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Research Article

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Antimicrobial sensitivity profile of nosocomial uropathogens in a tertiary care hospital of South India

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ABSTRACT

Urinary tract infections (UTIs) refers to the presence of microbial pathogens within the urinary tract. UTIs are also the most common nosocomially acquired infection which accounts for almost 40% of all nosocomial infections. The spectrum and susceptibility of these infections is different from that of community-acquired infections and they are more difficult to treat. This was a retrospective study conducted in Shri B M Patil Medical College, Bijapur, India over a period of 3 years. Patients with an episode of UTI that was not present in first 48 hours of admission, and became apparent after 48 hours of admission was diagnosed as nosocomial UTI, and were included in the study. Species were identified by conventional biochemical tests and were tested for antimicrobial susceptibility by the standard disc diffusion method recommended by the Clinical and Laboratory Standards Institute (CLSI). The prevalence of UTI was more among male patients. The majority of the isolates were from > 50 years age group. E. coli was the most predominant organism (43.3%), followed by Klebsiella spp. and Citrobacter spp. Piperacillin-tazobactum , amikacin, nitrofurantoin were the most active agents against the majority of Gram negative bacilli. E. coli, which was the commonest organism, isolated also showed similar sensitivity patterns. Piperacillin-tazobactum and linezolid were most effective drugs against Gram positive cocci. Sensitivity pattern of the pathogen should be ascertained before prescribing an antimicrobial agent for a meaningful therapy and to avoid fast emergence of resistant mutants. Appropriate usage of antimicrobials should be implemented by formulating hospital antibiotic policy through a close collaboration between clinicians and microbiologists.

Key words: Antibiotic Sensitivity Tests, Antibiotic policy, *Escherichia coli* , Microbial resistance, Urinary tract infections (UTI)

INTRODUCTION

Urinary tract infections (UTIs) refers to the presence of microbial pathogens within the urinary tract. Usually classified by the site of infection (the bladder [cystitis], kidney [pyelonephritis], or urine [bacteriuria]), UTIs can be asymptomatic or symptomatic, characterized by a wide spectrum of symptoms ranging from mild irritative voiding to bacteremia, sepsis, or even death. [1] UTIs are among the most common community-acquired infection; in some regions, however, a rising resistance rate is a cause of concern. UTIs are also the most common nosocomially acquired infection [1-3] which accounts for almost 40% of all nosocomial infections. The spectrum and susceptibility of these infections is different from that of community-acquired infections and they are more difficult to treat. [4-5]

UTIs often results in serious complications like secondary bacteremia and sepsis leading to a rise in the hospital costs and mortality. It is therefore, necessary to treat UTI empirically in relevant situations where indwelling

catheter for long duration is inevitable. Empiric antimicrobial therapy reduces the incidence of post operative UTI, prevents the development of sepsis and reduces the average hospital stay and the associated cost of treatment. [6]

Before seventies multiple drug resistance was practically nonexistent and was restricted to mutation of chromosomal genes. However during the last two decades bacterial drug resistance mediated by extra chromosomal genetic elements (plasmids), which simultaneously carry gene for resistance to number of antibiotics has made the position miserable, specifically in gram negative bacteria. The multiple drug resistance is increasing at an alarming rate, especially under the selective antibiotic pressure in the hospital environment. [7]

It is important to realize that there may be marked differences between various geographic areas within a vast country like India. Since most UTIs are treated empirically the selection of antimicrobial agent should be determined not only by the most likely pathogen but also by its expected susceptibility pattern. [8] Therefore the current study was undertaken to know the microorganisms responsible for nosocomial UTIs and their antimicrobial resistance pattern in our tertiary care hospital.

EXPERIMENTAL SECTION

Study design, setting:
This was a retrospective study conducted in the Department of Microbiology, Shri B M Patil Medical College, Bijapur, India over a period of 3 years from January 2010 to December 2012.

Analysis :
Presence of at least two of the following with no other recognized cause: fever, urgency of urination, dysuria or suprapubic tenderness; with at least one of the following: pyuria or positive urine culture. Patients with an episode of UTI that was not present in first 48 h of admission, and became apparent after 48 hours of admission was diagnosed as nosocomial UTI, and were included in the study.

Sample collection:
The samples included midstream urine specimen, catheterized urine samples, supra-pubic aspirates collected in sterile universal bottles (approximately 15 ml) The urine specimens were transported to the bacteriology laboratory within 2 hours of collection. [9]

Microbiological analysis:
All urine samples were examined by routine microscopic examination by wet mount of urine sediment after centrifuging urine for 10 minutes at 1000 revolution per minute. Presence of pus cells, red blood cells, epithelial cells, casts, and crystals were noted as supportive findings of urinary infection. Simultaneously all urine samples were cultured over routine culture media; MacConkey agar and Cysteine lactose electrolyte deficient agar with a sterile standard loop. These plates were incubated at 37°C for 2 consecutive days. Culture results were interpreted according to the standard criteria and a growth of $\geq 10^5$ CFU/ml was considered as significant bacteriuria. [10] To avoid duplication, repeated isolates of the same species from individual patients were excluded from the survey. Cultures with more than three colonies were discarded, as contaminants and their antibiotic susceptibility were not tested. Species were identified by conventional biochemical tests according to standard microbiological techniques. [9]

Antimicrobial susceptibility testing:
All isolates were tested for antimicrobial susceptibility on Mueller Hinton agar by the standard disc diffusion method recommended by the Clinical and Laboratory Standards Institute (CLSI). [11] Antimicrobial agents (disks) were obtained from HiMedia laboratories, Pvt Ltd, Mumbai. Appropriate quality control strains were used to validate the results of the antimicrobial disk. *E. coli*, ATCC 25922, and *Pseudomonas aeruginosa*, ATCC 27853, were used as quality control strains. [11]

RESULTS

A total of 682 culture positive isolates with significant growth were recovered. Of these 427 (62.6%) were from male patients and 255 (37.4%) were from female patients. Table 1 shows age and sex wise distribution of the uropathogens. The prevalence of UTI was more among male patients. Overall the majority of the isolates were from

> 50 years age group. Among females maximum numbers of isolates were from 21-50 years age group followed by > 50 years age group. Among males, elderly patients (57.8%) were more commonly affected followed by 21-50 years age group.

Table 2 shows the etiological agents of nosocomial UTI. *E. coli* was the most predominant organism (43.3%) and also the most prevalent organism isolated from male as well as female patients, followed by *Klebsiella* spp. and *Citrobacter* spp. Gram positive cocci accounted for 7.9 % of the total isolates causing CA-UTI. *Candida* spp. (6.5%) were isolated in small numbers.

Table 3 shows antibiotic sensitivity of the isolates causing nosocomial UTI. Piperacillin-tazobactum , amikacin, nitrofurantoin were the most active agents against the majority of Gram negative bacilli. Ampicillin, cephalexin and nalidixic acid were the least active antibiotics against the majority of the Gram negative bacilli.. *E. coli*, which was the commonest organism, isolated also showed similar sensitivity patterns with piperacillin-tazobactum, amikacin showing sensitivity of more than 80 %. Piperacillin-tazobactum and linezolid were most effective drugs against Gram positive cocci and the least active drugs against Gram positive cocci were penicillin and cloxacillin.

Table 1: Age and sex wise distribution of uropathogens

Age in years	Male		Female		Total	
	Number	%	Number	%	Number	%
1-20	27	6.32	39	15.3	66	9.68
21-50	153	35.8	142	55.7	295	43.3
> 51	247	57.8	74	29	321	47.1
Total	427	100	255	100	682	100

Table 2: Frequency of uropathogens isolated

Organism	Number (%)					
	Male		Female		Total	
	No.	%	No.	%	No.	%
E.coli	184	43.1	111	43.5	295	43.3
***Klebsiella* spp.**	60	14.1	51	20	111	16.3
***Citrobacter* spp.**	63	14.8	26	10.2	89	13
Other Gram negative bacilli *	58	13.6	31	12.2	89	13
Gram positive cocci	37	8.67	17	6.67	54	7.92
***Candida* spp.**	25	5.85	19	7.45	44	6.45
Total	427	100	255	100	682	100

**Protius* spp. *Acenetobacter* spp. *Pseudomonas* spp.

Table 3: Antibiotic sensitivity of the isolates

Antibiotics	Sensitivity (%)			
	All Gram negative bacilli	*E. coli*	*Klebsiella* spp.	*Citrobacter* spp.
Ampicillin	5.2	6.78	4.5	2.25
Co -trimoxazole	16.3	18.6	18.9	12.4
Norfloxacin	15.8	12.5	23.4	14.6
Ciprofloxacin	23	15.6	36	30.3
Gentamicin	28.9	35.9	25.2	20.2
Nalidixic acid	8.2	7.12	18	3.37
Amoxyclav	11.1	12.9	12.6	6.74
Amikacin	65.4	85.8	59.8	51.9
Cephalexin	6.4	7.46	5.41	6.74
Cefoparazone – salbactam	46.3	55.9	38.7	34.8
Piperacillin-tazobactum	76.5	84.5	70.5	57.7
Ofloxacin	28.6	23.4	40.5	36
Nitrofurantoin	56.8	67.2	47.9	45.3

Antibiotics	Sensitivity (%)
	Gram positive cocci
Penicillin	14.8
Erythromycin	25.9
Tetracycline	33.3
Cephalexin	20.4
Cloxacillin	13
Piperacillin-tazobactum	72.2
Cefoparazone – salbactam	44.4
Gentamicin	33.3
Ciprofloxacin	24.1
Amoxyclav	40.7
Cefuroxime	18.5
Azithromycin	24.1
Linezolid	64.8

DISCUSSION

Urinary tract infections (UTIs) are the most common bacterial infection in patients of all ages with high risk in young women resulting in significant morbidity and health care costs. [12] With the constantly shifting trends in drug resistance, antibiotic options, and pharmacoeconomic considerations, UTIs continue to be one of the most frequently diagnosed cases, having an estimated figure of 150 million per annum worldwide. [13]

In the current study , *Enterobacteriaceae* were responsible for more than 70 % of the nosocomial UTI cases. Among these *E. coli* was the most common organism isolated followed by *Klebsiella* spp. which correlates well other studies conducted across our country and around the world. [6,14,15] and also, a national survey of nosocomial UTIs in the United states found *E.coli*, *Pseudomonas* and *Klebsiella* spp. among the top 5 pathogens [16]. *Enterobacteriacae* have several factors responsible for their attachment to the uroepithelium. These gram-negative aerobic bacteria colonise the urogenital mucosa with adhesin, pili, fimbriae and P1-blood group phenotype receptor.[14]

The age wise distribution of the patients diagnosed with nosocomial UTI revealed the following characteristics. In all age groups, except those aged more than 50 years, females were more frequently affected than males. Among females, frequency of UTI was more among 21-50 years age group and among males, elderly patients were more commonly affected, which could be because of prostatic hypertrophy and neurogenic bladder in the elderly males. [17] The prevalence of UTIs which was more among reproductive age groups in females could be attributed to short length of urethra in females, termination of urethra beneath the labia and proximity of the urethral opening to anus.[17]

Uropathogens and their susceptibility may vary from time to time and from one institution to another, each hospital or institution must have its own evaluation for such infection so that any change in the susceptibility pattern can be detected and managed accordingly. Such evaluation is also useful for the setting up of an antibiotic policy. [18] Antibiotic resistance pattern in our study revealed that, ampicillin, cephalexin, nalidixic acid were the least active antibiotics against the Gram negative bacilli, followed by amoxyclav ,co –trimoxazole, norfloxacin which showed resistance rate of more than 70%. Piperacillin-tazobactum and amikacin were the most active agents against the Gram negative bacilli.

The *Enterobacteriaceae*, exhibited relatively higher resistance rates in general to amoxyclav and co –trimoxazole than those that have been reported in previous studies [16] our study correlates well with previous one [19] in which, Piperacillin-tazobactum , amikacin and nitrofurantoin remained very active drugs against most *E. coli* isolates. The highest resistance was shown by *Citrobacter* spp which was the third most common organism isolated from the UTIs. *Citrobacter* spp was resistant to commonly-used antibiotics, except Piperacillin-tazobactum which was the second line antibiotic according to hospital antibiotic policy. A similar pattern were observed for *Klebsiella* spp. majority of which were susceptible to Piperacillin-tazobactum and amikacin.

The quinolones viz Nalidixic acid, norfloxacin and ciprofloxacin, which are most commonly used drugs against UTI were least effective against all the uropathogens encountered during the study period. This observation consistent the previous reports.[20] It has been reported that since the mechanism of action of these quinolones is almost same, emergence of resistance against one will also decrease the activity of other quinolones. [7]

To summarize, *E. coli* was the most predominant organism (43.3%), followed by *Klebsiella* spp. Piperacillin-tazobactum , amikacin, nitrofurantoin were the most active agents against the majority of Gram negative bacilli. *E. coli*, which was the commonest organism, isolated also showed similar sensitivity patterns. Piperacillin-tazobactum and linezolid were most effective drugs against Gram positive cocci.

To conclude, sensitivity pattern of the pathogen should be ascertained before prescribing an antimicrobial agent for a meaningful therapy and to avoid fast emergence of resistant mutants. Appropriate usage of antimicrobials should be implemented by formulating hospital antibiotic policy through a close collaboration between clinicians and microbiologists.

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