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Trends in Antibiotic Susceptibility Pattern of Community-Acquired Uropathogens in the Nashik Division of Maharashtra

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Abstract

Background: Antibiotic resistance of urinary tract pathogens has increased worldwide. Knowledge of the antibiotic resistance patterns of uropathogens in specific geographical locations is an important factor for choosing an appropriate empirical antimicrobial treatment. The aim of this study is to provide information regarding local resistance patterns of urinary pathogens to the commonly used antibiotics in Nashik division of Maharashtra, India. *Methodology:* Urine samples collected and submitted to microbiology laboratories in Tambe hospital, Sangamner and SMBT IMSRC, Igatpuri, Nashik were identified by conventional methods over a period from August 2016 to March 2017. Antimicrobial resistance testing was performed by the standard technique in accordance with the recommendations of the Clinical and Laboratory Standards Institute. *Results:* Of the total 1575 mid-stream urine samples collected from suspected cases of urinary tract infection, 750 (47.61%) were positive for pathogenic bacteria. Escherichia coli (E. coli) was the most common isolate (68.8%) followed by Proteus spp. (13.7%), and Klebsiella spp. (7.46%). E. coli isolates were mostly susceptible to imipenem,meropenem(99.5%), followed by amikacin(92%), flouroquinolones(79-89%) ,nitrofurantoin (82%); however, only 69% of E. coli isolates were susceptible to trimethoprim-sulfamethoxazole and around 50% were susceptible to third generation cephalosporins. *Conclusion:* Nitrofurantoin and flouroquinolones may be considered as a first-line empiric antibacterial agent for urinary tract infections in outpatients in Nashik division of Maharashtra, India.

Keywords: Urinary Tract Infection; Antimicrobial Susceptibility; Uropathogens; India.

Introduction

Urinary tract infections (UTIs) are a commonly encountered diseases by general practitioners and hospital doctors in developing countries with an estimated annual global incidence of at least 250 million [1,2]. It has been estimated that globally symptomatic UTIs result in as many as 7 million visits to outpatient clinics, 1 million visits to emergency departments, and 100,000 hospitalizations annually [3]. Many different microorganisms can cause UTIs the most common pathogens being Escherichia coli and other Enterobacteriacae, which accounts approximately 75% of the isolates. In complicated urinary tract infections and hospitalized patients, organisms such as Enterococcus faecalis and highly resistant Gram-negative rods including

Pseudomonas spp. are comparatively more common. The relative frequency of the pathogens varies depending upon age, sex, catheterization, and hospitalization [4]. 10-20% of women have recurrent Urinary Tract Infection (UTI) at sometime in their life [5,6]. UTI in males is less common and primarily occurs after 50 years of age. It has been observed that 7.0 % of children with UTI develop renal scarring. It also has been observed that UTI in pregnancy may be associated with an increased neonatal mortality [7]. Although the majority of infections are acute and short lived, they contribute to a significant amount of morbidity in the population. Treatment of UTIs cases is often started empirically and therapy is based on information determined from the antimicrobial resistance pattern of the urinary pathogens [3]. However, a large proportion of uncontrolled antibiotic usage has contributed to the emergence of resistant bacterial infections [8,9]. As a result, the prevalence of antimicrobial resistance among urinary pathogens has been increasing worldwide. Associated resistance, i.e. the fact that a bacterium resistant to one antibiotic is often much more likely to be resistant to other antibiotics, drastically decreases our chances of getting a second empirical attempt right [10]. Resistance rates to the most common prescribed drugs used in the treatment of UTIs vary considerably in different areas world-wide. The estimation of local etiology and susceptibility profile could support the most effective empirical treatment [11]. E.coli has a relatively large potential for developing antibiotic resistance. Increasing rates of resistance among E.coli is a growing concern in both developed and devel-oping countries [12]. There is a substantial geographic variation in the antibiotic susceptibility profiles of E.coli to com-monly used antibiotics [13]. Therefore, investigating epidemiology of UTIs (prevalence, risk factors, bacterial isolates and antibiotic sensitivity) is fundamental for care givers and health planners to guide the expected interventions. Thus, the aim of this study was to determine bacterial etiologic agent of uropathogens and evaluate their in vitro susceptibility pattern to commonly used antimicrobial agents. We hope this study will help the clinicians to become familiar with the common pathogens responsible for UTIs and their antimicrobial susceptibility patterns which definitely help the clinicians to choose the proper empirical antimicrobial management of UTI.

Materials and Methods

Study Design

We carried out a prospective study in the Department of Urology in association with the Department of Microbiology on all of the bacterial strains isolated from the urine sample of patients who attended the Tambe Hospital, Sangamner, Ahmednagar and SMBT Institute of Medical Sciences and Research Center, Igatpuri, Nashik with a suspected case of urinary tract infection between August 2016 and March 2017. This study was approved by the Institutional Review Board of both the hospitals. A total of 1575 samples were processed and 750 showed positive growth in the laboratory for bacterial culture and sensitivity testing during the study period.

Culture

All clean catched midstream urine samples were collected and inoculated onto the blood agar and Mac Conkey agar using sterile loop. The plates were observed for bacterial growth after 24 hours of aerobic incubation at 37 degree Celsius. The bacteria were identified based on the colony characteristics, gram staining findings and biochemical reactions [14,15]. Only patients who had significant bacteriuria ($>10^5$ cfu/mL) were included in the microbiological analysis. The demographic datas were recorded and tabulated.

Antibiotic Susceptibility Testing

Susceptibility test was performed to currently used antibiotics using Kirby Bauer disc diffusion technique on Mueller–Hinton Agar (MH) or MH agar + 5% sheep blood, as recommended by the Clinical Laboratory Standards Institute (CLSI) guidelines. Antibiotics tested were ampicillin + sulbactum, amoxicillin + clavulanic acid, amikacin, cifixime, cefadroxil, cefuroxime, ceftriaxone, cefotaxime, cefoperazone, ciprofloxacin, cotrimoxazole, gentamicin, imipenem/meropenem, levofloxacin, nitrofurantoin, ofloxacin, piperacillin + tazobactum, tigecycline, vancomycin.

The results were interpreted according to CLSI (formerly NCCLS) 2000 [9].

Statistical analysis was performed using SPSS, version 13.

Results

In the present study 750 urine samples showed significant bacterial growth. The results are discussed based on these samples. The study showed that UTI is more common in females than males.

Table 1: Gender Distribution of the Study Group

Sex	Number	Percentage
M	298	39.73
F	452	60.26

Table 2: Age Distribution of the Study group

Age (years)	Number	Percentage
Less than 10 to 18	46	6.13
19 to 39	347	46.26
40 to 59	187	24.93
More than 60	170	22.66

Table 3: Frequency of community-acquired uropathogens

Organism	No of Isolates	Percentage
E. coli	516	68.8
Proteus spp.	103	13.7
Klebsiella spp.	56	7.46
Pseudomonas spp.	32	4.26
Streptococcus spp. 1	21	2.8
Enterococcus spp.	9	1.2
Coagulase-Negative Staphylococci 2	5	0.66
Staphylococcus aureus	4	0.53
Enterobacter spp.	2	0.26
Citrobacter spp.	2	0.26

Table 4: Percentage of Resistant Uropathogens to Commonly Used Antibiotics*

	E.coli	Proteus spp	Klebsiella spp	Pseudomonas spp	Streptococcus spp	Enterococcus spp	Enterobacter spp	Citrobacter spp	Acinetobacter spp	Staphylococcus spp
Ampicillin+Sulbactum	75	60	82	71	10	70	70	63	100	30
Amoxicillin+Clavulanic Acid	85	60	94	86	15	82	80	73	100	40
Amikacin	8	10	18	20	ND	48	12	9	60	ND#
Cefixime	49	33	47	ND	ND	ND	40	42	70	ND
Ciprofloxacin	21	10	13	14	ND	46	14	18	30	ND
Cefadroxil	54	28	52	ND	ND	ND	44	32	67	ND
Cefuroxime	50	12	39	29	54	48	39	26	52	60
Ceftriaxone	57	31	50	28	ND	50	40	18	58	ND
Cotrimoxazole(Trimethoprim-Sulphamethoxazole)	31	66	7	14	100	60	24	21	ND	90
Cefotaxime	48	32	49	ND	ND	ND	15	34	74	ND
Cefoperazone	47	41	38	26	51	50	44	38	71	70
Gentamicin	7	ND	19	24	ND	ND	24	9	61	0
Imipenem/Meropenem	0.5	0.4	0.4	0.5	1	0	0	0	0.4	1.5
Levofloxacin	11	5	8	12	42	31	15	18	32	45
Nitrofurantoin	18	20	9	38	2	ND	40	42	80	40
Ofloxacin	12	18	11	12	40	38	14	18	33	42
Piperacillin+Tazobactum	16	14	12	1	20	2	7	5	20	25
Tigecycline	7	ND	ND	ND	ND	ND	ND	8	13	ND
Vancomycin	ND	ND	ND	ND	15	ND	ND	ND	80	20

* All figures are rounded off to nearest value.
# ND = Not Done

Female/male ratio was 1.5:1 (Table 1). The present study showed that a high percentage of organisms were isolated from both the males and females within the age group19-39, 40-59 and more than 60 years of age (Table 2). Of the total 750 positive cultures E. coli was the predominant bacterial isolate and accounted for 68.8 % of the total isolates followed by Proteus spp (13.7%) and Klebsiella spp (7.46%) (Table 3). Ampicillin + sulbactum and amoxicillin + clavulanic acid showed higher level resistance to the commonly isolated pathogens. The study showed alarming results for the third generation cephalosporins that around 50% of the pathogens were resistant to them. Moreover, the pathogens have started developing resistance to Imipenem/Meropenem. However, they are still found sensitive to Amikacin, Levofloxacin, Ofloxacin and Nitrofurantoin (Table 4).

Discussion

Bacterial infection of the urinary tract is one of the common causes for seeking medical attention in the community [16]. Effective management of patients suffering from bacterial UTIs commonly relays on the identification of the type of organisms that caused the disease and the selection of an effective antibiotic agent to that particular organism [17].

In this study, the isolation rate of bacteria from urine was 47.61 % which is in line with other studies [16-20].

In our study, as in several previous reports, the most commonly isolated organism in UTI was E. coli, involving 68.8% of the positive samples. The proportion of bacterial species isolated was similar to those described in several previous studies [21-24]. Proteus spp. was the second most common organism followed by Klebsiella spp. and Pseudomonas spp.

The frequency of UTI is greater in women as compared to men [22,25], and our results were similar to these reports; 60.26% of all patients were female.

The main differences between our results and the results of studies conducted in other places were the resistance patterns of uropathogens. Antibiotic sensitivity pattern of organisms change rapidly over a short period. It is especially true for developing country where antibiotics are prescribed irrationally not only by the medical practitioners but the antibiotics are also purchased directly from the chemist (Medicine shop keepers) without prescription. It has been advised that clinicians should be aware of the rising resistance of urinary pathogens to commonly prescribed antibiotics.

Resistance to antimicrobial agents has been noted since the first use of these agents and is an increasing world-wide problem [5]. This study revealed that a higher prevalence rate of resistance to the commonly prescribed antibiotic agent. The finding that around 80% of E. coli and K. pneumonia isolates were resistant to Amoxicillin+clavulanic acid and Ampicillin+sulbactum is of great importance and implies that these antibiotics cannot be used as empirical therapy for urinary tract infection particularly in the study area.

According to a Turkish study [26], E. coli isolates were highly resistant to ampicillin (47.8% to 64.6%) and higher resistance rates to ampicillin have been reported in other studies [27,28]. In our study, the ampicillin resistance rate was around 75%. The beta (β)-lactam antibiotics such as ampicillin have other problems besides resistance. They are found to have relatively poor action in treating symptomatic cystitis. One hypothesis is that it is rapidly excreted and the duration of significant drug concentration in the urine is short. The other reason is that â-lactams are relatively ineffective in clearing Gram-negative rods from the vaginal and colonic mucosa, thus possibly predisposing to recurrences when used to treat UTI [29,30].

On the other hand very low levels of resistance were detected to antibiotics such as ciprofloxacin, nitrofurantoin and gentamicin and a comparable rate of sensitivity has been reported for these drugs in previous studies done [11,19,31-33]. Thus, these drugs could be considered as alternative options in the empirical treatment of UTIs.

Trimethoprim-sulfamethoxazole, fluoroquinolone, or nitrofurantoin are recommended for empirical treatment of uncomplicated UTI [29,35]. However, studies from the United States of America and worldwide indicate the emergence of high levels of trimethoprim-sulfamethoxazole resistance in a significant percentage (> 20%) of community-acquired E. coli UTI isolates [36,37]. We also found a high level of resistance to this antimicrobial agent [31%]. These findings indicate that initial empirical treatment with trimethoprim-sulfamethoxazole is no longer appropriate.

The fluoroquinolones tested in this study (ciprofloxacin,levofloxacin and ofloxacin) show relatively good activity against E. coli, finding that around 21%, 11% and 12% of the E. coli strains were resistant to ciprofloxacin, levofloxacin and ofloxacin, respectively. These findings indicate that the empiric use of fluoroquinolones can still be considered in

our region, and strategies to counteract increasing resistance to these antibiotics must be developed.

Nitrofurantoin demonstrated better activity against E. coli isolates (around 18% resistance), but this drug would not be recommended for serious upper urinary tract infections or for those cases with systemic involvement [38].

Another important finding to note in our study is the emerging resistance to the imipenem amd meropenem, the higher end antibiotics. Especially E.coli, Klebsiella spp and Pseudomonas spp have started showing resistance towards these antibiotics.

Conclusion

The isolation of bacterial uropathogens with a higher resistance rates for commonly used antimicrobials leaves the clinicians with very few options to choose drug used for empirical treatment of UTIs. Therefore, it is important to urge physician and other health worker in the field on the need of re-evaluation of empiric treatment of UTI. As drug resistance among pathogens is an evolving process, routine surveillance and monitoring studies should be conducted to provide physicians with knowledge about the most effective empirical treatment of UTIs'.

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