Clinical Profile and Antibiotics Sensitivity in Childhood Urinary Tract Infection at Dhulikhel Hospital

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ABSTRACT

Background

Urinary Tract Infection implies presence of actively multiplying organisms in the urinary tract. Although it is infrequently associated with mortality, it is still a significant cause of morbidity. Early diagnosis is critical to preserve renal function of growing kidney.

Objective

Our purpose was to determine the clinical, microbiologic profile and antibiotic sensitivity of such infections in pediatric Urinary Tract Infection (UTI) patients at Dhulikhel Hospital.

Methods

A hospital based prospective descriptive study of 135 children from 2 months to 16 years, with clinical diagnosis of urinary tract infection who visited the pediatric department of Dhulikhel Hospital over the period of 15 months were enrolled in the study. All patients underwent routine urine analysis and culture. Children with recurrent UTI underwent micturating cystourethrogram (MCUG). Children with recurrent UTI of more than two years and with feature of pyelonephritis underwent USG abdomen as well. Complications and response of the treatment was observed in all cases of UTI. All data were entered in Epidata and data analysis was done using spss 16 version.

Results

Among 135 children, 32.5% were male and 67.4% were female. Fever was the most common presenting symptom in 74.80% of patients followed by dysuria in 54.1%. Among these children 95.6% had significant pyuria and 45% had culture positive infection. Children who showed positive for bacteriuria, Escherichia coli (78.7%) was the most common organism and are more than 80% sensitive to Amikacin, Gentamicin, Ceftriaxone, Ofloxacin, Nalidixic acid, Imipenem and Vancomycin. Co-trimoxazole was the most common drug used for treatment with a mean drug respond time of (mean±S.D) of 2.21±.78 days. 2±±. Children who had recurrent UTI were more prone to develop culture positive UTI (p=0.0001).

Conclusion

Urinary Tract Infection in female was almost twice more common than in male. Co-trimoxazole was the most common drug used for treatment, sensitivity of this drug was less than 50% for all organisms.

KEY WORDS

Bacteriuria, pyuria

INTRODUCTION

Reported rates of urinary tract infection (UTI) in children consulting for any acute condition varies widely from 2% -20% depending on setting and inclusion criteria.[1,2] UTI implies presence of actively multiplying organisms in the urinary tract.[3]

UTI occurs in 3-5% of girls and 1% of boys during childhood, while it is more common in boys during the first year of life.[4] The male to female ration varies with age, observed as 2.8-5.4:1.0 in the first year of life and changing to 1:10 in the second year of life.[4] The patient with UTI in early infancy presents with abnormal crying, malodorous urine, vomiting, diarrhea and jaundice.[5]

Fever remain a more common presentation in neonates, infants and younger children, whereas older children present with classic signs of UTI.[6] Renal scarring has been cited as one of the most common causes of end stage renal disease in both adults and children.[7]

Seventy to ninety percent of female children are suffering with UTI, the causative organism is usually *Escherichia coli* (*E.coli*) followed by *Klebsiella* and *Proteus* while in males older than one year *Proteus* is as common as *E. coli* as a bacterial cause of UTI. Early diagnosis is critical to preserve renal function of the growing kidney.[4] Antibiotic therapy is the main stay of treatment.[8]

The aim of present study was to record the common clinical presentation for UTI at Dhulikhel Hospital. The distribution of bacterial strains isolated from UTI and their resistance pattern against commonly used antibiotics at our setting was also studied.

METHODS

This was a prospective hospital-based study conducted in collaboration with microbiology department in Dhulikhel Hospital, Kathmandu University Teaching Hospital from January 2012 to March 2013. After ethical approval from institutional review Committee, this hospital based prospective study was conducted. Verbal consent was taken from the parents before enrolling them in study. Patients from 2 months to 16 years were admitted to the pediatric ward and visited in outpatient department (OPD) with diagnosis of UTI based on history with routine and microscopic examination of urine were considered for this study. Data were collected using a questionnaire regarding demographic and clinical data. A clean catch mid stream specimen in wide mouthed container to hold around 20ml specimen was collected. In routine and microscopic examination of urine report if white blood cell count were more than 5 per high power field then it is considered as significant pyuria and culture will be send. A urine specimen was considered positive for culture positive UTI, if a single organism was cultured at concentration of more than 10^5 colony forming unit per ml of urine. History, clinical examination and findings of culture sensitivity were recorded in a questionnaire. Treatment with appropriate drug, response to the drug and complication were also recorded. Vesico ureteric reflux was excluded in cases of recurrent UTI in children less than two years of age.

All data were entered in Epidata. Data analysis was done with spss version 16.0 program. Categorical data were analyzed by using Chi-square test. Mean and proportion were calculated as needed. Continuous data were analyzed by using independent sample T test. Data were presented as mean±SD (standard deviation). The p value was considered significant if it is less than 0.05.

RESULTS

Out of 135 patients who had complaints related to UTI and who were subjected to routine urine and culture, there were (32.5%) males and 91(67.4%) females .The ratio of male to female was 1:2. Female children between 1-5 years constituted 36.3% of total infected patients (Table 1).

Table 1. Age and Sex Distribution of UTI.

Sex	2 months to 1 year	1 to 5 years	6 to 10 years	>10 years	Total
Male	13 (9.6%)	15 (11.1%)	10 (7.4%)	6 (4.4%)	44 (32.5%)
Female	23 (17%)	49 (36.3%)	10 (7.4%)	9 (6.7%)	91 (67.4%)
Total	36 (26.7%)	64 (47.4%)	20 (14.8%)	15 (11.1%)	135 (100%)

Fever was the most common presenting symptom accounting for 74.80% of patients. This is followed by dysuria (54.1%), increased frequency of micturation (53.3%), nausea and vomiting (52.6%), abdominal pain (51.9%) and anorexia (51.1%) (Table 2).

Table 2. Clinical Manifestation of UTI.

Symptoms	Total	Percentage (%)
Fever	101	74.8
Headache	24	17.8
Nausea/vomiting	71	52.6
Pain abdomen	70	51.9
Frequency of urine	72	53.3
Dysuria	73	54.1
Dribbling	24	17.8
Anorexia	69	51.1
Myalgia	5	3.7
Back pain	10	7.4

Patient may present to one or more sign and symptom

Lower urinary symptoms were more common in children older than five years. Urine analysis was done in all suspected cases of UTI. Among all urine samples 64.4% had WBC >10/hpf, followed by 87(31.1%) which had WBC between 6-10/hpf. Only 6 (4.4%) had WBC 5 or less. Among

all urine analyses 68 (50.4%) sample revealed RBCs in the urine. In terms of urine culture, 61 (45.2%) subjects had positive urine culture (Table 3).

Among those who showed positive for bacteriuria, *E. coli* (78.7%) was the most common organism found followed by *Klebsiella pneumonia* (13.1%), *Proteus mirabilis* (4.9%)and 3.3% were other pathogens like *Enterococcus species* and *pseudomonas aeroginosa* (Fig 1).

Table 3. Result of Urine Analysis and Urine Culture.

Urine RME and Culture	Number (%)
Urine WBC	
WBC < 5/HPF	6 (4.4)
WBC 6-10/HPF	42 (31.1)
WBC > 10/HPF	87 (64.4)
Urine RBC	
Present	68 (50.4)
Absent	67 (49.6)
Urine Epithelial Cell	
Present	83 (61.5)
Absent	52 (38.5)
Urine Culture	
Positive	61 (45.2)
Negative	74 (54.8)

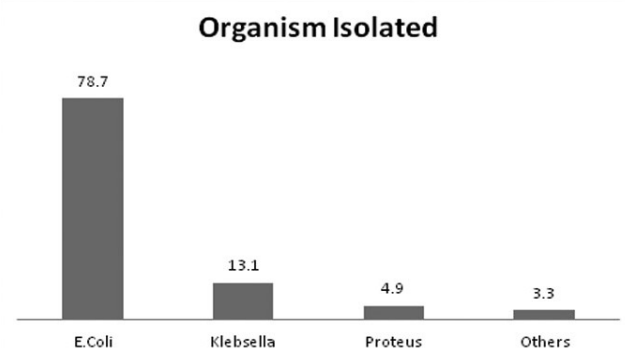

Figure 1. Bacteria isolates in UTI.

Other laboratory work ups requested for our subjects were ultrasonography (USG) of abdomen and micturating cystourethrogram (MCUG). USG was done in 24 cases (Table 4). Among them, only 6 (25%) had abnormal finding like hydronephrosis, calculi, intra renal pelvis, enlarged and inflamed kidney, thicken bladder wall and multiple internal echoes. MCUG was done in 21 cases, 7(33.3%) had abnormal MCUG including Grade 3 to Grade 5 refluxes.

All isolated *E. coli* was sensitive to Imipenem, Nalidixic acid, Netilmicin and Vancomycin. *E.coli* were 80-90% sensitive to Amikacin, Ceftriaxone, Cefuroxime, Ofloxacin, Gentamicin and Nitrofurantoin. Only 13.9% of *E. coli* was sensitive to Ampicillin. Though Co-trimoxazole was drug of choice for UTI, only 41.9% of *E. coli* cases were sensitive to it. *Klebsiella* and *Proteus* were 100% sensitive to Amikacin and Imipenem. *Proteus* was even more sensitive to the Cephalosporin group of drugs in comparison to *Klebsiella*, while *Klebsiella* is more sensitive to the Penicillin group

Table 4. Radiological finding in UTI.

Investigation	Normal	Abnormal	Total
USG	18 (75%)	6 (25%)	24
MCUG	14 (66.7%)	7 (33.3%)	21

of drug (p=0.004). The sensitivity patterns of different organisms to the drugs Gentamicin and Amikacin were slightly significant.(Table 5)

Table 5. Antimicrobial Sensitivity Pattern of Isolates.

Antibiotic	E. coli	Klebsiella	Proteus
Amikacin	82.6%	100%	100%
Ampicillin	13.9%	40%	0
Cefazolin	45.5%	20%	0
Cefixime	38.5%	20%	100%
Cefpirome	50%	0	100%
Cefotaxime	61.5%	50%	NT
Ceftazidime	66.7%	50%	100%
Ceftriaxone	80%	100%	NT
Ofloxacin	80%	50%	NT
Ciprofloxacin	57.5%	20%	50%
Cloxacillin	27.3%	50%	NT
Cotrimoxazole	41.9%	28.6%	50%
Gentamicin	86.8%	57.1%	33.3%
Nalidixic acid	100%	100%	0
Nitrofurantoin	91.7%	50%	33.3%
Norfloxacin	63.3%	50%	66.7%
Netilmicin	100%	100%	50%
Vancomycin	100%	100%	NGT

NT-Not tested

Mean response time of the drug in days was 2.36±1.09 days. Among all of the drugs used, Amoxicillin and Norfloxacin responded quickest.

In the present study, previous history of UTI was also recorded. Among all UTI cases, 28 (20.7%) cases had a previous history of UTI. There were significantly high chance of having culture positive UTI in those cases who had previous history of UTI (p=.0001). There were no complications observed in any cases.

DISCUSSION

The predominance of females among children affected with acute UTI in this study is consistent with many previous reports.[9-11] This can be easily attributed due to short urethra in female. In these studies male:female ratio were 1:2 and 1:1.9 respectively. Such findings have been reported in the present study as well. UTI was more common in the age group to one to five years (47.7%), other studies also showed a common age for UTI was between one to five years.[12,13]

There was no consistent symptom common to all patients

with UTI other than fever. In the present study, among all these children, 74.8% presented with febrile UTI. UTI is recognized increasingly as a common cause of fever in young children.[9,13,14] Dysuria and vomiting were the predominant symptoms. Urinary symptom like dysuria (54.1%), increase frequency (53.3%) and dribbling of urine (17.8%) were noted. Other studies also indicate high association of these symptoms and urinary tract infection.[14-16] Other symptoms were pain abdomen (51.9%), nausea and vomiting (52.6%),anorexia (51.1%), back pain (7.4%) and myalgia (3.7%). Another study done by Bayin Philippine and Sharma in Nepal also found abdomen pain in almost half of the cases.[13,15] These findings indicate that clinical presentation plays a very important role in diagnosing UTI. Although clinical presentation are very strong enough, urine culture and sensitivity is essential to diagnose UTI.

In the present study urine analysis was done in all 135 cases of UTI. Among all urine analysis 95.8% had significant pyuria which was very similar to another study done at Mymensigh Medical colleage,where pyuria was detected in 91%.[17] Pyuria detected in our study was very high in comparison to another study done in the Philippines,which was 35.2 % only.[15] In the Philippines, the diagnosis of UTI is based on the clinical presentation of the patient; it is often times supported by urinalysis, but rarely confirmed by urine culture and sensitivity. Here, at Dhulikhel hospital UTI was diagnosed based on clinical presentation of the patient and urine analysis was done in 100% UTI suspected cases. In the present study during urine analysis microscopic hematuria was found in 50.4% patients. This finding was high in comparison to the study done at Manipal College of Medial Sciences where hematuria was present in 10.7% and in Philippines where hematuria was present in only 6.4% of cases.[9,15] The microscopic hematuria is quite high in our study .This is possibly, we consider hematuria even RBC was 0-1/hpf in microscopic examination of urine.

Study done by Zamir and Colleague have questioned the yield of routine renal ultrasound (RUS) in the management of young children with first simple UTI.[18] The author concluded that RUS should only be performed in children in whom complication such as renal parenchyma disease and renal obstruction are suspected based on an unfavorable clinical course or in children in whom VUR has been found in order to look for renal structure abnormalities. In the present study also RUS was done in suspected renal parenchyma disease and in those children whom calculi were suspected. Ultra sonogram was done in only 24 cases. Among them six (25%) had abnormal findings including enlarged and inflamed kidney, hydronephrosis and calculi. According to revised AAP Guideline routine micturating cystourethrogram is no longer recommended after the first UTI.[19] According to revised AAP Guideline micturating cystourethrogram (MCUG) should be done in recurrent UTI.[19] In the present study also MCUG was done in recurrent UTI only. We performed 21 MCUG and7 patent (33.3%) has vesicoureteral reflux (VUR) Grade 3 to Grade 5 refluxes, which is in agreement with the findings of previous studies.[20,21] This study shown that it is highly recommended that children with recurrent UTI should undergo RUS and MCUG for early detected of complication and prevention of severe complication like renal scar.

In keeping with other studies, Gram negative organism accounted for over 90% of the isolates with E.coli predominating.[13,17,20] *Klebsiella spp* accounted for around 13% of all isolates which was true in some of the other studies as well.[22,23] *Proteus spp* was the third isolate in our study occupying 4.9% of the total isolates. Different studies have shown the growth of *Proteus spp* in urine from 3.9-10%.[13,24] A case having calculi also found to have significant pyuria and positive urine culture growth of *Proteus spp mirabilis*. The recurrent UTI association with secondary urolithiasis, Proteus bacteria are most likely to be found in urine culture. UTI with *Proteus spp* species are more often found in males than in females because of frequent colonization of the prepuce.[25]

E. coli showed more than 80% sensitivity to Nitrofurantoin (91.7%), Ceftriazone (80%), Amikacin (82.6%), Gentamicin (86.8%), and Ofloxacin (80%) while less than 50% sensitivity to Ampicillin and Co-trimoxazole. Antibiotic susceptibility patterns of Mymensigh Medical Collage shown *E.coli* was more than 80% sensitive to Amikacin, Cefotaxime and Nitrofurantoin.[17] A different study done at the Nepal Medical College showed that *E.coli* was more than 80% sensitive to Nitrofurantoin, Cefotaxime and Amikacin.[13] In the same study *E.coli* was sensitive to Co-trimoxazole in only 34.6% of patients, which was close to our study where sensitivity was 41.9%. In our study, *E. coli* was sensitive to Ampicillin in 13.9% of cases. Among all common medications, *E. coli* was highly resistant to Ampicillin as well as Co-trimoxazole.*13,23*

Klebsiella spp and *Proteus spp* showed 100% sensitivity to Amikacin. This finding was comparable to the study done in one of the tertiary centers of eastern Nepal where *Klebsiella spp* and *Proteus spp* were 96.0% and 92.1% sensitive to Amikacin respectively.[26] Another study done at the Nepal Medical Collage 13 also showed that *Klebsiella spp* and *Proteus spp* were 100% sensitive to Amikacin. In our study, *Proteus spp* was 100% resistance to Nalidixic acid which was comparable to another study, done in Nepal where *Proteus spp* also was 100% resistant to Nalidixic acid.[13]

Imipenem and Vancomycin were 100% sensitive to all organisms isolated in our study. *E coli* was more sensitive to Nitrofurantoin(91.7%) and Norfloxacin (63.3%) in comparison to *Klebsiella spp* and *Proteus spp*. Similar finding were also shown in the study done at Nepa Medical Colleage.[13] The drug of choice used in UTI treatment was Co-trimoxazole and Amoxycillin. The sensitivity to the isolated organisms to these commonly used drugs is low. Amikacin, Ceftriaxone, Nitrofurantoin and Norfloxacin were the antibiotics with the highest sensitivity. Though Co-trimoxazole and Amoxicillin can be used for empirical

therapy in UTI, the urine of all suspected cases of UTI should be cultured and sensitivity pattern determined for appropriate treatment.

The most common antibiotics used for the subjects in this study were Co-trimoxazole, Amoxicillin and Norfloxacin. Among all antibiotics used for UTI, Amoxicillin yielded the fastest response time to the symptoms. The mean response time of the drugs prescribed was 2.36±1.09 days. In this study, recurrence of UTI after first or second attack occurred in 28(20.7%) patients and was more common in female 22(16.3%) in comparison to male 6(4.4%). In another study the recurrence of UTI after first attack is approximately 30% and can be as high as 75% in children after second or third episode of UTI.[27] This study showed that with the recurrence of the UTI, there will be a greater chance of developing a positive culture for UTI (p=.0001).

Although small, randomized controlled trials have reported that antibiotics prophylaxis can be beneficial in high risk group.[28] There is clearly a need for well designed, prospective, randomized, controlled trials focusing on group with different risk stratification in females with fever being the most common presenting symptom followed by lower urinary symptoms.

According to Revised AAP Guideline on UTI in Febrile Infants and Young children, diagnosis now requires evidence of infection from abnormal urinalysis result and positive urine culture result (the criteria for a positive urine culture has been reduced from at least 100,000 colony-forming units per ml to at least 50,000 colony- forming units per ml).[19] So, in all study done before the revised AAP Guideline, the culture positive UTI was under diagnosed. In AAP Guideline oral treatment now is considered to be as effective as parenteral treatment. Prophylaxis antibiotic was not recommended in first episode of UTI.

CONCLUSION

UTI is a common childhood illness at Dhulikhel Hospital. Males were almost twice more common than in females with fever being the most common presenting symptom followed by lower urinary symptom. *E. coli* was the most common organism cultured in the urine of these children. The drug of choice used in UTI treatment was Co-trimoxazole and Amoxicillin. The sensitivity to the isolated organisms to these commonly used drugs is low. Amikacin, Ceftriaxone and Norfloxacin were the antibiotics with the highest sensitivity. Though Co-trimoxazole and Amoxicillin can be used for empirical therapy in UTI, the urine of all suspected cases of UTI should be cultured and sensitivity pattern determined for appropriate treatment. MUCG should be done only in recurrent UTI cases and UTI with abnormal USG finding.

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