Scholars Journal of Applied Medical Sciences (SJAMS)
Abbreviated Key Title: Sch. J. App. Med. Sci.
ISSN 2320-6691 (Online)
ISSN 2347-954X (Print)

A Unit of Scholars Academic and Scientific Society, India
www.saspublisher.com

Microbiology

Bacterial Isolates and Their Antibiotic Susceptibility Pattern of Uropathogens in Outpatients and Inpatients with Urinary Tract Infection in Tertiary Care Centre, Bikaner - Implications on Empiric Therapy

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Original Research Article

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Article History
Received: 19.12.2017
Accepted: 25.12.2017
Published: 30.01.2018

DOI:
10.36347/sjams.2018.v06i01.013

Abstract: Urinary Tract Infections (UTI) are the common infections after the respiratory tract infections. The present study was designed to isolates the bacterial uropathogens and their antibiotic susceptibility pattern in outpatients and inpatients of our tertiary care and to determine an empirical treatment pattern for patients with UTI. A total of 500 urine samples were obtained with a clinical diagnosis of UTI. The samples were cultured and antibiotic susceptibility of isolates determined by disc diffusion method. Of 500 urine samples processed (310 from inpatients and 190 from outpatients), 176(35.20%) yielded bacterial isolates. About 136(43.87%) samples from inpatients and 40 (21.05%) from outpatients showed significant bacteriuria. *Escherichia coli* predominated organism isolated in both groups, followed by *Klebsiella spp*. and Pseudomonas spp., Acinetobacter spp., and Enterobacter spp., which were isolated from only the inpatient urine samples. Sensitivity to Nitrofurantoin varied from 65% to 90% and fluoroquinolone resistance was documented as 25%-50%. Resistance to amikacin, ceftazidime, and ceftriaxone was less than 25%. Imipenem was found no resistance of the bacterial isolates. E. coli and Klebsiella spp. are the major bacteria uropathogens. Resistant strains are prevalent in the community, as evident by the fact that there is not much difference in resistance patterns of isolates from inpatients and outpatients. Taking into account the resistant pattern, Nitrofurantoin represents the option of first choice for empirical therapy of uncomplicated UTI.
Keywords: Antibiotic susceptibility, *E.coli*, Nitrofurantoin, Urinary Tract infection.

INTRODUCTION

Urinary tract infections (UTIs) are the second most common infections encountered in clinical practice after respiratory tract infection [1]. The most common bacterial agent involved in cause of urinary tract infection is *Escherichia coli*; this is the principal pathogen both in the community as well as in the hospital [2, 3]. Urinary Tract Infections (UTI) constitute a great proportion of prescription of antibiotics. With the use of antibiotics, though a significant reduction in the prevalence of infectious diseases was seen worldwide in the initial years, eventually a new form of infectious diseases caused by drug-resistant bacteria has evolved. The use of an antibiotic has been correlated with the subsequent development of resistance to it [4,5]. The common organisms causing UTI are the normal part of intestinal flora [6]. Antibiotic resistance occurs commonly in intestinal bacteria due to treatment therapy for infection other than UTI [7]. The organisms causing UTI are normal part of intestinal flora. Escherichia coli is the predominant organism isolates, accounting for 75% to 90% of uncomplicated UTI among patients [8, 9]. Staphylococcus saprophyticus, Klebsiella spp., Proteus spp., Enterococcus spp., and Enterobacter spp. are organisms less commonly isolated from outpatients.In the initial years, the prevalence of infectious disease was significantly reduced due to use of novel antibiotic , later a new form of infectious diseases caused by drug-resistant bacteria has evolve. The drug resistance in bacteria developed subsequently use of antibiotic [10,11]. In last 30 years Antibiotic resistance among uropathogens has increased [12-14]. In Britain, 1971 to 1992 ampicillin resistance increased from 12% to 43%. A study conducted in Turky, the resistance found in different antibiotic was 56% to ampicillin, 24% to ampicillin/sulbactam, 15% to ciprofloxacin, 36% to trimethoprim-sulfamethoxazole and 75% to cefuroxime [15]. The resistance rates among uropathogens were very high, third-generation cephalosporins were found resistance in 76% strains, a

recent study in India [16]. The present study was, therefore, designed to to determine the etiology a of uropathogens profile. Antibiotic sensitivity pattern was also done so as to guide the clinicians of our hospital to select appropriate antimicrobial agents and to aid them for designing effective empiric treatment, in patients with UTI.

MATERIALS AND METHODS

Study Design & Setting

This descriptive study was conducted in the department of microbiology, Sardar Patel Medical College, Bikaner from July 2017 to September 2017 over a period of three months. The urine samples were obtained from inpatients and outpatients of P.B.M. hospital with a clinical diagnosis of suspected UTI. Only samples which had been submitted by adult, non-pregnant females in the outpatient department were considered.

Clinical Isolates

The samples consider are midstream urine specimen, catheterized urine samples, supra-pubic aspirates collected in sterile universal container. A total of 500 samples were processed during the study period.

Microbiological Analysis

The uncentrifuged samples were inoculated with a calibrated loop delivering 0.001 ml of urine sample onto Blood agar and MacConkey agar plates. The inoculated culture plates were incubated at 37°C for 24 hour. A significant bacterial count was taken as any count equal to or more than 10^5/ml of urine for Gram-negative bacteria and 10^3-10^4 /ml of urine for Gram-positive bacteria. The isolates were identified by biochemical tests as per standard methods [17].

RESULTS

A total of 500 urine samples were processed in which 310 and 190 were from inpatients and outpatients respectively. Out of these samples, 176 (35.20%) specimens yielded bacterial isolates. About 136 (43.87%) samples from inpatients and 40 (21.05%) from outpatients showed significant bacteriuria. Gram negative organisms isolate mostly 91.48% and Gram positive organisms formed only 8.52% of the isolates in present study.

E. coli predominated in both groups followed by Klebsiella spp. and Citrobacter spp. (Table 1). *Proteus* spp. and *Staphylococcus aureus* were isolated from both groups, whereas *Pseudomonas spp*., *Acinetobacter spp*., and *Enterobacter spp*. were isolated from only the inpatient samples.

Table-1: Distribution of organisms in outpatients and inpatients

Urine sample	Outpatient	Inpatient	Total
	190	310	500
Escherichia coli	19	35	54
Klebsiella spp.	12	23	35
Citrobacter spp.	05	13	18
Pseudomonas spp.	00	25	25
Acinetobacter spp.	00	15	15
Enterobacter spp.	00	09	09
Proteus spp.	00	05	05
Staphylococcus aureus	04	11	15

Table-2: Sensitivity of organisms to antimicrobials (numbers sensitive)

Antibiotic	E. coli (n=54)	Klebsiella (n=35)	Pseudomonas aeruginosa (n=25)	Acinatobacter spp. (n=15)	Citrobacter spp. (n=18)	Enterobacter spp. (n=09)	Proteus spp. (n=05)	S.aureus (n=15)
	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive
Amikacin	30 (55.55%)	23 (65.70%)	18 (72%)	11 (73.33%)	11 (61.11%)	5 (55.55%)	3 (60%)	10 (66.66%)
Amoxycillin +clavunic acid	35 (64.81%)	19 (54.28%)	Not Applied	10 (66.66%)	10 (55.55%)	7 (77.77%)	3 (60%)	11 (73.33%)
Polymyxin B	Not Applied	Not Applied	23 (92%)	Not Applied	Not Applied	Not Applied	Not Applied	Not Applied
Ciprofloxacin	26 (48.14%)	22 (62.85%)	15(60%)	10 (66.66%)	10 (55.55%)	5 (55.55%)	3 (60%)	11 (73.33%)
Ceftazidine	35 (64.81%)	25 (71.42%)	17 (68%)	11 (73.33%)	9 (50%)	7 (77.77%)	3 (60%)	Not Applied
Ceftriaxone	46 (88.46%)	27 (77.14%)	18 (72%)	11 (73.33%)	12 (66.66%)	7 (77.77%)	2 (40%)	Not Applied
Piperacillin +Tazobactum	48 (88.88%)	28 (80%)	20 (80%)	13 (86.66%)	15 (83.33%)	8 (88.88%)	4 (80%)	Not Applied
Nitrofuration	43 (79.62%)	27 (77.14%)	Not Applied	Not Applied	14 (77.77%)	8 (88.88%)	4 (80%)	10 (66.66%)
Linezolid	Not Applied	Not Applied	Not Applied	Not Applied	Not Applied	Not Applied	Not Applied	15 (100%)
Vancomycin	Not Applied	Not Applied	Not Applied	Not Applied	Not Applied	Not Applied	Not Applied	15 (100%)
Imipenem	54 (100%)	35 (100%)	25 (100%)	15 (100%)	18 (100%)	09 (100%)	05 (100%)	Not Applied

In gram positive bacteria, fifteen strains of *Staph.aureus* isolated, out of them oxacillin resistant strains are five. All *Staph. aureus* strains were sensitive to linezolid and vancomycin.

DISCUSSION

Most common gram negative bacteria isolates from urine sample was Eishcheria coli., Klebisella spp., Citrobacter spp., Acinatobacter spp. and Pseudomonas spp. were isolated only in hospitalized patients. The proportion of bacterial isolated was similar to some previous studies [18, 19].

Gram-negative organisms were more pathogenic and common isolates other than Gram-positive organisms in our tertiary care hospital which is similar to reports from other study. *Pseudomonas* spp. is commonly survive and thrives well in soaps and other disinfectants used for urethral catheterization [20]. Gram-positive bacteria *Staphylococcus Aureus* was isolated from out and in patients.

The degree of resistance to routinely used antibiotics in both groups was almost similar. This is in contrast to some previous studies, which showed that resistance is more in isolates from hospitalized patients than the outpatients [19, 21]. Recent studies have shown results similar to the present study [18]. This indicates that the drug-resistant strains have spread in the community.

The aminoglycoside, amikacin was sensitive to >60% of gram negative bacteria .Similar findings was as also reported from other studies [22, 23].

Many antibiotics are used many years to treat UTI infection due to use of these drugs high degree of resistance to amikacin, amoxyclav, ceftazidine and ciprofloxacin was found. Ceftrixone and pipercillin+ tazobactum are have low resistant to other antibiotics. On the other hand, resistance to a Piperacillin-tazobactum and Ceftrixone are low, likely reflecting lower usage of these drugs.

In the present study, ceftriaxone & ceftazidime 3rd generation cephalosporins have high sensitivity rate more than 60% to all gram negative organisms. 3rd generation cephalosporins have good activity against the gram negative strains. This low resistant to ceftriaxone and ceftazidime (<25%) indicate that most of the bacterial strains in our tertiary care are not Extended-Spectrum Beta-Lactamase (ESBL) producers. This is dissimilar to other studies that have isolated >76% of UTI bacteria are ESBL producers. This is a new finding and interesting to us to learn that ESBL producers are present in low concentration in our community. Third-generation cephalosporin may be considered as the first line of therapy for UTI [22]. Resistance to pipercillin tazobactum was very low (<20%). The resistance to this drug was seen with *Klebsiella* spp., *Pseudomonas* spp., and *Proteus* spp. (20%)

Most commonly used urinary antibiotic is Nitrofurantoin. This antibiotic cannot be used for other infection outside the urinary tract. So this antibiotic has not occurred high drug resistance in urinary tract infection patients. In our study we found 78% overall drug sensitivity to all pathogens. This study same similar trend previous Indian studies that have shown lower resistance rates [24, 25]. Due to intrinsic resistance to this urinary antibiotic Pseudomonas spp. and Acinetobacter spp. strains are not tested in our study. We recommend Nitrofurantoin as an empirical therapy antibiotic for UTI because this drug has good sensitivity to *E. coli, Klebsiella spp., Proteus spp., Staph aureus*.

Imipenem is highly sensitive (100%) to all uro-pathogens of gram negative bacteria. Carbapenem is the final therapeutic option for any infection, and hence cannot be given for empirical therapy.

Uncontrolled use of oral antibiotics creates high resistance rate in our community in last decades. These resistance trends have similarity to other studies [26, 27].

The trend of antibiotic empirical therapy for treating UTI in world may not consider for specific region such as India. In India antibiotic susceptibility rates are decreased have documented for common urinary pathogens.

So in present study, we recommend that for Indian region, routine urine culture and antibiotic susceptibility pattern may be necessary, since treatment failure with empirical therapy is likely to occur. In India, UTI treatment plan can no longer acceptable as international guidelines and specific guidelines on local susceptibility patterns are necessary. In India continuous regional surveillance programme is necessary to known local susceptibility pattern and provide information which can be used for development of Indian guidelines in UTI patients.

In conclusion, present study shows that antibiotic resistance trends continuously increasing in UTI patients indicate that it is imperative to rationalize the use of antimicrobials and to use these conservatively. This study it is too alarming that all the bacterial pathogen were found resistance to three or four antibiotics. Antibiotics resistance is becoming a life threatening like problem in our country for the public health; therefore it is very important issue to be addressed by the government and local governing body to formulate a strict antibiotics prescription policy in our country.

CONCLUSION

E. coli and Klebsiella spp. are the major bacterial uropathogens. Resistant strains are prevalent in the community, as evident by the fact that there is not much difference in resistance patterns of isolates from inpatients and outpatients. Taking into account the resistant pattern, Nitrofurantoin represents the option of first choice for empirical therapy of uncomplicated UTI. This along with the alarming rate of resistance to ciprofloxacin, amikacin and amoxicillin-clavunic acid, avoiding the use of these antibiotics for empiric treatment of UTI in India. This study is useful for clinician to in order to improve the empirical treatment.

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