

Original Research Article

Etiology and antimicrobial susceptibility pattern in children with community acquired urinary tract infection

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ABSTRACT

Background: Urinary tract infection (UTI) is represented as one of the most common disease encountered in medical practice today, occurring from neonate to geriatric age group. It is an important cause of morbidity in children and affects up to 10% of the childhood population.

Methods: After properly cleaning ano-genital area, in infants and young children up to 3 years of age, urine sample was collected in proper aseptic way. Midstream urine sample were collected from children older than 3 years in a sterile container. Isolation of bacteria was done on blood agar and MacConkey agar using semi quantitative methods. Antibiotic sensitivity test was carried out by disc diffusion method using Mueller-Hinton (MH) agar.

Results: Over a study period of eighteen months, one hundred eighty diagnosed cases of culture positive UTI were recruited in our study. It was found that UTI was more commonly seen in females than males with male to female ratio of 0.8:1. It was more commonly seen in children with age group from one month to one year of age and least commonly seen in children's above 4 years of age. Most commonly isolated microorganism on urine culture was *Escherichia Coli* (86.7%), followed by *Klebsiella pneumoniae* (11.7%). Maximum sensitivity was to nitrofurantoin (95%) as oral antibiotics and to meropenem (97.8%) for intravenous use. Ampicillin and cefotaxime were the least sensitive antibiotics.

Conclusions: *E. coli* was the most common uropathogen for UTI. Nitrofurantoin and meropenam were the antibiotics with maximum sensitivity.

Keywords: Urinary tract infection, *Escherichia coli*, Nitrofurantoin, Meropenam

INTRODUCTION

UTIs are common infections seen in children of all ages. UTI is defined using symptomatic urinary tract infection (SUTI) criteria or asymptomatic urinary tract infection (ASUTI) criteria. SUTI is defined as at least 1 of the following signs or symptoms: fever ($>38^{\circ}\text{C}$), suprapubic tenderness, costovertebral angle pain or tenderness and a positive urine culture of $\geq 10^5$ colony-forming units (CFU) per ml and with no more than 2 species of microorganisms.¹

UTI is a common bacterial infection in infants and children, the risk of having a UTI before the age of 14 years is approximately 1-3% in boys and 3-10% in girls.² The diagnosis of UTI is often missed in infants and young children, as urinary symptoms are minimal and often non-specific.

UTI represents a standard reason behind morbidity that in association with abnormalities of the urinary tract, contribute to the future complications, which includes cardio-vascular disease and chronic kidney disease. The diagnosis of UTI should be made only in patients with a

positive urine culture since this has implications for detailed evaluation and follow up.³

UTIs are most commonly caused by bacteria and may occasionally be caused by viruses and fungi. *E. coli* account for about 60% of infections, followed by *Klebsiella*, *Proteus spp*, *Enterococcus*, *Pseudomonas aeruginosa*, *Enterobacter*, *Staphylococcus saprophyticus*, *Salmonella spp*.

E. coli accounts for about 50% of infections in hospitalized patient and *Klebsiella*, *Enterobacter*, *Citrobacter*, *Serratia*, *Pseudomonas*, *Providencia*, *Enterococcus* and *Staphylococcus epidermidis* account for the rest. Fungal infections occur almost exclusively in hospitalized patients.¹⁻⁵

Antimicrobial resistance is a growing problem due to inappropriate use of antibiotics. In patients with suspected UTI, antibiotic is usually started empirically before culture reports are available. For empirical therapy we should know regional antibiotic resistance pattern especially, in the underdeveloped and developing countries. Due to inappropriate use of antibiotic, resistance is increasing and treatment of UTIs becomes more difficult.³

METHODS

This cross sectional study was carried out in TNMC and BYL Nair Ch. hospital of Mumbai, India over a period of 18 months, from June 2014 to December 2015. 180 culture positive cases of UTI, who were admitted in the hospital were included in this study. Inclusion criteria were one month to 12 years of age patients, cases of UTIs, diagnosed by positive urine culture for bacteria. Nosocomial UTIs were excluded from study.

The study was initiated after obtaining ethical clearance from the institutional ethics committee. The study included 180 children between the ages 1 month to 12 years who were admitted with urine culture positive UTI. Detailed history was taken and clinical examination was done in each case. Mid-stream clean catch urine sample was collected in a sterile container under all aseptic measures. As urine sample is good culture media for many bacteria to grow, it was transported and processed immediately within an hour of collection. Semi quantitative culture method was used, using blood agar and Mac Conkeys agar. The numbers of colonies grown were counted and interpreted as CFU per ml of urine. Colony counts exceeding 105 CFU per ml were taken as significant bacteriuria.

Antimicrobial sensitivity test was carried out by disc diffusion method on MH agar. The antibiotic discs contained in cartridges were taken out from the refrigerator half an hour earlier and brought to the room temperature. Antibiotic discs were applied to the MH agar surface seeded with test bacterium and incubated at

37°C overnight. The antibiotic discs used were ampicillin, cotrimoxazole, nitrofurantoin, norfloxacin, cefuroxime, cefotaxime, ceftazidime, cefixime, piperacillin-tazobactam, meropenam and imipenam.

Statistical analysis

Qualitative data was given in the form of frequency and percentage. Association between qualitative variables will be assessed by Chi-square test with continuity correction for all 2×2 tables and with or without continuity correction in rest and Fisher's exact test for all 2×2 tables where p value of Chi-square test is not valid due to small counts.

Quantitative data was analysed using mean±standard deviation and the percentages and median and amp, IQR (interquartile range). Analysis of quantitative data between a qualitative variable with 2 subgroups was done using unpaired t test if data passes normality test and by Mann-Whitney test if data fails normality test. Results were graphically represented where deemed necessary. SPSS version 19 was used for most analysis.

RESULTS

Over a period of 18 months, 180 admitted cases of culture positive UTI were recruited in our study. There were 79 (43.9%) males and 101 (56.1%) females (male:female ratio was 0.8:1) (Table 1). Their ages ranged from 2 month to 12 years. The age distribution of the patients, maximum number of children in the study group 68 (37.8%) were in the age group of 1 month to 1 year, followed by 41 (22.8%) in the age group of 2 to 4 years of age, followed by 38 (21.1%) in the age group of 1 to 2 years of age and 33 (18.3%) in the age group of more than 4 years of age (Table 2). Minimum age of child with UTI was 2 months old and maximum age of child with UTI was 12 years. With mean age of 2.79 years, median age of 2.0 years with standard deviation of 2.73 years of age.

Most commonly isolated microorganism in both male and female was *E. coli*. In male 70 (88.6%) out of 79 were *E. coli* and in females 86 (85.1%) were *E. coli*. Most commonly isolated organism was *E. coli*, followed by *K. pneumonia*, *Enterobacter* and *Proteus vulgaris* (Table 3).

Overall sensitivity by all isolated organisms was ampicillin (0%), cotrimoxazole (37.5%), nitrofurantoin (95%), norfloxacin (72%), cefixime (58.9%), ceftazidime (34.4%), cefotaxime (4.4%), cefuroxime (34.4%), piperacillin-tazobactom (66.1%), meropenem (97.8%) and imipenam (95%) (Table 4).

Susceptibility pattern of *E. Coli* was ampicillin (S=0%, R=100%), cotrimoxazole (S=89.1%, R=10.9%), nitrofurantoin (S=96.1%, R=3.8%), norfloxacin (S=76.3%, R=23.7%), cefuroxime (S=32.05%, R=67.95%), cefotaxime (S=4.5%, R=95.5%), ceftazidime

(S=34.6%, R=64.7%), cefixime (S=61.5%, R=11.0%, IS=27.5%), piperacillin-tazobactam (S=67.3%, R=19.2%, IS=13.5%), imipenem (S=96.6%, R=0%, IS=3.8%) and meropenam (S=97.4%, R=2.6%). Maximum sensitivity was to meropenem, imipenem and nitrofurantoin (Table 4).

Susceptibility pattern of *K. Pneumoniae* was ampicillin (S=0%, R=100%), cotrimoxazole (S=61.9%, R=38.1%), nitrofurantoin (S=90.47%, R=9.53%), norfloxacin

(S=52.38%, R=47.62%), cefuroxime (S=42.85%, R=57.14%), cefotaxime (S=4.76%, R=95.24%), ceftazidime (S=33.33%, R=66.66%), cefixime (S=42.85%, R=26.55%, IS=23.8%), piperacillin-tazobactam (S=52.38%, R=33.34%, IS=14.28%), imipenem (S=85.7%, R=4.78%, IS=9.52%) and meropenam (S=100%, R=0%) (Table 5).

Maximum isolates of *E.Coli* and *K. Pneumoniae* were sensitive to meropenem, imipenem and nitrofurantoin and major resistance were to ampicillin and cefotaxime.

Table 1: Demographic variables.

Demographics	Frequency	Percentage (%)
Male	79	43.9
Female	101	56.1
Total	180	100.0

Table 2: Age distribution of the study groups.

Age distribution	Frequency	Percentage (%)
1 month to 1 year	68	37.8
1-2 years	38	21.1
2-4 years	41	22.8
>4 years	33	18.3
Total	180	100.0

Table 3: Organisms isolated on urine culture.

Organisms	Frequency	Percentage (%)
<i>E. coli</i>	156	86.7
<i>Enterobacter</i>	2	1.1
<i>K. pneumonia</i>	21	11.7
<i>P. vulgaris</i>	1	0.6
Total	180	100.0

Table 4: Association between organisms isolated on urine culture and their sensitivity pattern.

Sensitivity	E. coli			Other than E. coli			Chi-square	P value
	Sensitivity (%)	Resistant (%)	I/S (%)	Sensitivity (%)	Resistant (%)	I/S (%)		
Ampicillin	0	156 (100)	0	0	24 (100)	0	-	-
Cotrimoxazole	139 (89.1)	17 (10.9)	0	15 (62.5)	9 (37.5)	0	-	-
Nitrofurantoin	150 (96.16)	6 (3.84)	0	21 (87.5)	3 (12.5)	0	3.279	0.002
Norfloxacin	119 (76.3)	37 (23.7)	0	12 (50)	12 (50)	0	7.252	0.007
Cefuroxime	50 (32.05)	106 (67.95)	0	12 (50)	12 (50)	0	-	-
Cefotaxime	7 (4.5)	149 (95.5)	0	1 (4.17)	23 (95.83)	0	0.005	0.943
Ceftazidime	54 (34.6)	101 (64.74)	1 (0.64)	8 (33.33)	16 (66.66)	0	0.176	0.916
Cefixime	96 (61.53)	17 (10.9)	43 (27.56)	10 (41.66)	8 (33.33)	6 (25)	9.398	0.024
Piperacillin-tazobactam	105 (67.3)	30 (19.23)	21 (13.5)	14 (58.33)	7 (29.16)	3 (1.92)	1.267	0.531
Meropenam	152 (97.44)	0	4 (2.56)	24 (100)	0	0	0.629	0.428
Imipenem	150 (96.15)	0	6 (3.84)	21 (87.5)	1 (4.16)	2 (8.33)	8.224	0.042

Table 5: Association between organisms isolated on urine culture klebsiella and their sensitivity pattern.

Sensitivity	Sensitive (%)	Resistant (%)	I/S (%)	Chi-square	P value
Ampicillin	0	21 (100)	0	-	-
Cotrimoxazole	13 (61.9)	8 (38.09)	0	10.761	0.001
Nitrofurantoin	19 (90.47)	2 (9.52)	0	1.024	0.312
Norfloxacin	11 (52.38)	10 (47.61)	0	4.992	0.025
Cefuroxime	9 (42.85)	12 (57.14)	0	-	-
Cefotaxime	1 (4.76)	20 (95.23)	0	-	-
Ceftazidime	7 (33.33)	14 (66.66)	0	0.006	0.940
Cefixime	9 (42.85)	7 (33.33)	5 (23.8)	0.151	0.927
Piperacillin-tazobactam	11 (52.38)	7 (33.33)	3 (14.28)	7.934	0.047
Meropenam	21 (100)	0	0	2.582	0.275
Imipenam	18 (85.71)	1 (4.76)	2 (9.52)	0.540	0.462

DISCUSSION

This study was carried out primarily to determine etiology and antimicrobial sensitivity pattern in children with community acquired UTIs. UTI is a major health problem due to complications of hypertension and chronic kidney disease.

UTI was more commonly seen in females than males. The observed female preponderance in this study is similar to previous studies.⁶⁻⁹ This is attributed to easy entry of organism from vulva to bladder due to short length of urethra in the female urinary tract. UTI was more commonly seen in children with age group in between one month to one year of age and least commonly seen in age group of more than 4 years of age.

E. coli was most commonly isolated microorganism followed by *K. pneumoniae*, *Enterobacter* and *P. vulgaris*. Palak et al reported most commonly isolated microorganism on urine culture was *E. coli* accounting for 156 (86.7%) out of 180, followed by *K. pneumoniae* 21 (11.7%), *Enterobacter* 2 (1.1%) and *P. vulgaris* 1 (0.6%).¹⁰ Similar results were seen in other studies.^{6,8,11,12}

On antimicrobial testing, there was 100% resistant to ampicillin by all isolated organisms. Maximum sensitivity for oral antibiotics to nitrofurantoin (95%) followed by cotrimoxazole (85.6%) and for IV antibiotics, maximum sensitivity to meropenem (97.8%) followed by imipenem (95%).

In our study sensitivity pattern by all isolated organisms was ampicillin (0%), cotrimoxazole (37.5%), nitrofurantoin (95%), norfloxacin (72%), cefixime (58.9%), ceftazidime (34.4%), cefotaxime (4.4%), cefuroxime (34.4%), piperacillin-tazobactam (66.1%), meropenem (97.8%) and imipenem (95%). These reports are similar to other reports.^{6,8,9,11}

In our study resistant ratio of *E. coli* to antibiotics was ampicillin (R=100%), cotrimoxazole (R=10.9%), nitrofurantoin (R=3.8%), norfloxacin (R=23.7%),

cefuroxime (R=67.95%), cefotaxime (R=95.5%), ceftazidime (R=64.7%), cefixime (R=11.0%), piperacillin-tazobactam (R=19.2%), imipenem (R=0%) and meropenem (R=2.6%). Yolbas et al found out the antibiotic resistance against *Escherichia* was amikacin (3%), imipenem (0%), meropenem (0%), nitrofurantoin (9%), trimethoprim-sulfamethoxazole (58%), piperacillin (83%), amoxicillin/clavulanate (50%), ampicillin/sulbactam (65%), cefazolin (54%), cefotaxime (51%), cefuroxime sodium (51%) and tetracycline (68%).⁶

The resistance pattern of *Klebsiella* to antibiotics in our study was ampicillin (R=100%), cotrimoxazole (R=38.1%), nitrofurantoin (R=9.53%), norfloxacin (R=47.62%), cefuroxime (R=57.14%), cefotaxime (R=95.24%), ceftazidime (R=66.66%), cefixime (R=26.55%), piperacillin-tazobactam (R=33.34%), imipenem (R=4.78%) and meropenem (R=0%). In the study of Yolbas et al the resistance ratios of *Klebsiella* are amikacin (0%), imipenem (0%), levofloxacin (0%), meropenem (0%), amoxicillin/clavulanate (57%), ampicillin/sulbactam (79%), ceftriaxone (68%), cefuroxime sodium (74%) and trimethoprim/sulfamethoxazole (61%).⁶ Ahangarzadeh et al found amikacin and ciprofloxacin as the most active antibiotic against gram-negative and gram-positive organisms.¹¹

Antibiotic resistance of urinary pathogen is increased worldwide. Inappropriate guidelines about use of antibiotics, poor surveillance, self-medication, poor diagnosis, poor quality of antibiotics, wrong dose have all contributed to increase in antimicrobial resistance.¹³ Regular reportage of the antimicrobial susceptibility pattern of uropathogens may be a helpful guide for appropriate initiating empiric medical aid of UTIs in children.

Limitations

We couldn't do sensitivity testing to ceftriaxone and amoxicillin which are commonly used for empirical

treatment due to non-availability of kit to test their sensitivity pattern.

CONCLUSION

UTI is a common disease in children. The incidence is more common in females than males and in age group from 1 month to 1 year. In our study, *E. coli* is the leading pathogen (86.7%) followed by *K. pneumoniae* (11.7%), *Enterobacter* and *P. vulgaris*. Uropathogens were mainly resistant to ampicillin and cefotaxime, thus they should not be used empirically to treat UTIs. *E. coli* and other isolates were more sensitive to oral drugs like nitrofurantoin, cotrimoxazole, norfloxacin, cefixime and to IV medicines like imipenem and meropenem. Therefore, these may be the drug of choice for the treatment of community acquired UTIs. IV medications like meropenem and imipenem can be used in complicated community acquired UTIs. Choice of antibiotics for treatment of UTIs will depend on local resistance pattern.

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