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URINARY TRACT INFECTIONS-BACTERIOLOGICAL PROFILE AND ANTIBIOTIC SENSITIVITY PATTERN IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Introduction: Bacterial urinary tract infections (UTIs) can involve the urethra, prostate, bladder, or kidneys. Diagnosis is based on analysis and culture of urine. Treatment is with antibiotics and removal of urinary tract catheters and obstructions. *E. coli* account for 75 to 95% of cases followed by Klebsiella species. Susceptibility patterns for the bacteria causing acute uncomplicated UTIs have generally been predictable until recently, with most susceptible to Trimethoprim-Sulfamethoxazole (TMP-SMX). Consequently, the traditional approach to therapy has been empirical short-course regimens with TMP-SMX. However, increasing antimicrobial resistance among uropathogens causing acute uncomplicated cystitis has had important ramifications for traditional empirical approaches.

Materials and methods: A retrospective study of urinary isolates was done for a period of one year from November 2016 to October 2017. The study was conducted in a tertiary care hospital in Central Kerala. The organisms isolated from urine samples of patients received in the microbiology laboratory with features of urinary tract infection were analysed. The samples included midstream urine sample (MSU), Suprapubic aspirates (SPA), Cathterised urine sample.

Results: A total of 8473 samples were processed during the one year period. Out of which 832 significant isolates obtained (9.8%). Isolates were maximum from patients above 45 years. *E.coli* and Klebsiella (560 &198) together accounted 91.1% of the total isolates. Among the orally acting drugs Nitrofurantin showed maximum sensitivity, followed by TMP-SMX. A total of 503 isolates (both E.coli, and Klebsiella together) were Extended Spectrum Betalactamase (ESBL) producing.

Discussion: The microbial etiology of urinary infections has been regarded as well established and reasonably consistent. *Escherichia coli* remains the predominant uropathogen. In our study, *E. coli* has a high percentage of resistance to Ampicillin, Cephalosporins and to TMP-SMX, so these antibiotics are not suitable as empirical agents. The emergence of these resistance patterns is concerning, because they are mostly resistant to oral antibiotics. Around 60% of urinary isolates showed ESBL production

Conclusion: Although the etiology of UTI remains constant, knowledge of local resistance trends is now an integral component in the successful empiric treatment of uncomplicated UTI. Selection of a therapeutic agent must now take in to account the in vitro susceptibility, in addition to potential adverse effects and cost effectiveness.

KEYWORDS : UTI, ESBL, E.coli, Trimethoprim-sulfamethoxazole (TMP-SMX)

Introduction

Bacterial UTIs can involve the urethra, prostate, bladder, or kidneys. Symptoms may be absent or include urinary frequency, urgency, dysuria, lower abdominal pain, and flank pain. Systemic symptoms and even sepsis may occur with kidney infection. Diagnosis is based on analysis and culture of urine. Treatment is with antibiotics and removal of urinary tract catheters and obstructions. The urinary tract, from the kidneys to the urethral meatus, is normally sterile and resistant to bacterial colonization despite frequent contamination of the distal urethra with colonic bacteria. The major defense against UTI is complete emptying of the bladder during urination. Other mechanisms that maintain the tract's sterility include urine acidity, vesicoureteral valve and various immunologic and mucosal barrier[1].

About 95% of UTIs occur when bacteria ascend the urethra to the bladder and, in the case of pyelonephritis, ascend the ureter to the kidney. The remainder of UTIs are hematogenous. Systemic infection can result from UTI, particularly in the elderly. About 6.5% of cases of hospital-acquired bacteremia are attributable to UTI.

In normal GU tracts, strains of *Escherichia coli* with specific attachment factors for transitional epithelium of the bladder and ureters account for 75 to 95% of cases. The remaining gram-negative urinary pathogens are usually other enterobacteria, typically Klebsiella or Proteus mirabilis, and occasionally Pseudomonas aeruginosa. Among gram-positive bacteria, Staphylococcus saprophyticus is isolated in 5 to 10% of bacterial UTIs. Less common gram-positive bacterial isolates are Enterococcus faecalis (group D streptococci). In hospitalized patients, E. coli accounts for about 50% of cases. The gram-negative species Klebsiella, Proteus, Enterobacter, Pseudomonas, and Serratia account for about 40%, and the gram-positive bacteria cocci like E. faecalis, S. saprophyticus, and Staphylococcus aureus account for the remainder[2].

Susceptibility patterns for the bacteria causing acute uncomplicated UTIs in women have generally been predictable until recently, with most susceptible to trimethoprim-sulfamethoxazole (TMP-SMX). Consequently, the traditional approach to therapy has been empiric short-course regimens with TMP-SMX. However, increasing antimicrobial resistance among uropathogens causing acute uncomplicated cystitis has important ramifications for traditional empiric approaches[1-2].

Material methods:

A retrospective study of urinary isolates was done for a period of one year from November 2016 to October 2017. The study was conducted in a tertiary care hospital in Central Kerala. The organisms isolated from urine samples of patients received in the microbiology laboratory with features of urinary tract infection were analysed. The samples included midstream urine sample (MSU), Suprapubic aspirates (SPA), Cathterised urine sample. The urine samples were inoculated into Blood Agar and Mac Conkey agar. Direct microscopy of all urine sample were done. Bacterial isolates obtained in significant numbers ($>10^5$ CFU/ml),$<10^5$in case of patients on antibiotics and suprapubic aspirated samples identified by biochemical tests. Antibiotic sensitivity tests were done for all significant isolates according to CLSI guideline 2016.

Results: A total of 8473 sample were processed during the one year period. Out of which 832 significant isolates obtained (9.8%). Isolates were maximum from patients above 45 years. 711 isolates obtained from I.P patients and 121 isolates from O.P patients. E. coli was the commonest isolate (67.4%) in both O.P and I.P samples followed by Klebsiella (23.8%).

Table 1 Age wise distribution of urinary isolates

Age group	Significant growth
<15 years	98
15-45 years	251
>45years	483

Table 2. Age wise distribution of each isolate

Age group	E. coli	Klebsiella	Pseudomonas Sp	Staphylococcus aureus	Enterococci	Others
<15years	62	20	10	0	4	2
16-45years	164	65	8	3	7	4
>45 years	334	113	18	4	11	3

Table 3 Bacterial isolates.

Isolates	Number	Percentage
E.coli	560	67.4
Klebsiella species	198	23.8
Pseudomonas species	36	4.4
Enterococci	22	2.6
Staphylococcus aureus	7	0.8
Acinetobacter species	5	0.6
Staphylococcus saprophyticus	2	0.2
Proteus mirabilis	2	0.2

Table 4 Antibiotic Sensitivity pattern in percentage

Isolates	Ampicillin	Cefazolin	TMP-SMX	Nitrofurantoin	Gentamicin	Ciprofloxacin	Ceftriaxone
E.coli	2.7	15.9	51	80	81	55	39
Klebsiella species	0	12	46	67	67	47	32
Pseudomonas sp	NT	NT	NT	NT	44	25	NT
Enterococcus sp.	80	NT	NT	87	NT	66	NT

Table 5 Antibiotic Sensitivity pattern in percentage

Isolate	Piperacilln+Tazobactam	Amikacin	Imipenam
E.coli	85	90	100
Klebsiella sp	67	78	88
Pseudomonas	65	50	52
Enterococcus sp.	NT	NT	NT

NT- Not tested

Around 91.1% of the total isolates were E.coli and Klebsiella. Among the orally acting drugs Nitrofurantin showed maximum sensitivity, followed by TMP-SMX.

A total of 503 isolates (both E.coli, and Klebsiella together) were ESBL producing. ESBL production detected by disc diffusion and also checking sensitivity by Vitek system.

Discussion

The microbial etiology of urinary infections has been regarded as well established and reasonably consistent. *Escherichia coli* remains the predominant uropathogen. In our study, also *E.coli* was the predominant isolate .*E. coli* has a high percentage of resistance to Ampicillin, first and third generation Cephalosporins and to TMP-SMX, so these antibiotics are not suitable as empirical treatments. Around 60% of our isolates were ESBL producing. Among antibiotics that have a high activity against *E. coli*, Nitrofurantoin is the only one active orally. As a result, selection of an antibacterial must consider both susceptibility and known efficacy. It should be noted that fluoroquinolone susceptibility also decreasing. Although susceptibility is of critical importance in selecting an appropriate antimicrobial agent, clinicians must also first consider the established range of coverage for each agent. Despite established susceptibility, Nitrofurantoin has not been shown to be effective in patients with acute pyelonephritis. In addition, Nitrofurantoin is rarely the agent of choice in patients diagnosed with urinary infections other than acute cystitis[2]. The emergence of these resistance patterns is concerning, particularly in community-onset UTIs, because they are mostly resistant to oral antibiotics[3-11].One study from Spain reported a 3-fold increase in community-onset UTIs caused by ESBL-producing *E coli* over a 3-year period, most of which were also resistant to TMP-SMX and Fluoroquinolones[5].Another study from the United Kingdom revealed a similar trend, with24% of 291 CTX-M–producing, *E coli* isolates (mostly urinary in origin) came from the community. Most of isolates were also resistant to Fluoroquinolones, TMP-SMX, and Tetracycline[11]. Resistance to commonly prescribed oral antibiotics leads to inadequate empirical therapy and potential development of more severe infections, including bacteremia. A series of non-hospitalized patients with UTIs secondary to ESBL-producing *E coli* strains showed that 5 of 37 patients became bacteremic requiring hospitalization because of treatment with inadequate initial empirical therapy[9].Clinicians and patients need to accept that the initial empiric treatment choice may be incorrect and a switch in therapy may be needed, depending on full susceptibility results and the clinical response. For uncomplicated cystitis secondary to ESBL organisms, treatment options involve a return to UTI-specific antibiotics, such Fosfomycin and Nitrofurantoin. Auer and colleagues[12]examined 100 ESBL-producing *E coli* from urinary samples and found high rates of co resistance with other antimicrobials, such as Aminoglycosides, Fluoroquinolones, and TMP-SMX. The isolates retained high rates of susceptibility to Fosfomycin, Nitrofurantoin, and Ertapenem. The increasing resistance trends are likely to influence the clinical outcome when TMP-SMX is used empirically in uncomplicated UTI. As a result, alternative antimicrobials, including a Fuoroquinolone (3 days), Nitrofurantoin (7 days), or Fosfomycin (single-dose treatment), are preferred for cystitis.[12]Antimicrobial resistance among uropathogens has been widely documented. Resistance to commonly used antimicrobials, even in community-associated uncomplicated cystitis, has been described for more than a decade. However, the prevalence of multidrug-resistant organisms in the outpatient setting is increasing, and the problem of uncomplicated UTIs requiring intravenous therapy because of the lack of oral options is a new challenge for clinicians, complicating a once simple to-treat infection[9].

Conclusion

Although the etiology of UTI remains constant, knowledge of local resistance trends is now an integral component in the successful empiric treatment of uncomplicated UTI. Selection of a therapeutic agent must now take into account geographic location and in vitro susceptibility, in addition to potential adverse effects and cost effectiveness. Substituting a Fluoroquinolone or Nitrofurantoin for TMP&SMX in uncomplicated UTI may be necessary. Although there have been minimal changes in the predominant uropathogens over the past decades, there have been significant changes in the resistance patterns to antimicrobials. The changes in resistance patterns need to be considered when determining the most appropriate empiric therapy.

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