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Childhood Urinary Tract Infection: Clinical & Laboratory Profile in a Tertiary Care Hospital of Bangladesh

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Authors' contributions

This work was carried out in collaboration between all authors. Author NIN designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors MRA and FJ managed the analyses of the study. Author NNF managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Urinary Tract Infection (UTI) implies presence of actively multiplying organisms in the urinary tract. Although it is infrequently associated with mortality, it is still an important cause of morbidity in the paediatric age group. Prompt diagnosis and early initiation of appropriate antibiotics in children reduce the morbidities associated with UTI.
Objective: This study was undertaken to observe the clinical and laboratory profile of UTI in children attending outpatient department (OPD) of Combined Military Hospital (CMH) Dhaka.
Methods: This observational cross sectional study was carried out in CMH Dhaka within the period of June 2015 to May 2016. A total of 120 children aged 0 months to 12 years attending paediatric OPD with symptoms of suspected UTI were included in this study. All the children were subjected to do urine analysis including microscopy and culture-sensitivity. Other relevant workups were also

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done. After enrollment, clinical and laboratory profile were obtained and recorded in case record form.

Results: Among 120 patients, 63.3% were females and 36.7% were males. Overall highest number of cases was within the age group of 0 to 5 years (62.5%). The most common clinical presentation was fever (64.2%). Common risk factors were wiping of genital area from back to front (91.7%), irregular antihelminthic intake (70.8%), intake of inadequate drinking water (51.7%), infrequent voiding habit (37.5%) and constipation (32.5%). Patients having previous urethral instrumentation and uncircumcised boys had significantly higher rate of UTI. Among all urine analyses 75% urine samples revealed pyuria. Urine culture was positive in 58 (48.3%) subjects and Escherichia coli (62%) was the commonest isolated organism. The common organisms were highly sensitive to Ciprofloxacin and Levofloxacin. Ultrasonography(USG) of whole abdomen showed abnormal findings in 17.5% cases. High Erythrocyte Sedimentation Rate (ESR) and neutrophilic leukocytosis was evident in 25% cases.

Conclusion: This study revealed that UTI was more common in female & under five children. Fever was the commonest symptom and uncircumcised boys had significantly higher rate of UTI. Escherichia coli were the commonest isolated organism but it was resistant to commonly used antibiotics like Amoxycillin and Cephalosporines. In the outdoor set up of CMH Dhaka, Ciprofloxacin and Levofloxacin can be used empirically for UTI treatment after sending urine culture and sensitivity, as most of the organisms are sensitive to these drugs.

Keywords: Urinary tract infection; clinical and laboratory profile; pyuria; culture and sensitivity.

1. INTRODUCTION

Urinary tract infection (UTI) causes significant illness in children. UTI is mainly due to the ascending infection from the urethra. Early diagnosis of UTI in young children is important to preserve renal function of the growing kidney [1]. Diagnosis of UTI in most developing countries is often difficult. Misdiagnosis may lead to renal damage and hypertension, which could be avoided with early diagnosis and proper management [2]. The incidence of UTI varies according to age, race and sex. It is estimated that 1% of boys and 3% of girls develop UTI during the first ten years of life. It affects male children more than female in the first year of life and mostly female after 1 year of age [3].

Fever remains a more common presentation in the neonates, infants and younger children whereas older children present with other symptoms [1]. Dysuria can also be the main symptom of UTI in younger children, but most of the time, it indicates cystitis. Dysuria may be associated with enuresis and foul smelling turbid urine. Some newborns and infants may show nonspecific symptoms such as jaundice, poor feeding, irritability and weight loss [4]. A variety of conditions lead to an increase predisposition to UTI. These include female gender as they have short urethra which is in close proximity with anus and wiping from back to front. Uncircumcised male have 4-20 times more chance of developing UTI [5].

Urine culture & sensitivity is the gold standard for the diagnosis of UTI [5]. On culture, a colony count of more than 10^5 colony forming units /ml organisms of a single species in midstream urine of girls and $>10^4$ CFU/ml organisms in boys are considered confirmatory of UTI. A pure growth of $\geq 10^2$ CFU/ml from catheterized urine sample or growth of any number of uropathogen from urine obtained by suprapubic aspiration is considered as significant bacteriuria [6]. Although *E. coli* has been reported to account for most of the cases of symptomatic UTI in children, studies from some other parts of the world however, have shown a changing trend in the bacteriology of UTI [5,6,7].

The result of urine culture and sensitivity test can be achieved 48 hours following sampling. However sometimes it may take longer and as in most of cases, the urine culture and susceptibility testing costs more than antibiotic treatment itself [8]. Furthermore, the etiology of UTI and their antibiotic sensitivity have been shown geographical variation; Therefore, in suspected UTI cases, it is appropriate to begin empiric treatment after collecting urine specimens for culture and sensitivity. The selection of antibiotics should be based on the pattern of urinary pathogens and their antimicrobial sensitivities in the local environment [9].

Demonstration of bacteria microscopically is the most reliable and fastest mean to establish the diagnosis of UTI before results of urine cultures are available. Again in the resource poor

settings, the diagnosis of UTI is mostly based on the clinical presentation of the patient; often supported by urinalysis, but rarely confirmed by urine culture and sensitivity. It is more applicable in outdoor establishments [10]. Some studies have shown statistically significant increased levels of ESR and leukocytosis with acute pyelonephritis when compared with those with acute cystitis [1,11].

UTI is a common cause for a significant number of outpatient visits [10]. Keeping in view the high incidence of UTI in children and its associated morbidity, it is imperative to diagnose UTI early and to treat the infection promptly. The aim of this study therefore was to evaluate the clinical symptoms, risk factors, laboratory findings of UTI and antimicrobial sensitivity of uropathogens in children attending OPD of CMH Dhaka.

2. METHODS

This is an observational cross sectional study. A total of 120 children aged 0 months to 12 years attending paediatric OPD of CMH Dhaka between June 2015 to May 2016 with symptoms of suspected UTI like fever, abdominal pain, dysuria, frequency of urine, smelly urine, dribbling of urine, nocturnal enuresis, vomiting, anorexia were included in this study.

The infants were advised to collect urine samples by using sterile plastic bags or wide-opened mouth container. Older children and adolescent were asked to collect mid-stream urine samples after proper cleaning of the external urethra and perineum with fresh water without soap. Urine samples thus collected were sent for microscopic examination and bacteriological culture and antibiotics sensitivity tests to the laboratory of Armed Forces Institute of Pathology (AFIP) after taking informed consent from the parents or guardians. Samples were advised to process within half an hour to one hour of collection. The results of urine microscopy and bacterial isolates and antibiotic sensitivity were retrieved from the microbiology laboratory of AFIP. Pyuria was defined by presence of ≥5White blood cells/High power field in centrifuged urine or ≥10WBC/HPF in uncentrifuged urine. A urine specimen was considered as culture positive case, if a single organism was cultured at concentration of more than 10^5 colony forming unit (CFU) per ml of a clean-catch midstream single urine sample.

Other investigations like Complete blood count (CBC), Ultrasonography (USG) of whole abdomen were also advised to all patients to support diagnosis of UTI as well as to identify risk factors. Children with suspected vesicoureteral reflux (VUR) underwent micturating cystourethrogram (MCUG).

After enrollment, relevant information such as age, sex was obtained and recorded in case record form. The following cases were excluded: other causes of pyuria like acute interstitial nephritis, glomerulonephritis (acute, chronic), other inflammatory diseases like vasculitis (SLE & others), asymptomatic bacteriuria, known urinary malformations (according to prenatal ultrasound and previous medical records), vesicoureteric reflux (VUR), chronic illness, or current prophylactic treatment with antibiotics and children having antibiotic treatment within seven days of sample collection. SPSS version 19.0 for windows (SPSS Inc, Chicago) was used for data analysis. Categorical data were analyzed by using Chi-square test. The p value was considered significant if it is less than 0.05. Ethical issues were addressed duly.

3. RESULTS

From June 2015 through May 2016, there were 120 patients (aged 0 days to 12 years), clinically suspected as cases of UTI attending OPD of CMH Dhaka. Among 120 patients, 63.3% were females and 36.7% were males, with a female to male ratio of 1.7:1. Female children between 0-5 years constituted 38.3% of total patients. Overall highest number of suspected UTI cases was within the age group of 0 to 5 years (62.5%). (Table 1) The most common clinical presentation was fever (64.2%) followed by frequency of urine (53.3%), anorexia (49.2%), vomiting (44.2%), abdominal pain (38.3%) and dysuria (36.7%). The detail is given in Table 2.

Different risk factors were associated with UTI like wiping of genital area from back to front (91.7%), irregular antihelminthic intake (70.8%), intake of inadequate drinking water (51.7%), infrequent voiding habit (37.5%), constipation (32.5%) and others described in Table 3. Previous urethral instrumentation like catheterization had significant relation with UTI and uncircumcised boys had significantly higher rate of urinary tract infection.

Urine analysis was done in all suspected cases of UTI. Among them 75% cases had pyuria (more than 5 WBCs/HPF), therefore had

presumptive UTI. Among all urine analyses, 32 (26.7%) urine samples revealed RBCs and 109 (90.8%) samples revealed epithelial cells. In terms of urine culture, 58 (48.3%) subjects had positive urine culture (Table 4).

Other laboratory work ups requested for our subjects were USG of abdomen, complete blood count (CBC) and micturatng cystourethrogram (MCUG). USG was done in 93 (77.5%) cases. Among them 21 (17.5%) had abnormal finding like cystitis (15 cases), hydronephrosis (3 cases), calculi (1 case), enlarged and inflammed kidney (1 case) and thickened bladder wall and multiple internal echoes (1 case). High ESR was & neutrophilic leukocytosis was evident in 30 cases (25%) and in 12 (10%) cases there was no record of ESR or WBC count. MCUG was done in 3 cases of hydronephrosis which revealed normal study (Table 5).

Table 1. Age & sex distribution of UTI

Sex	0-5 years n (%)	5-10 years n (%)	>10 years n (%)	Total N (%)
Male	29 (24.2)	8 (6.7)	7 (5.8)	44 (36.7)
Female	46 (38.3)	23 (19.2)	7 (5.8)	76 (63.3)
Total N (%)	**75 (62.5)**	**31 (25.9)**	**14 (11.6)**	**120 (100)**

Table 2. Clinical presentation of UTI in children

Presentation	Total	%
Fever	77	64.2
Frequency of urine	64	53.3
Anorexia	59	49.2
Vomiting	53	44.2
Abdominal pain	46	38.3
Dysuria	44	36.7
Malodorous urine	24	20
Failure to thrive	17	14.2
Headache	11	9.2
Myalgia	9	7.5
Diarrhea	8	6.7
Dribbling of urine	5	4.2
Others*	14	11.7

**Other symptoms include back pain, seizure, reluctant to feed, lethargy, irritability, high colour urine, nocturnal enuresis.*

***Patients presented with one or more sign and symptoms*

Table 3. Risk factors of UTI in children

Risk factors	Male n (%)	Female n (%)	Total N (%)	P value
Wiping from back to front	42 (35)	68 (56.7)	110 (91.7)	.253
Irregular antihelminthic	29 (24.2)	56 (46.7)	85 (70.8)	.367
Inadequate drinking water	21 (17.5)	41 (34.2)	62 (51.7)	.400
Infrequent voiding habit	13 (10.8)	32 (26.7)	45 (37.5)	.171
Constipation	10 (8.3)	29 (24.2)	39 (32.5)	.082
Unhygienic sanitation	14 (11.7)	22 (18.3)	36 (30)	.741
Circumcision not done in male	35 (29.2)	NA	35 (29.2)	**.000***
Past history of UTI	8 (6.7)	18 (15)	26 (21.7)	.481
Previous urethral instrumentation	3 (2.5)	0 (0)	3 (2.5)	**.021***
Tight undergarments	0 (0)	3 (2.5)	3 (2.5)	.182

NA-not applicable

Table 4. Result of urine analysis and urine culture

Urine RME & culture	Age			Total N (%)	P value
	0-5 yrs N (%)	5-10 yrs N (%)	>10 yrs N (%)		
Urine WBC					
WBC <5/HPF	18 (15)	6 (5)	6 (5)	30 (25)	.335
WBC 6-10/HPF	27 (22.5)	15 (12.5)	3 (2.5)	45 (37.5)	
WBC >10/HPF	30 (25)	10 (8.3)	5 (4.2)	45 (37.5)	
Total	**75 (62.5)**	**31(25.8)**	**14(11.7)**	**120(100)**	
Urine RBC					
Present	20 (16.7)	7 (5.8)	5 (4.2)	32 (26.7)	.456
Absent	55 (45.8)	24 (20)	9 (7.5)	88 (73.3)	
Total	**75 (62.5)**	**31 (25.8)**	**14 (11.7)**	**120 (100)**	
Urine Epithelial Cell					
Present	66 (55)	30 (25)	13 (10.8)	109 (90.8)	.349
Absent	9 (7.5)	1 (0.8)	1 (0.8)	11 (9.2)	
Total	**75 (62.5)**	**31 (25.8)**	**14 (11.7)**	**120 (100)**	
Urine culture					
Positive	40 (33.3)	13 (10.8)	5 (4.2)	58 (48.3)	.341
Negative	35 (29.2)	18 (15)	9 (7.5)	62 (51.7)	
Total	**75 (62.5)**	**31 (25.8)**	**14 (11.7)**	**120 (100)**	

Table 5. Other investigation findings

Name of investigation	Normal n (%)	Abnormal n (%)	Not done n (%)	Total N (%)
CBC*	78 (65)	30 (25)	12 (10)	120(100)
USG abdomen†	72 (60)	21 (17.5)	27 (22.5)	120(100)
MCUG‡	3 (2.5)	0 (0)	117 (97.5)	120(100)

** Abnormality was Leukocytosis with high ESR*

†Abnormality was Cystitis (15 cases) & hydronephrosis, calculi, enlarged and inflamed kidney, thickened bladder wall and multiple internal echoes. (6 cases)

‡ Vesicoureteral reflux (VUR) cases diagnosed by MCUG were excluded from the study

Among those who showed positive for bacteriuria, *Escherichia coli* (62%) was the most common organism found, followed by *Enterococcus* (19%), *Klebsiella* (10%) and others (9%). Other organisms included *Pseudomonas* (4%), *Acinetobacter* (3%) and *Proteus* (2%). (Fig. 1) *Escherichia coli* (*E. coli*) was found to be most sensitive to Ciprofloxacin (50%), Nitrofurantoin (47%), Levofloxacin (41%) and Amikacin (31%) in descending order. Enterococcus was found to be most sensitive to Vancomycin (73%), Amoxycillin (55%), Ciprofloxacin (36%) and Ceftriaxone (36%). Klebsiella was found to be most sensitive to Ciprofloxacin (83%), Nalidixic acid (83%) and Levofloxacin (67%). The common organisms were highly sensitive to Ciprofloxacin and Levofloxacin (Table 6).

4. DISCUSSION

The present study showed that the majority of patients belonged to the age group 0 to 5 years (62.5%). (Table 1) This value will approximate the findings of other international studies [12,13]. This could be because of younger children are not well toilet trained and likelihood of ascending infection with faecal flora is more common in this age group [13]. The finding was contrary to another study of Philippine where the majority of patients belonged to the age group 7 to 12 years (42.6%) or the school-age group [10]. In our studied patients, there was an obvious preponderance of female (1.7 times more frequent in girls). This is in accordance with other studies performed in Iran as well as in other countries [1,2,10]. The reason of UTI being more common in female child is probably short urethra in female besides others factors. In early infancy though, males are more susceptible because of higher incidence of congenital malformation but as the age increases the gender ratio is reversed [10,13].

Similar to previous studies, fever was the most common presentation of UTI (64.2%) in our study [1,2,10,12]. Other common clinical presentations

were frequency of urine (53.3%), anorexia (49.2%), vomiting (44.2%), abdominal pain (38.3%) and dysuria (36.7%). (Table 2). Dysuria was another commonly reported clinical presentation by several authors specially in older children [1,12,14]. Abdominal or flank pain though a non specific finding in patients having UTI; it was documented as a common symptom of UTI in many studies, as in ours [2,10,14]. There was a diverse pattern of clinical presentations of UTI in infants and children depicted in different international studies like vomiting, diarrhea, irritability, anorexia, failure to thrive, myalgia and headache [1,10,14]. Again newborns may show non-specific symptoms such as poor feeding , irritability, weight loss, jaundice or other signs of sepsis [4,5].

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 [14]. Nevertheless, the diagnosis of UTI is based mostly on the clinical presentation of the patients in resource poor settings; it is often times supported by urinalysis, but rarely confirmed by urine culture and sensitivity because bacterial growth is not always evident and culture & sensitivity is a costly test too [10].

In this study, different risk factors were associated with UTI like wiping of genital area from back to front, irregular antihelminthic intake, intake of inadequate drinking water, infrequent voiding habit, constipation, unhygienic sanitation and others (Table 3) which was more or less similar in other studies [1,2,7,15]. Previous urethral instrumentation like catheterization had significant association with UTI as risk factor which is consistent with a study by Zorc JJ et al. [16]. Again uncircumcised boys have 4-20 times more chance of developing UTI and in our study there was significantly higher rate of UTI in uncircumcised male child [5,15,16]. In two reviews by Laila K and Hamid F et al. some other

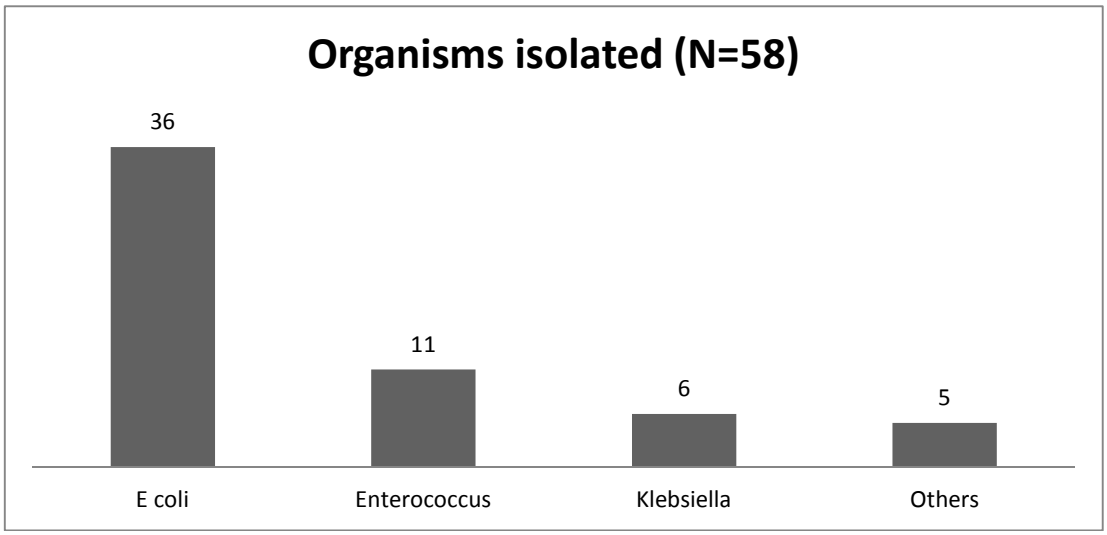

Fig. 1. Bacterial isolates in UTI

**Others- Pseudomonas (4%), Acinetobacter (3%) and Proteus (2%)*

Table 6. Antibiotic sensitivity of commonly detected uropathogens (%)

Bacterial isolates	AMK	AMO	AZT	CEF	CER	CEZ	CIP	GEN	LEV	NAX	NIT	PIP	VAN
E coli (n=36)	31	3	22	11	17	6	**50**	22	**41**	19	**47**	8	0
Enterococcus (n=11)	18	**55**	27	18	**36**	0	**36**	18	27	0	9	18	**73**
Klebsiella (n=6)	17	0	34	50	50	50	**83**	17	**67**	**83**	34	0	0

AMK-Amikacin, AMO-Amoxycillin, AZT-Azythromycin, CEF-Cefixime, CER-Ceftriaxone, CEZ-Ceftazidime, CIP-Ciprofloxacin, GEN-Gentamicin, LEV-Levofloxacin, NAX-Nalidixic acid, NIT-Nitrofurantoin, PIP-Piperacillin, VAN-Vancomycin

risk factors were known to be associated with UTI like children having anatomic anomaly, voiding dysfunction, neurogenic bladder, uninhibited detrusor contraction, urolithiasis, lack of toilet training, labial adhesion, sexual activity and children receiving broad spectrum antibiotics (e.g., amoxicillin, cephalexin) that are likely to alter gastrointestinal (GI) and periurethral flora [5,15].

In the present study urine analysis was done in all 120 cases of UTI. Among them pyuria was revealed in 90 (75%) cases and microscopic hematuria in 32 (26.7%) cases. (Table 4) Incidence of pyuria was higher than another study done in the Philippines (35.2%) [10] and lower than two other studies done at Mymensigh Medical college, Bangladesh (91%) and Dhulikhel hospital, Nepal (95.8%) [7,14]. Microscopic hematuria was found in 50.4% cases in a study done in Nepal which was higher in comparison to another study done in Philippines (6.4%) [10,14]. Urinalysis should be performed in all suspected UTI cases so that treatment can be started early and before the results of culture. However, absence of significant pyuria (>5 WBCs/HPF) does not rule out UTI [15]. Therefore, the treating physician should proceed to urine culture as the child may present with suggestive symptoms of UTI despite negative urinalysis [1].

Of the 120 urine samples, 58 samples were having culture positive accounting 48.3% of the total sample studied. (Table 4) In our present study culture positivity rate is more than that of two studies conducted in Nepal (28% and 19.5% respectively), which may be attributed to the sample size and urine collection method [2,13]. Significant association of acute phase reactants (ESR, CRP) and leukocytosis in children with febrile UTI & acute pyelonephritis have been previously reported [1,17]. However, only a few studies addressed the issue of specificity of these tests to confirm the diagnosis of acute pyelonephritis [11,12]. In our study, high ESR & neutrophilic leukocytosis were evident in 30 cases (25%) only (Table 5).

In present study, USG was done in 93 (77.5%) cases. Among them 21 (17.5%) had abnormal finding like cystitis, hydronephrosis, calculi, enlarged and inflammed kidney and thickened bladder wall and multiple internal echoes. The finding was almost similar to other studies [1,18]. USG should be done to demonstrate the size and shape of the kidneys, the presence of duplication and dilatation of the ureters, and the existence of gross anatomic abnormalities, post voidal residue & to detect obstruction by fungal ball [6,18]. Zamir and Colleague concluded that renal USG should only be performed in children in whom complicaton such as renal parenchyma disease and renal obstructon 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 [19]. USG was advised for all included patients of current study, but 27 (22.5%) patients could not show reports to further follow up. MCUG is indicated if renal ultrasound reveals hydronephrosis, scarring, or other findings that would suggest either high-grade VUR or obstructive uropathy, as well as in other atypical or complex clinical circumstances such as recurrent UTI [15]. In our study, MCUG was done in 3 cases of hydronephrosis which revealed normal study (Table 5).

The high prevalence of gram negative bacteria with *E.coli* as the predominant organism in this study is in agreement with previous reports [3,6]. In this study, *E. coli* was followed by *Enterococcus* (19%), *Klebsiella* (10%) and others as shown in Fig. 1. This finding was almost similar in a study reported by Ladhini and Grandsen [20]. However the pattern of isolated organisms greatly varies in different international studies. *E. coli* was followed by *Enterobacter spp.* (16.7%), and *Pseudomonas* (11.1%) in a study of Philippine, [10] it was followed by *Proteus* (20%), *Klebsiella* (5.4%) and *Pseudomonas* (1.8%) in a study of Nepal [3]. The pattern of antibiotic susceptibility in some cases differed from other reports. While Rabasa and Shattima reported less than 30% sensitivity of *E. coli* to Nitrofurantoin, more than 81.2% isolates were susceptible to this antibiotic in another study by Ayazi et al. [1,21]. In our study this rate was 47%. Our result also showed that *E. coli* isolates demonstrated a substantial reduction in susceptibility to Cephalosporin groups (Cefixime, Ceftriaxone and Ceftazidime), which is in close agreement with other studies [8,13]. While *E. coli* and other common organisms (*Enterococcus* and *Klebsiella*) were highly sensitive to Ciprofloxacin and Levofloxacin in present study, sensitivity to these drugs were low in some studies [8,22].

Cephalosporins and Ciprofloxacin were the least active agents against *Enterococcus* found in different studies which contradicts the finding of ours [22]. Vancomycin was 100% sensitive to all organisms isolated in a study done at Dhulikhel

hospital, Nepal [14]. But in our study, only *Enterococcus* showed sensitivity to Vancomycin. In an Indian study, *Klebsiella* was the second most common organism and was found to be highly sensitive to Amikacin and the sensitivity was 100% in two other studies [2,14]. But Amikacin sensitivity was only 17% to *Klebsiella* in the present study.

The prevalence of organisms and their sensitivity pattern to different antibiotics has a wide range of variation according to geographic establishment. The use of an inappropriate antibiotic delays effective treatment and increase the risk of renal scarring and chronic renal failure later in life. So, empiric treatment with a "best guess" antibiotic should be started in all cases of suspected UTI according to local antibiotic guideline [9].

5. CONCLUSION

UTI is one of the most common infections in paediatric patients. In present study, UTI was common in female and under five children. This study revealed variable risk factors and clinical presentations associated with UTI. Fever was the commonest symptom and uncircumcised boys had significantly higher rate of UTI. Urine analysis is mandatory for diagnosing UTI, although absence of pyuria doesn't rule out UTI. *E. coli* was the commonest isolated organism but it was resistant to commonly used antibiotics like Amoxycillin and Cephalosporines. In the outdoor set up of CMH Dhaka, Ciprofloxacin and Levofloxacin can be used empirically for UTI treatment after sending urine culture and sensitivity, as most of the organisms are sensitive to these drugs.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

"All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki."

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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