

Urinary Tract Infections in Children: Clinical Profile, Bacteriology and Antibiotic Sensitivity Pattern

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Abstract :

Introduction : Urinary tract infection(UTI) is a common bacterial infection in children. Early diagnosis, treatment based on the antibiotic sensitivity pattern of the causative bacteria and evaluation for underlying congenital anomalies of the urinary tract are important to prevent complications and renal insufficiency. **Objectives:** To study the current clinical profile, bacteriology and antibiotic sensitivity pattern of urinary tract infections in children in a part of the western region of India. **Material and Methods:** A prospective study was conducted from August 2014 to July 2015. Patients from the age of 1 month to 14 years presenting with urinary symptoms and fever without a focus were investigated for UTI and analyzed. **Results:** Out of 207 patients enrolled, 56 (27.1%) patients had UTI. Females outnumbered males. Fever was the most common presenting complaint noted in 39 (69.6%) patients, followed by pain in abdomen in 26 (46.4%) and dysuria in 21(37.5%) patients. 6 (10.4%) had complicated UTI and 9 (16.1%) had recurrent UTI. The most common bacterium isolated was E.coli (58.9%) followed by Klebsiella (16.1%). E.coli showed high resistance to co-trimoxazole (75.8%), cephalosporins (varying from 66.7 to 72.7%), ciprofloxacin (66.7%) and amoxicillin-clavulanic acid (51.5%). Maximum sensitivity was for imipenem, nitrofurantoin, amikacin, cefepime-tazobactam, cefoperazone-sulbactam, piperacillin-tazobactam and levofloxacin. 15 (26.8 %) of the pathogens isolated were Extended Spectrum Beta Lactamase producers. **Conclusion:** Bacteria causing UTI showed high resistance to antibiotics like cephalosporins, ciprofloxacin and amoxicillin-clavulanic acid in our region. Large scale studies are required to monitor the changes in the antibiotic sensitivity pattern to help formulate appropriate empirical pharmacotherapy.

Key words: Paediatric, Resistance, Urinary tract infection.

Introduction :

Urinary tract infection is a common bacterial infection in children. The risk of having a UTI before the age of 14 years is approximately 1-3% in boys and 3-10% in girls. ⁽¹⁾ Complications include renal parenchymal damage and renal scarring that can lead to hypertension and progressive renal insufficiency in later life.^(2, 3) In children, UTI may be the first presentation of an underlying congenital anomaly of the urinary tract. Therefore rapid diagnosis, institution of early treatment and further evaluation by imaging modalities is important to preserve the function of the growing kidney.

The clinical and laboratory diagnosis of UTI in children poses some difficulties. Presentation varies among different age groups. Diagnosis is often missed in

infants and young children because urinary symptoms are minimal and often nonspecific.⁽¹⁾ Collection of appropriate samples of urine for investigations is also often difficult in this age group. The presence of significant bacteriuria in urine culture is essential to diagnose UTI and patients then have to be evaluated for anomalies of the urinary tract to prevent recurrence and complications.⁽⁴⁾

Gram negative enteric bacilli are the leading pathogens in community acquired UTI in children.⁽⁵⁾ In suspected cases of UTI, empirical treatment with antibiotics is started after collecting urine samples for culture and antimicrobial sensitivity.⁽¹⁾ The selection of antibiotics should be based on amongst other factors, the commonly prevalent urinary pathogens and their antibiotic sensitivity in the region. This is important because injudicious use of antibiotics has led to bacterial resistance to antibiotics like cephalosporins, ciprofloxacin, amoxicillin-clavulanic acid and co-trimoxazole. Depending upon the extent of use and misuse of antibiotics, antibiogram pattern is different in

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different countries and in different regions of the same country.

This study was therefore undertaken to study the current scenario of UTI in children in a part of the western region of India. Our aim was to study the clinical profile, bacteriology and antibiotic sensitivity pattern of bacteria causing UTI in children attending our hospital.

Material and Methods :

This prospective study was carried out in the Pediatric department of a tertiary care private hospital in Ahmedabad, India over a period of one year from August 2014 to July 2015. Patients from the age of 1month to 14 years presenting with urinary symptoms (dysuria, urgency, frequency, incontinence, hematuria and suprapubic pain) and those with fever without a focus were enrolled in the study. History was noted and clinical examination done. Complicated UTI (involvement of upper urinary tract) was diagnosed if there was presence of any one or all of the following- fever > 39°C, systemic toxicity, persistent vomiting, dehydration, renal angle tenderness and raised serum creatinine.^(1,2) Recurrent UTI was considered if there was a previous history of one or more episodes of proven UTI.^(1,4)

Complete blood count, blood urea, serum creatinine and electrolyte levels were done in all the patients. Blood culture of infants was sent to rule out septicemia. Wet mount microscopy of urine was done to detect pyuria, hematuria and presence of any other abnormal cells. Clean catch midstream urine samples were collected in older children while transurethral bladder catheterization was done to obtain urine samples in infants and younger children. Urine culture was done on Mac conkey agar, Nutrient agar and Hichrome UTI agar with a calibrated loop.⁽⁵⁾ A growth of greater than 10⁵ colony forming units/ml of a single organism for midstream urine samples and greater than 5x10⁴ colony forming units/ml for samples obtained by catheterization was considered significant bacteriuria and UTI.^(1,6) The antibiotic sensitivity test was done on Mueller-Hinton agar by Kirby-Bauer disc diffusion test and ESBL (Extended Spectrum Beta Lactamase) production was detected by double disc synergy tests as

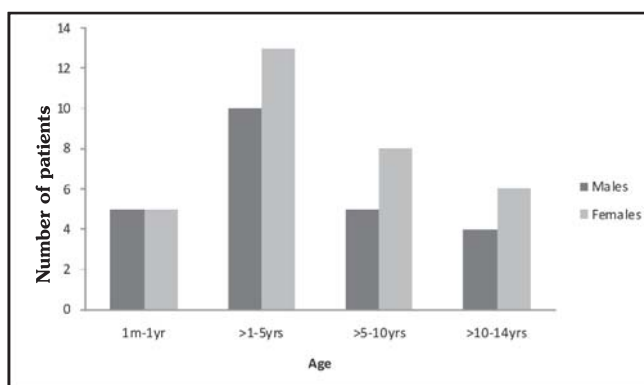
per the recent Clinical and Laboratory Standard Institute (CLSI) guidelines.⁽⁷⁾

Ultrasonography of the abdomen was done in patients who showed significant bacteriuria on urine culture and those with abnormal renal sonography were advised MCU (Micturating cystourethrography), DMSA (Dimercaptosuccinic acid) renal scan and other imaging modalities as per recommendations.⁽¹⁾ Patients were treated with cefixime, ceftriaxone or amoxicillin-clavulanic acid while their urine culture and sensitivity reports were awaited for.⁽¹⁾ The clinical features and investigation reports of patients with UTI were analyzed.

Results :

Out of 207 patients enrolled and evaluated for possible urinary tract infection, 56 (27.1%) showed significant bacterial growth in urine culture and were diagnosed to have UTI and analyzed. 24 were males and 32 were females with a male: female ratio of 1:1.3. Agewise, maximum patients in our study were in the age group of >1-5 years (41.07%), followed by >5-10 years age group (23.21%). Figure 1 shows age and genderwise distribution of the patients.

Figure 1: Age and gender wise distribution of patients



The most common complaint was fever which was found in 39 (69.6%) patients. This was followed by pain in abdomen in 26(46.4%), dysuria in 21(37.5%), vomiting in 17(30.4%) and increased frequency of urination in 14(25%) patients. Table 1 shows the clinical features of the patients. 6(10.7%) patients had features of complicated UTI while 9 (16.1%) patients had recurrent UTI.

Table 1: Clinical features of patients with urinary tract infections

Clinical Features	Number of patients (n = 56)	Percentage *
Fever	39	69.6
Pain abdomen	26	46.4
Dysuria	21	37.5
Vomiting	17	30.4
Frequency of urination	14	25.0
Poor feeding/ Decreased appetite	13	23.2
Diarrhoea	11	19.6
Urgency of urination	9	16.1
Irritability	8	14.3
Incontinence	5	8.9
Hematuria	4	7.1
Malodorous urine	3	5.4
Constipation	3	5.4

*Percentage values have been rounded to the nearest first decimal

Leucocytosis with neutrophilia was found in 8(14.3%) patients, out of which 6(75%) were patients with complicated UTI. 2(33.3%) of the latter were infants with a positive blood culture. Blood urea, serum creatinine and electrolyte levels were normal in all the patients. Significant pyuria (>5 WBCs /high power field of centrifuged urine sample)⁽⁶⁾ was found in 51 (91.1%) patients and hematuria (>5 RBCs /high power field of centrifuged urine sample)⁽⁶⁾ in 9(16.1%) patients. 10(17.9%) patients had abnormal ultrasonography findings. 7(12.5%) patients had hydronephrosis, 6(10.7%) had hydroureter, 2(3.6%) had calculi and 1(1.8%) each had enlarged kidneys and thickened bladder with internal echoes on ultrasonography. MCU was abnormal in 6(10.7%) patients. 4(7.1%) patients had primary VUR(Vesico Ureteral Reflux) and 1(1.8%) each had posterior urethral valves and neuropathic bladder. 2(3.6%) patients, one with grade 4 VUR and another with myelomeningocele and neuropathic bladder showed renal scarring on DMSA scan. The

most common bacteria isolated on urine culture were *E.coli* in 33 (58.9%) patients, followed by *Klebsiella spp.* in 9(16.1%) patients. The most common gram positive organism was *Enterococcus spp.* which was isolated in 6(10.7%) patients. Table 2 shows the different bacteria isolated in the 56 patients.

Table 2: Bacteria isolated from patients with urinary tract infections

Bacterial isolates	Number of isolates	Percentage *
<i>Escherichia coli</i>	33	58.9
<i>Klebsiella spp.</i>	9	16.1
<i>Enterococcus spp.</i>	6	10.7
<i>Proteus mirabilis</i>	3	5.4
<i>Citrobacter diversus</i>	3	5.4
<i>Pseudomonas aeruginosa</i>	1	1.8
<i>Staphylococcus aureus</i>	1	1.8

*Percentage values have been rounded to the nearest first decimal

In our study, *E.coli* showed high resistance to co-trimoxazole (75.8%), cephalosporins (varying from 66.7 -72.7% for various third and fourth generation cephalosporins), ciprofloxacin (66.7%) and amoxicillin-clavulanic acid (51.5%). Maximum sensitivity was for imipenem (100%), nitrofurantoin (100%), amikacin (90.9%), cefepime-tazobactam (90.9%), cefoperazone-sulbactam (90.9%), piperacillin-tazobactam (87.9%) and levofloxacin (87.9%). *Klebsiella spp.* also showed high resistance to co-trimoxazole (100%), cephalosporins (55.6-77.8%), ciprofloxacin (66.7%) and amoxicillin-clavulanic acid (66.7%). However, *Proteus mirabilis* and *Citrobacter diversus* showed 100% sensitivity to all the tested antibiotics except co-trimoxazole to which both showed 33.3% sensitivity. The antibiotic sensitivity pattern of *E.coli* and *Klebsiella spp.* to the various antibiotics is shown in Table 3.

Table 3: Antibiotic sensitivity pattern of *E. coli* and *Klebsiella spp.*

Antibiotic	<i>E. coli</i> n=33 Number (%) sensitive	<i>Klebsiella spp.</i> n=9 Number (%) Sensitive
Cefixime	9 (27.3)	2 (22.2)
Cefotaxime	9 (27.3)	2 (22.2)
Ceftriaxone	9 (27.3)	3 (33.3)
Ceftazidime	10 (30.3)	3 (33.3)
Cefoperazone	10 (30.3)	3 (33.3)
Cefepime	11 (33.3)	4 (44.4)
Cefpirome	11 (33.3)	4 (44.4)
Ciprofloxacin	11 (33.3)	3 (33.3)
Ofloxacin	11 (33.3)	3 (33.3)
Norfloxacin	11 (33.3)	3 (33.3)
Co-trimoxazole	8 (24.2)	0 (0)
Ampicillin-sulbactam	15 (45.5)	3 (33.3)
Amoxicillin-clavulanic acid	16 (48.5)	3 (33.3)
Piperacillin-tazobactam	29 (87.9)	7 (77.8)
Cefoperazone-sulbactam	30 (90.9)	7 (77.8)
Cefepime-tazobactam	30 (90.9)	7 (77.8)
Levofloxacin	29 (87.9)	7 (77.8)
Gentamicin	21 (63.6)	4 (44.4)
Amikacin	30 (90.9)	7 (77.8)
Nitrofurantoin	33 (100)	8 (88.9)
Imipenem	33 (100)	9 (100)

Among the gram positive isolates, *Enterococcus spp.* showed 100% resistance to cephalosporins, aminoglycosides and co-trimoxazole. Resistance to ampicillin-sulbactam, ciprofloxacin and amoxicillin-clavulanic acid was 50%, 66.7% and 75%, respectively. All the isolates were 100% sensitive to vancomycin, teicoplanin and linezolid.

15 (26.8%) of the isolates were ESBL producers, out of which 13 (23.2%) were *E.coli* and 2 (3.6%) were *Klebsiella*. 4 (7.1%) of the isolates were AmpC beta lactamase producers.

Discussion :

UTI is a common infection in children. Out of 207 patients enrolled and investigated for UTI, 56 (27.1%) had significant bacteriuria. The male to female ratio in our study was 1:1.3, with females more than males in all the age groups except in infants where both were equal in number. Other studies have also shown a female preponderance with a male: female ratio varying from 1:1.3 to 1:2.⁽⁸⁻¹⁴⁾ Males are more susceptible to UTI in the first year of life. Thereafter, females are at increased risk due to a shorter urethra and its proximity to the

anus which encourages contamination and ascent of fecal flora into the urinary tract.⁽²⁾

Maximum number of patients (41.07%) in our study were in >1-5 years age group. Sharma et al,⁽¹¹⁾ Malla et al,⁽¹²⁾ Singh et al,⁽¹³⁾ and Benachinmardi et al⁽¹⁵⁾ have also reported maximum number of patients (varying from 35-50%) in this age group. However, Gupta et al⁽¹⁶⁾ and Gadge et al⁽¹⁷⁾ found maximum number of patients (56.5% and 37.7%, respectively) in the age group of less than 1 year.

Fever was the most common symptom in our study (69.6%). Other studies have also found it to be the most common symptom present in 45-87% of their patients.⁽⁸⁻¹³⁾ The other common symptoms noted were pain in abdomen, urinary symptoms and vomiting which correlates with other studies.^(8,9,11,12,13) Infants presented with nonspecific symptoms like fever, vomiting, poor feeding, diarrhoea and irritability while older children had urinary symptoms and pain in abdomen with or without fever. UTI is an important cause of fever without a focus especially, in children less than 2 years old.^(1,2) In our study, 6(10.7%) patients had complicated UTI. All of them had leucocytosis with neutrophilia and 2(33.3%) of them were infants with a positive blood culture. Sepsis is common in pyelonephritis in infants and so blood culture should be done.⁽²⁾

Pyuria was seen in 91.1% and hematuria in 16.1% of patients with positive urine culture. In studies by Singh et al⁽¹³⁾ and Islam et al,⁽¹⁸⁾ 95.8% and 91% of patients with significant bacteriuria respectively, had pyuria. Presence of pyuria is useful for screening of UTI. It has a sensitivity of 74% and specificity of 86% to detect UTI.⁽⁴⁾ Microscopic hematuria can occur in acute cystitis and due to calculi in the urinary system.

9 (16.1%) patients had recurrent UTI, out of which 5 (55.6%) showed underlying structural abnormality or voiding dysfunction on imaging studies. 3(33.3%) patients had VUR and 1(11.1%) each had posterior urethral valves and neuropathic bladder. Singh et al have reported structural anomalies in 33.3% of patients with recurrent UTI.⁽¹³⁾ The risk of recurrence varies between 12% to 30% in the first 6-12 months after the

initial episode.⁽⁴⁾ All patients with recurrent UTI should be investigated for a structural abnormality or voiding dysfunction to prevent complications.⁽⁴⁾

In our study, *E.coli* (58.92%), was the most common bacterium isolated in both the genders and in all the age groups, followed by *Klebsiella spp.* (16.07%). This finding has also been observed in studies from other parts of India^(9, 15, 16, 17, 19) and other countries across the world.^(11, 12, 13, 14, 20, 21) Therefore, *E. coli* still remains the most common uropathogen all over the world. As also reported in other studies, in our study *Proteus mirabilis* was isolated only in males. This is because of frequent colonization of the prepuce in males.⁽²⁾ In our study, gram positive organisms constituted 12.4% of the isolates, the commonest being *Enterococcus species*.

E.coli in our study showed high resistance to antibiotics commonly used in the treatment of UTI in children. Resistance to various third and fourth generation cephalosporins varied from 66.7-72.7%. High resistance was also noted for co-trimoxazole (75.8%), ciprofloxacin (66.7%) and amoxicillin-clavulanic acid (51.5%). Similar pattern of resistance varying from 61.3-79.8% for cephalosporins, 52-88% for amoxicillin-clavulanic acid, 63.3-71.4% for ciprofloxacin and 54-75.6% for co-trimoxazole has been observed in recent studies in different regions.^(8, 12, 15, 19) However Singh et al⁽¹³⁾ and Ibeneme et al⁽²⁰⁾ have reported higher sensitivity of *E.coli* to ceftriaxone (80% and 85.7%, respectively) in their regions. Similarly, Edlin et al⁽²¹⁾ have reported higher sensitivity of *E.coli* to co-trimoxazole (76%) and ciprofloxacin (90%) in the United States. In our study, maximum sensitivity of *E.coli* was for imipenem (100%), nitrofurantoin (100%), amikacin (90.9%), cefoperazone-sulbactam (90.9%), cefepime-tazobactam (90.9%), piperacillin-tazobactam (87.9%) and levofloxacin (87.9%), which has also been noted in other studies.^(8, 12, 15, 19) Table 4 shows the antibiotic sensitivity pattern of *E.coli* in different studies. The pattern of high resistance of *Klebsiella spp.* to antibiotics noted in our study has also been observed in other regions.^(8, 15, 19)

Table 4: Antibiotic sensitivity pattern of *E. coli* in various studies

Antibiotics	Our study % sensitive	Gupta et al ⁽⁸⁾ % sensitive	Benachinmardi et al ⁽¹⁵⁾ % sensitive	Sharan et al ⁽¹⁹⁾ % sensitive
Cefixime	27.3	*	*	*
Cefotaxime	27.3	35	22.7	26.5
Ceftriaxone	27.3	*	*	26.5
Ceftazidime	30.3	*	20.2	38.7
Cefoperazone-Sulbactam	90.9	*	72.3	78.6
Amoxicillin-clavulanic acid	48.5	48	18.5	12
Piperacillin-tazobactam	87.9	*	79	57.8
Ciprofloxacin	33.3	30	28.6	36.7
Levofloxacin	87.9	*	*	93.8
Co-trimoxazole	24.2	46	38.7	24.4
Gentamicin	63.6	41	58	83.6
Amikacin	90.9	72	94.1	78.6
Nitrofurantoin	100	72	86.5	100
Imipenem	100	96	98.3	58.1

*Antibiotic not tested for sensitivity in the study.

The number of gram positive isolates in our study was less, only 7 (12.5%) and mainly consisted of *Enterococcus spp.* which showed 100% resistance to cephalosporins, aminoglycosides and co-trimoxazole. No resistance was found for vancomycin, teicoplanin and linezolid. Rekha et al ⁽²²⁾ and Benachinmardi et al ⁽¹⁵⁾ have also noted similar sensitivity pattern of *Enterococcus spp.* in their regions.

15(26.8%) of the bacteria isolated were ESBL producers while 4 (7.1%) were Amp C beta lactamase producers. Rekha et al ⁽²²⁾ and Benachinmardi ⁽¹⁵⁾ et al found 30% and 20.45% of their isolates to be ESBL producers, respectively. Out of 9 patients with recurrent UTI in our study, 6(66.7%) showed ESBL producing isolates on urine culture. Production of ESBLs and Amp C beta lactamases are the most common mechanisms of antimicrobial resistance in gram negative bacilli which make them resistant to antibiotics like third generation cephalosporins.⁽²³⁾ Cephalosporins used in combination with beta lactamase inhibitors like clavulanic acid, sulbactam or tazobactam are effective against beta lactamase producing bacilli. Amp C beta lactamase producing bacilli are typically associated with

multiple antibiotic resistance. They pose a challenge in choosing appropriate antibiotics and increase the cost of treatment.⁽²³⁾ Drug resistance among uropathogens has increased over a past few decades because of the widespread indiscriminate use, easy availability and over the counter sale of antibiotics. As per our study, antibiotics like cefixime, cefotaxime, ceftriaxone, amoxicillin-clavulanic acid, ciprofloxacin and co-trimoxazole which have been recommended for treatment of UTI ⁽¹⁾ would not cover majority of bacteria causing UTI in our region. However, large scale studies would be required to study the resistance of bacteria to various antibiotics in our region. This would help formulate a policy for empirical treatment with the aim to minimize evolution of resistant bacterial strains and at the same time to ensure effective treatment.

Conclusion:

Urinary tract infection is a common bacterial infection in children. Females are more affected than males. High prevalence of fever and other nonspecific symptoms especially in infants and young children supports the need for screening all febrile young children for UTI. Diagnosis must be based on a positive urine culture as this has implications for detailed evaluation for

congenital abnormalities and follow up. *E.coli* as the most common causative organism for UTI has not changed but its sensitivity for cephalosporins, ciprofloxacin and amoxicillin-clavulanic acid is low in our region. ESBL producing *E.coli* and *Klebsiella spp.* are now being increasingly isolated especially in those with recurrent UTI. Large scale studies are required to monitor the pattern of antibiotic resistance to help formulate appropriate empirical pharmacotherapy for UTI.

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