter samples from UTI cases were cultured by semiquantitative wire loop method on cysteine lactose electrolyte deficient medium (CLED) and incubated aerobically at 37° C for 24-48 hours [5]. Pure isolates of 10⁵ organisms/ml with presence of albumin and pus cells in the urine were taken as acute UTI. The isolates were identified by standard method [6]. The antibiotic sensitivity tests were carried out on Mueller Hinton agar by Stokes disc diffusion method. The antibiotic discs were procured from HI Media or prepared in the department from pure powders as per recommendations [7]. The control strains used were NCTC 10418(*E coli*) and NCTC 10662 (*P aeruginosa*). The isolates from out patient clinics were taken as community acquired strains and isolates from the patients admitted in the hospital with complications and intervention of the urinary tract were taken as hospital acquired strains. These patients did not have UTI during or within 48 hours of admission.

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Results

67% of acute UTI isolates were due to *E coli* followed by *Staph aureus* in 11% of cases where as *E coli* contributed for only 40% of nosocomial UTI followed by *K pneumoniae* (11%). *Acinetobacter*, *Citrobacter spp* and *Strep fecalis* are more commonly seen in nosocomial UTI (Table 1). There is increase in the resistance of the isolates to β -lactams particularly to ampicillin though *K pneumoniae* are also resistant to third generation cephalosporin, cefotaxime (75% for hospital strains and 54% for community strains (Table 2). There is relatively less resistance of *Pseudomonas aeruginosa* to carbenicillin. *Proteus* show much higher resistance to both norfloxacin and ofloxacin as compared to *P aeruginosa* which show less resistance to these antibiotics. There is distinctly higher resistance to commonly used aminoglycosides like gentamicin and netilmicin but less so to amikacin (Table 3). *E coli* isolates from acute and nosocomial UTI show almost equal percentage of resistance to norfloxacin but *Proteus spp* show higher resistance to the fluoroquinolones (Table 2). Similar is the observation to other first line antibiotics (Table 3). *K pneumoniae* hospital isolates are 100% resistance to sulphamethoxazole and trimethoprim. The ranking of antibiotics for empirical treatment to community isolates is amikacin 89.5%, followed by cefotaxime 86.7%, gentamicin 79.4%, piperacillin 74.4% and ofloxacin 73% depending on the susceptibility of all types of isolates. (Table 4). The ranking of the antibiotics for hospital isolates are amikacin 81.5% followed by cefotaxime 58% (Table 5).

TABLE 1

Common isolates from acute and nosocomial UTI

	Acute UTI		Nosocomial UTI	
<i>E coli</i>	97	(67)	78	(40)*
<i>Staph aureus</i>	16	(11)	18	(9)
<i>K pneumoniae</i>	08	(5.5)	21	(11)
<i>Citrobacter sp</i>	08	(5.5)	17	(8.8)
<i>Pseudomonas aeruginosa</i>	07	(05)	15	(7.7)
<i>Acinetobacter sp</i>	—	—	18	(09)
<i>Str faecalis</i>	—	—	16	(08)
Others	09	(06)	10	(6.5)
Total	145	(100)	193	(100)

* Figures in brackets indicate percentage

Discussion

E coli continued to be the predominant cause of acute UTI (67%) followed by *Staph aureus* (11%) both of which contribute to 70% of community acquired infections (Table 1). This is because in community acquired UTI the *E coli* are a select group of uropathogens which are attributed with multiple viru-

TABLE 2

Antibiotic resistant pattern of urinary isolates to β -lactams, aminoglycosides and quinolones (%)

Organism		Amp	Cef	Ceft	Car	Gen	Amk	Net	Nor	Ofi	Nal
<i>E coli</i>	(C)	66	10	—	—	29	14	24	55	40	56
	(H)	81	23	—	—	51	18	51	56	56	67
<i>Kleb pneumoniae</i>	(C)	88	54	—	—	47	56	63	47	47	59
	(H)	94	75	—	—	73	65	76	56	53	88
<i>Proteus spp.</i>	(H)	89	22	—	—	73	45	77	78	82	92
<i>Pseudo aeruginosa</i>	(C)	—	—	24	10	33	0	78	08	17	—
	(H)	—	—	30	40	67	29	80	33	26	—

(C) Community strains, (H) Hospital strains

Amp : Ampicillin, Cef : Cefotaxime, Ceft : Cefotazidime, Car : Carbenicillin, Gen : Gentamicin, Amk : Amikacin, Net : Netilmicin, Nor : Norfloxacin, Ofi : Ofloxacin, Nal : Nalidixic acid

TABLE 3

Antibiotic resistant pattern of urinary isolates to miscellaneous antibiotics (%)

Organism		TET	CHL	SUL	TMP	NFT	POLY B
<i>E coli</i>	(C)	67	42	72	75	60	—
	(H)	82	62	73	83	63	—
<i>K pneumoniae</i>	(C)	81	79	50	75	70	—
	(H)	86	88	100	100	72	—
<i>Proteus spp.</i>	(H)	92	—	88	92	80	—
<i>P aeruginosa</i>	(C)	—	—	—	—	—	11
	(H)	—	—	—	—	—	15
(Study AFMC 1989)							
Coliforms		66.4	50.7	78.1	71.5	37.9	51.1
<i>Proteus spp.</i>		80.5	43.9	92.7	82.9	26.8	78
<i>P aeruginosa</i>		—	—	—	—	—	14

(C) - Community strains; (H) - Hospital strains; TET - Tetracyclines; CHL - Chloromycetin; SUL - Sulphamethoxazole; TMP - Trimethoprim; NFT - Nitrofurantoin

TABLE 4

Susceptibility pattern community urinary pathogens to various antimicrobials (%)

Name of Antibiotic	Grunberg 1971	Grunberg 1992	AFMC 1991	AFMC 1995-96
Ampicillin	88.2	56.7	24.9	27.6
Tetracycline	72.5	63.6	33.6	41.3
Trimethoprim	94.0	75.0	28.5	26.4
Sulphonamide	76.4	63.1	21.9	53.2
Nitrofurantoin	85.6	86.2	62.1	71.0
Nalidixic acid	90.7	77.9	62.1	62.2
Ciprofloxacin	—	89.9	—	52.4
Norfloxacin	—	—	—	58
Ofloxacin	—	—	—	73
Piperacillin	—	—	—	74.4
Cefotaxime	—	—	—	86.7
Gentamicin	—	—	44.5	79.4
Netilmicin	—	—	—	74
Amikacin	—	—	—	89.5
Chloramphenicol	—	—	49.3	67.0

TABLE 5

Susceptibility pattern hospital urinary pathogens to various antimicrobials (%)

Name of Antibiotic	Grunberg 1971	Grunberg 1992	AFMC 1995-96
Ampicillin	66.1	53.5	10.7
Tetracycline	55.8	55.7	25.1
Trimethoprim	79.9	63.4	17.8
Sulphonamide	61.9	56.1	29.5
Nitrofurantoin	70.3	78.8	36.3
Nalidixic acid	84.8	63.3	24.8
Ciprofloxacin	—	79.4	43.3
Norfloxacin	—	—	37.2
Ofloxacin	—	—	49.5
Cefotaxime	—	—	58.0
Gentamicin	—	—	44.8
Netilmicin	—	—	56.9
Amikacin	—	—	81.5
Chloramphenicol	—	—	35.3

lent factors like increased adherence to vaginal and uroepithelial cells, resistance to serum bactericidal activity, higher quantity of K antigen, presence of aerobactin and haemolysin production [8-10]. Similar study in 1991 in this institute also isolated *E coli* in 63% of UTI cases [11]. However in a hospital setting where the patients with structural abnormalities of the urinary tract eg. benign hyperplasia of prostate, stricture of urethra or calculi, the bacteria are found to be attributed with less virulent factors and a natural selection of uropathogens absent [13].

The antibiotic resistant pattern of the major isolates

are given in Table 2. There is an overall increase in resistance to various antibiotics as compared to the previous study at AFMC in 1991 [13]. The fall in the resistance of *Pseudomonas spp* to carbenicillin is possible due to its lesser use in the hospital, for patient management. Similar observation have been made in an extensive study abroad [13]. There is relatively less resistance to the newly introduced antibiotics eg. third generation cephalosporins and fluoroquinolones as well as less commonly used aminoglycosides like netilmicin and amikacin. Though mutation confers resistance to a single antibiotic but multidrug resistance is usually transmitted by horizontal transfer via plasmids and transposons from same or different species. According to our observation multidrug resistance is more commonly seen in the hospital isolates of *E coli*, *K pneumoniae*, *Citrobacter* and *Acinetobacter spp*

The ranking of various antibiotics for empirical treatment of community acquired UTI is given in Table 4. The overall susceptibility to amikacin, cefotaxime, gentamicin, piperacillin, netilmicin and nitrofurantoin are 89.5%, 86.7%, 79.4%, 74.4%, 74% and 71% respectively. However from a study conducted abroad in 1992 ciprofloxacin and nitrofurantoin ranked highest with 89.9% and 86.2% susceptibility [14]. The ranking of drugs for empirical treatment of hospital isolates (Table 5) are amikacin, cefotaxime, netilmicin and ofloxacin with 81.5%, 58%, 56.9% and 49.5% susceptibility respectively. While starting empirical treatment, the effectiveness of the drug, the cost of treatment and affordability should be kept in mind. Once the sensitivity result are available, it is better to switch over to the specific treatment.

Microbial resistance is a constant threat to any drug and it is unlikely that any totally new antibiotic remains to be discovered since those of recent origin have similar properties to others already known. Unless adequate discretion is exercised in judicious use of these antibiotics, multidrug resistant strains will become increasingly common and this may very well lead to "the end of the antibiotic era" [15].

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