

CLINICAL AND LABORATORY PROFILE OF CHILDREN BIRTH TO 12 YEARS PRESENTING WITH FIRST URINARY TRACT INFECTION (UTI) AT A TERTIARY CARE HOSPITALYengkhom Rameshwor Singh¹, Okram Pusparani Devi², Tonjam Hemchand Singh³**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: Urinary tract infection (UTI) is a common infection in infants and children. The clinical manifestations of UTI are varied and the etiology of UTI and the antibiotic resistance of uropathogens have been changing over the past years, both in community and nosocomial infections. However, there are not much information on etiology and resistance pattern of community acquired UTIs in India. This study was designed and conducted in the department of Pediatrics, BVDU Medical college hospital, Pune during the period from July 2009 to August 2011 to study children from birth to 12 years of age presenting with their first UTI with respect to their age and sex distributions, clinical manifestations, laboratory parameters, uropathogens and their antibiotic sensitivity patterns of 52 patients who attended our tertiary care centre. This study showed highest incidence of first UTI among infants with male preponderance among <2 years of age. The commonest risk factor for UTI was identified as obstructive uropathy, followed by VUR. The commonest symptom of UTI was found to be fever followed by dysuria and pain abdomen. The commonest sign was pyrexia. On urinalysis most patients had significant pyuria (>5WBCs/mm³). E. coli was the commonest organism found in urine culture in all the age groups followed by CONS, Klebsiella and Pseudomonas. Maximum Sensitivity of E. coli was to Imipenem, Meropenem, Amikacin, Gatifloxacin and Nitrofurantoin. E. coli was found resistant to commonly used oral antibiotics like cotrimoxazole, ampicillin, cephalexin, cefuroxime, cefixime, cepodoxim. Most isolates of Klebsiella, Pseudomonas and Proteus were highly sensitive to Piperacillin-Tazobactam, Imipenem, Aminoglycosides, Fluroquinolones and Nitrofurantoin. Also, Klebsiella isolates were found sensitive to third generation cephalosporins but Pseudomonas and Proteus isolates were resistant to it. CONS and Enterococci were highly sensitive to Co-amoxycylav, Ampicillin-sulbactam, Piperacillin-tazobactam, Imipenem, Amikacin and Gatifloxacin.

KEYWORDS: UTI, uropathogens, antibiotic sensitivity and resistance

INDRODUCTION: Urinary tract infection (UTI) is a common infection in infants and children. The risk of developing urinary tract infection (UTI) before the age of 14 years is approximately 1% in boys and 3-5% in girls. The incidence varies with age, being highest in the first year of life for all children (1%) but decreases substantially among boys after infancy.^(1,2) Screening studies in emergency departments suggest that upto 5% of children under the age of 2 presenting with fever have urinary tract infection (UTI), and over half of these would have been given alternative diagnoses such as otitis media had the urine not been screened as part of the study.^(3,4) During the first year of life, the male to female ratio is 3-5:1. Beyond 1-2 years, there is female preponderance with male to female ratio of 1:10.^(5,6) The diagnosis of urinary tract infection (UTI) is often clinically missed in young children, as symptoms are minimal and often non-specific.⁽⁷⁾

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Rapid evaluation and treatment of urinary tract infection (UTI) is important to prevent renal parenchymal damage (renal scarring) that can cause hypertension, toxemia of pregnancy, chronic renal failure and end-stage-renal disease later. Risk factors for renal scarring include: young age especially children less than one year old, delay in initiating antibacterial treatment, recurrent urinary tract infection (UTI), and presence of moderate to severe vesicoureteric reflux (VUR).^(8,9)

The clinical manifestations of urinary tract infection (UTI) are varied and the etiology of urinary tract infection (UTI) and the antibiotic resistance of uropathogens have been changing over the past years, both in community and nosocomial infections.⁽¹⁰⁾ However, there are not much information on etiology and resistance pattern of community acquired urinary tract infections (UTIs) in India. The present study was designed to study children from birth to 12 years of age presenting with their first urinary tract infection (UTI) with respect to their age and sex distributions, clinical manifestations, laboratory parameters, uropathogens and their antibiotic sensitivity patterns in our tertiary care centre.

MATERIAL AND METHODS: This observational study was conducted in the department of Pediatrics, BVDU Medical college hospital, Pune during the period from July 2009 to August 2011. After obtaining informed consent 52 patients from birth to 12 years of age with urine culture positive first urinary tract infection was enrolled. Inclusion criteria: Children birth-12 years of age with positive urine culture.

Exclusion Criteria:

1. Children with urinary symptoms, and or pyuria on urinalysis without positive urine culture.
2. Children with recurrent urinary tract infection (UTI). Detailed clinical history taking, general and systemic examinations were done.

Investigations that include hemoglobin, TLC, DLC, blood urea and serum creatinine, urinalysis, urine culture and sensitivity tests were done for all patients.

Five ml of urine collected aseptically by midstream urine collection or urine specimen collected by urethral catheterisation or suprapubic aspiration in a sterile test tube was sent to laboratory and plated immediately for culture and sensitivity.

RESULTS: Fifty two (52) children with first urinary tract infection (UTI) formed the study material and were evaluated. Male to female ratio was 1.47:1. UTI was most common in children less than 2 years of age with male to female ratio of 1.25:1.

The most common symptom was fever in 39(75%) cases, followed by burning micturition/crying during micturition in 15(28.8%) and flank or abdominal pain in 12(23%) cases. The least common presentations were jaundice, diarrhoea, haematuria in 1(1.9%) cases. Maximum number of patients presented with combination of 3 or more symptoms. 22(42.3%) cases presented with ≥ 3 symptoms, 19(36.5%) with 2 symptoms and 11(21.1%) with only one symptom. The most common risk factor for urinary tract infection (UTI) in this study was obstructive uropathy 10(19.2%) followed by vesicoureteral reflux (VUR) 10(19.2%). Pyuria was present in 33 (63.46%) patients. Nineteen (36.5%) patients did not have significant pyuria (<5 pus cell/hpf).

Commonest organism was E. Coli in 36 (69.2%) cases, followed by Coagulase negative staphylococcus (CONS), Klebsiella, Pseudomonas, Proteus, Enterococcus in that order.

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All isolates of *E. Coli* were resistant to ampicillin, cephalixin, cefixime, cepodoxime and cefdinir, 8% isolates were sensitive to amoxicillin, 36% to co-amoxiclav, 13.3% to piperacillin-tazobactam, 4% to cefuroxime, 21.7% to cefotaxime, 18% to ceftriaxone, 40% to ceftazidime, 42.3% to gentamicin, 33.3% to tobramycin, 85.7% to amikacin, 54.1% to netilmycin, 12.1% to norfloxacin, 11.4% to ciprofloxacin, 13.7% to ofloxacin, 33.3% to levofloxacin, 91.6% to gatifloxacin, 85.7% to nitrofurantoin, 25% to cotrimoxazole, 95.2% to fosfomycin, 100% to imipenem and meropenem, colistin and polymyxin.

Fifty percent (50%) of *Pseudomonas* isolates were sensitive to piperacillin-tazobactam, norfloxacin, ciprofloxacin and nitrofurantoin, 100% to amikacin, fosfomycin and imipenem. All were resistant to cefotaxime, ceftriaxone, ceftazidime, gentamicin, tobramycin, netilmycin and cotrimoxazole. Fifty percent (50%) of *Proteus* isolates were sensitive to ciprofloxacin, ofloxacin and fosfomycin, 100% sensitive to ampicillin-sulbactam, amikacin, gatifloxacin, nitrofurantoin and imipenem.

All were resistant to ampicillin, amoxicillin, piperacillin-tazobactam, cefotaxime, ceftriaxone, ceftazidime, gentamicin, tobramycin, cotrimoxazole.

33.3% of *Klebsiella* isolates were sensitive to piperacillin-tazobactam, cefuroxime, cefotaxime, ceftriaxone, ceftazidime, tobramycin, netilmycin and fosfomycin, 50% to norfloxacin and nitrofurantoin, 66.6% co amoxiclav, gentamicin, ciprofloxacin, ofloxacin and imipenem, 100% to cephalixin, amikacin, levofloxacin, gatifloxacin, cotrimoxazole, colistin and polymyxin.

100% of enterococci isolates were sensitive to ampicillin, amoxicillin, co-amoxiclav, piperacillin-tazobactam, fosfomycin and imipenem. All were resistant to cephalixin, cefuroxime, cefotaxime, ceftriaxone, ciprofloxacin, nitrofurantoin and cotrimoxazole. All the isolates of CONS were 100% sensitive to amoxicillin, co-amoxiclav, ampicillin-sulbactam, piperacillin-tazobactam, amikacin, netilmycin, gatifloxacin and imipenem. 66.6% were sensitive to cephalixin, cefuroxime, gentamicin, tobramycin, norfloxacin, ciprofloxacin and cotrimoxazole. Serum creatinine was estimated in all patients. 41(78.8%) patients had serum creatinine level in normal range and 11(21.1%) patients had a higher than the age related normal.

DISCUSSION: In this study the majority of the children with the first UTI were infants, a finding that is consistent with observations made by other groups.⁽¹¹⁾ Also, male preponderance in age group less than 2 years was found. The manifestations of urinary tract infection (UTI) are related to the age, severity of the infection and whether it is upper urinary tract infection (pyelonephritis) or lower urinary tract infection (Cystitis). In our study, most patients presented with fever (75%) followed by crying/burning sensation during micturition (28.8%) and pain in abdomen (23%). Young children, less than 2 years of age, presented with poor feeding (15.3%), crying during micturition (28.8%), jaundice (1.9%), diarrhoea (1.9%), vomiting (15.3%), febrile seizure (9.6%). Dysuria, urgency and increased frequency of micturition were present in (15.3%). Malodorous and turbid urine was present in (7.6%).

One (1.9%) young child (10 days old) had haematuria and oligouria as the only manifestation of urinary tract infection (UTI). Weak urinary stream and dribbling was found in (7.6%), all had PUVs.

Failure to thrive was found in 17 of 27 infants and children below 2 years (62.9%). Failure to thrive was a common finding in other studies also. In the study by Malla KK et al in Nepal also found fever as the single most common presenting symptom (86.9%), followed by pain abdomen (46.4%), burning/crying during micturition (26%), vomiting, dysuria and failure to thrive.

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In the study by Theodoros A et al, in children less than 2 years with UTI, fever was the most common presentation (83%), followed by poor feeding, lethargy and failure to thrive.⁽¹²⁾

In our study, on microscopic examination of a fresh centrifuged urine, (57.6%) had >10 WBCs/mm, 3(5.7%) had 5-10 pus cells/hpf, but a large number of them did not have pyuria (36.5%). This has also been remarked upon earlier i.e. predictive value of pyuria as an isolated feature is poor and it cannot be recommended for making a presumptive diagnosis of urinary tract infection (UTI).⁽³⁾

Isolated proteinuria, isolated pyuria, isolated bacteriuria and microscopic haematuria are not features of urinary tract infection in children. Urine culture can be more selectively done if the routine urinalysis is well interpreted. In the absence of dependable culture facilities, a routine urine examination can be reliably used in the diagnosis of urinary tract infection (UTI) in children.⁽¹³⁾

In our study, E. coli was commonest organism and was isolated in 36(69.2%) cases, followed by Coagulase negative staphylococcus (CONS) in 5(9.6%) patients, Klebsiella pneumonia in 4(7.6%) patients, Pseudomonas aeruginosa in 2(3.8%), Proteus in 2(3.8%), Enterococcus in 2(3.8%). In a study by Mohammad A, Mohammad Sh, Asad U Khan on causative organisms and antibiotic sensitivity pattern of UTI in JNMC Hospital Aligarh, E. Coli was most common organism isolated (61%), followed by Klebsiella (22%), Staphylococcus (7%) and Pseudomonas (4%).⁽¹⁴⁾ In the study by Malla KK et al in Nepal, E. Coli was most common organism isolated (50%), followed by Klebsiella (16.6%), Proteus (12.5%), Enterococcus (6.25%) and Staphylococcus.⁽¹⁴⁾

Findings similar to other studies, E. Coli the commonest organism causing UTI in children was found highly sensitive to Amikacin, Imipenem, Meropenem, Nitrofurantoin, Levofloxacin and Gatifloxacin, moderately sensitive to Norfloxacin, Ciprofloxacin, third generation Cephalosporins, other Aminoglycosides, Co-amoxiclav and Piperacillin-tazobactam and resistant to Ampicillin, Cotrimoxazole and first generation Cephalosporins.

Pseudomonas isolates were sensitive to pipozo, norfloxacin, ciprofloxacin, nitrofurantoin, amikacin, fosfomycin and imipenem. All were resistant to cefotaxime, ceftriaxone, ceftazidime, gentamicin, tobramycin, netilmycin and cotrimoxazole.

Proteus isolates were sensitive to ciprofloxacin, ofloxacin, fosfomycin, ampicillin-sulbactam, amikacin, gatifloxacin, nitrofurantoin and imipenem. All were resistant to ampicillin, amoxicillin, piperacillin-tazobactam, cefotaxime, ceftriaxone, ceftazidime, gentamicin, tobramycin and cotrimoxazole.

Klebsiella isolates were sensitive to piperacillin-tazobactam, cefuroxime, cefotaxime, ceftriaxone, ceftazidime, tobramycin, netilmycin, fosfomycin, norfloxacin and nitrofurantoin, co-moxiclav, gentamicin, ciprofloxacin, ofloxacin and imipenem, cephalixin, amikacin, levofloxacin, gatifloxacin, cotrimoxazole, colistin and polymyxin.

100% of enterococci isolates were sensitive to ampicillin, amoxicillin, co-amoxiclav, piperacillin-tazobactam, fosfomycin and imipenem. All were resistant to cephalixin, cefuroxime, cefotaxime, ceftriaxone, ciprofloxacin, nitrofurantoin and cotrimoxazole.

All the isolates of Coagulase negative staphylococcus (CONS) were 100% sensitive to amoxicillin, co-amoxiclav, ampicillin-sulbactam, piperacillin-tazobactam, amikacin, netilmycin, gatifloxacin and imipenem. Our antibiotic sensitivity pattern was found similar to other hospital based studies.

In the study by Mohammad A, Mohammad Sh, Asad U Khan in JNMC Hospital Aligarh, E. Coli was 100% sensitive to Imipenem, Amikacin, third generation Cephalosporins, followed by

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fluroquinolones, but highly resistant to Ampicillin, Cotrimoxazole, Nitrofurantoin. Klebsiella showed high sensitivity to Imipenem (88%), followed by Amikacin, Cefotaxime and Ceftriaxone, but resistant to Ampicillin, Cotrimoxazole, Cefpodoxime and Nitrofurantoin. Pseudomonas showed high sensitivity to Imipenem (100%), followed by Amikacin, Ciprofloxacin and Norfloxacin, but resistant to Cotrimoxazole, Cefpodoxime and Nitrofurantoin. Staphylococcus also was highly sensitive to Imipenem, Cefotaxime and Ceftriaxone.⁽¹⁴⁾

In the study by Malla KK et al in Nepal, E. Coli was showed high sensitivity to Aminoglycosides (96%), Fluroquinolone (80%) and Nitrofurantoin (88%), but high resistance to Cephalosporins, Ampicillin and Co-amoxiclav. Klebsiella and Proteus were highly sensitive to Cotrimoxazole (50%), Nitrofurantoin (50%) and Fluroquinolones (80%). Enterococcus was resistant to Amikacin, but sensitive to Co-amoxiclav (100%). Majority of organisms were resistant to Cephalosporins.⁽¹⁵⁾

In the present study, most patients had normal renal functions, indicating that function is essentially preserved in uncomplicated febrile urinary tract infection (UTI). 78.8% had normal serum creatinine.

Serum creatinine was elevated in 11(21.1%) cases and all were found in cases with complicated urinary tract infection (UTI). This elevated serum creatinine may be related to acute febrile illness and acute kidney injury in complicated UTI.

CONCLUSION: The present study showed highest incidence of first UTI among infants with male preponderance among <2 years of age. The commonest risk factor for UTI was identified as obstructive uropathy, followed by VUR. The commonest symptom of UTI was found to be fever followed by dysuria and pain abdomen. The commonest sign was pyrexia. On urinalysis most patients had significant pyuria (>5WBCs/mm³) concluding that urine culture can be more selectively done if the routine urinalysis is well interpreted. E. coli was the commonest organism found in urine culture in all the age groups followed by CONS, Klebsiella and Pseudomonas. Maximum Sensitivity of E. coli was to Imipenem, Meropenem, Amikacin, Gatifloxacin and Nitrofurantoin. E. coli was found resistant to commonly used oral antibiotics like cotrimoxazole, ampicillin, cephalixin, cefuroxime, cefixime, cepodoxime and cefdinir. Most isolates of Klebsiella, Pseudomonas and Proteus were highly sensitive to Piperacillin- Tazobactam, Imipenem, Aminoglycosides, Fluroquinolones and Nitrofurantoin. Also, Klesiella isolates were found sensitive to third generation cephalosporins but Pseudomonas and Proteus isolates were resistant to it. CONS and Enterococci were highly sensitive to Co-amoxycrav, Ampicillin-sulbactam, Piperacillin-tazobactam, Imipenem, Amikacin and Gatifloxacin.

Age (Years)	Male	Female	Total	Percentage (%)
≤2	15	12	27	51.9
>2-5	7	5	12	23.0
>5	9	4	13	25.0

Table 1: Age and Sex distribution (n=52)

Symptoms	Number of Patients	Percentage (%)
Fever	39	75
Burning/Crying during micturation	15	28.8
Flank pain/Abdominal pain	12	23
Vomiting	8	15.3
Lethargy and poor feeding	8	15.3
Urgency/Frequency	8	15.3
Seizure	5	9.6
Turbid/Foul smelling urine	4	7.6
Weak stream/Dribbling	4	7.6
Oliguria	2	3.8
Jaundice	1	1.9
Diarrhoea	1	1.9
Haematuria	1	1.9

Table 2: Distribution of patients according to presenting symptoms (n=52)

Type of UTI	Male	Female	Total	Percentage (%)
Simple UTI	16	9	25	48.0
Complicated UTI	15	12	27	51.9

Table 3: Case classification

Organisms	Number of patients	Percentage (%)
E. Coli	36	69.2
CONS	5	9.6
Klebsiella	4	7.6
Pseudomonas	2	3.8
Proteus spp.	2	3.8
Enterococcus	2	3.8
Gram negative cocco-bacilli	1	1.9

Table 4: Distribution of cases as per organisms in urine (n=52)

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