BANGLADESH J CHILD HEALTH 2017; VOL 41 (2): 77-83

Original Articles

Bacteriological Profile of Urinary Tract Infection in Children of a Tertiary Care Hospital

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Abstract:

Background: *Urinary tract infection (UTI) is an important cause of morbidity and mortality in the paediatric age group. The spectrum of etiologic agents causing UTI and their antimicrobial resistance pattern has been continuously changing over the years. It varies among geographical locations, hospitals and also in different age groups.*

Objective: *The aim of this study was to find out the causative agents of UTI and their antibiotic sensitivity pattern in paediatric patients in CMH, Dhaka.*

Methodology: *This is an observational cross sectional study. A total of 180 children aged 0 months to 15 years attending pediatric outpatient department or admitted in Department of Paediatrics CMH, Dhaka with suspected UTI were subjected for urine routine and microscopic examination between June 2015 to May 2016. Those having pyuria (n=120) were then sent for urine culture and sensitivity to the laboratory of Armed Forces Institute of Pathology (AFIP). Patients having significant growth of organism were enrolled as cases of confirmed UTI. After enrollment, relevant information such as age, sex, sociodemographic profile was obtained and recorded in case record form.*

Result: *In the present study, urine routine microscopy was done in all 180 cases of suspected UTI. Among all urine analysis 67% had significant pyuria (n=120). Of the 120 cases with pyuria, 58 cases were having culture positive accounting 48.3% of the total sample studied. Occurrence of urinary tract infections was highest in the age group below 5 year (62.5%). UTI was more prevalent in girls (63.3%) with male to female ratio 1:1.7. E. coli was the commonest isolate (62.1%) followed by Enterococcus (19.2%) and Klebsiella (10.2%). E. coli was found to be most sensitive to Ciprofloxacin, Nitrofurantoin, Amikacin, and Levofloxacin in descending order. There was a generally high level of resistance of isolates to Cotrimoxazole, Amoxycillin, Aminoglycosides, Azythromycin and the Cephalosporins like Cefuroxime, Ceftazidime, Cefixime and Ceftriaxone compared to Ciprofloxacin, Nitrofurantoin and Levofloxacin.*

Conclusion: *Based on our findings, Ciprofloxacin, Levofloxacin and Nitrofurantoin are appropriate for initial empirical therapy for UTI among Bangladeshi children.*

Keywords: *UTI, Children, Bacteriological profile*

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Received: 22 February 2017 **Accepted:** 31 May 2017

Introduction:

Urinary tract infection (UTI) is an important cause of morbidity and mortality in the paediatric age group.[1] The incidence of UTI varies according to age, race and sex. It is estimated that 1% of boys 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.[2] In 2007, a

meta analysis was carried out where the overall prevalence of UTI was 7.0% among infants presenting with fever.[3]

Although the outcome of UTI is usually benign, symptomatic UTI is associated with renal parenchymal involvement which predisposes to renal scarring with devastating consequences such as hypertension, CRF and ESRD.[2,4] Prompt diagnosis and early initiation of appropriate antibiotics in children reduce the morbidities associated with UTI. 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.[5]

Urine culture & sensitivity is the gold standard for the diagnosis of UTI.[6] 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.[7] 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.[5]

Although E. coli has been reported to account for most of the cases of symptomatic UTI in children,[6,7] studies from some other parts of the world however, have shown a changing trend in the bacteriology of UTI.[8-10] The spectrum of etiologic agents causing UTI and their antimicrobial resistance pattern have been continuously changing over the years, both in community and in hospitals.[10] It is especially true for developing countries where antibiotics are prescribed often irrationally. [11]

Little has been published regarding scenario of the range and antimicrobial susceptibility patterns of urinary tract pathogens particularly among children of Bangladesh so as to guide empiric antibiotic choice and prompt treatment. Therefore the objective of this study was to find out the spectrum of causative agents of urinary tract infections and their antibiotic sensitivity pattern in indoor and outdoor paediatric patients of CMH, Dhaka.

Methodology:

This is an observational cross sectional study. A total of 180 children aged 0 months to 15 years attending pediatric outpatient department or admitted in Department of Paediatrics CMH Dhaka with symptoms of suspected UTI like fever, abdominal pain, dysuria, frequency of urine, smelly urine, dribbling of urine, vomiting, anorexia were subjected for urine routine and microscopic examination between June 2015 to May 2016. Those with WBC >5 per high power field were then sent for urine culture and sensitivity.

The infants were advised to collect urine samples by using sterile plastic bags or wide-opened mouth container supplied by the laboratory. Catheterization was advised for critical hospital admitted patients. Older children and adolescent were asked to collect mid-stream urine samples after proper cleaning of the external urethra and perineum. 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.

Patients having pyuria were enrolled as presumptive UTI cases (n=120) and those having positive urine culture with significant growth of organism were enrolled as cases of confirmed UTI. After enrollment, relevant information such as age, sex, socio-demographic profile, was obtained and recorded in case record form. The following cases were excluded: recurrent UTI, 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), chronic illness, or current prophylactic treatment with antibiotics, children having antibiotic treatment within seven days of sample collection and samples with a mixture of two or more microorganisms. SPSS version 19.0 for windows (SPSS Inc, Chicago) was used for data analysis. Ethical issues were addressed duely.

Definition of Terms[12,13]

UTI suspect – with signs and symptoms that are associated with UTI**

Presumptive UTI – positive for pyuria on urinalysis

Confirmed UTI – positive for pyuria documented by positive urine culture

Recurrent UTI – occurrence of the disease at least twice a year

Pyuria – urinalysis with >5WBC/HPF of centrifuged urine or ≥10WBC/HPF of uncentrifuged urine

Positive urine culture – with $>10^5$ CFU/ml of urine of a single pathogen in bag urine samples and $\geq 10^2$ CFU/mL of a catheter specimen.

**Patients with fever, abdominal pain, dysuria, frequency of micturation, smelly urine, dribbling of urine, vomiting, anorexia were suspected as case of UTI and symptoms were non-specific and sometimes like sepsis in neonates and in early infancy

Result:

In the present study, urine routine microscopy was done in all 180 cases of suspected UTI. Among all urine analysis 67% had significant pyuria (n=120). Of the 120 cases with pyuria, 58 cases were having culture positive accounting 48.3% of the total sample studied. Occurrence of urinary tract infections was highest in the age group one day to 5 year (62.5%) and the lowest in the age > 10 years (11.7%). Culture positive cases were also highest in the age group <5 years (33.3%), but the result was not statistically significant (P>0.05). (Table-I)

There were 44 (36.7%) boys and 76 (63.3%) girls giving a total of 120 children who were enrolled in this study as presumptive UTI cases. The overall male to female ratio was 1:1.7. Urine culture negative cases mostly were females (39.2%) which was statistically significant (P<0.05). (Table-II)

E. coli was the commonest isolate (62.1%) followed by Enterococcus (19.2%), Klebsiella (10.2%), Pseudomonas (3.4%), Acinetobacter (3.4%) and Proteus (1.7%). (Table III) 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, Nalidixic acid and Levofloxacin. Acinetobacter was found to be most sensitive to Azythromycin and Levofloxacin. The two Psudomonas isolates were sensitive to Amikacin, Azythromycin, Ciprofloxacin, Ceftazidime, Gentamicin and others. The proteus (n=1) was sensitive to Azythromycin, Ciprofloxacin and Ceftriaxone. (Table-IV)

Table-I

Age distribution of study population (n=120)

Urine culture	Age				
	0-5 years	5-10 years	>10 years	Total	P value
Positive	40 (33.3)	13 (10.8)	5 (4.2)	58 (48.3)	
Negative	35 (29.2)	18 (15)	9 (7.5)	62 (51.7)	0.34
Total	75 (62.5)	31 (25.8)	14 (11.7)	120 (100)	

Table-II

Sex distribution of total patients (n=120)

Urine Culture	Male N (%)	Female N (%)	Total	P-value
Positive	29 (24.2)	29 (24.2)	58 (48.3)	0.003*
Negative	15 (12.5)	47 (39.2)	62 (51.7)	
Total	44 (36.7)	76 (63.3)	120 (100)	

Table-III

Prevalence of pathogens isolated on urine culture (n=58)

Pathogen	No. of isolates N (%)
E coli	36 (62.1)
Enterococcus	11 (19.2)
Klebsiella	6 (10.2)
Pseudomonas	2 (3.4)
Acinetobacter	2 (3.4)
Proteus	1 (1.7)
Total	58 (100)

Table-IV

Antibiotic sensitivity pattern of isolates

Antibiotics	E coli (n=36) N (%)	Enterococcus (n=11) N (%)	Klebsiella (n=6) N (%)	Acinetobacter (n=2) N (%)	Pseudomonas (n=2) N (%)	Proteus (n=1) N (%)
Amikacin	**11 (31)**	2 (18)	1 (17)	1 (50)	1 (50)	0 (0)
Amoxycillin	1 (3)	**6 (55)**	0 (0)	0 (0)	0 (0)	0 (0)
Azythromycin	8 (22)	3 (27)	2 (34)	**2 (100)**	1 (50)	**1 (100)**
Aztreonem	2 (6)	2 (18)	0 (0)	0 (0)	0 (0)	0 (0)
Ciprofloxacin	**18 (50)**	**4 (36)**	**5 (83)**	1 (50)	1 (50)	**1 (100)**
Ceftriaxone	6 (17)	**4 (36)**	**3 (50)**	1 (50)	0 (0)	**1 (100)**
Cotrimoxazole	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Cefixime	4 (11)	2 (18)	**3 (50)**	1 (50)	0 (0)	0 (0)
Cefuroxime	1 (3)	0 (0)	**3 (50)**	1 (50)	0 (0)	0 (0)
Cefepime	2 (6)	2 (18)	0 (0)	0 (0)	0 (0)	0 (0)
Ceftazidime	6 (17)	0 (0)	**3 (50)**	1 (50)	1 (50)	0 (0)
Collistin	3 (8)	2 (18)	1 (17)	0 (0)	0 (0)	0 (0)
Gentamicin	8 (22)	2 (18)	1 (17)	0 (0)	1 (50)	0 (0)
Levofloxacin	**15 (41)**	3 (27)	**4 (67)**	**2 (100)**	0 (0)	0 (0)
Meropenem	5 (14)	2 (18)	1 (17)	0 (0)	1 (50)	0 (0)
Netilmicin	6 (17)	2 (18)	1 (17)	1 (50)	1 (50)	0 (0)
Nalidixic acid	7 (19)	0 (0)	**5 (83)**	0 (0)	0 (0)	0 (0)
Nitrofurantoin	**17 (47)**	1 (9)	2 (34)	1 (50)	0 (0)	0 (0)
Piperecillin	3 (8)	2 (18)	0 (0)	1 (50)	0 (0)	0 (0)
Vancomycin	0 (0)	**8 (73)**	0 (0)	0 (0)	0 (0)	0 (0)

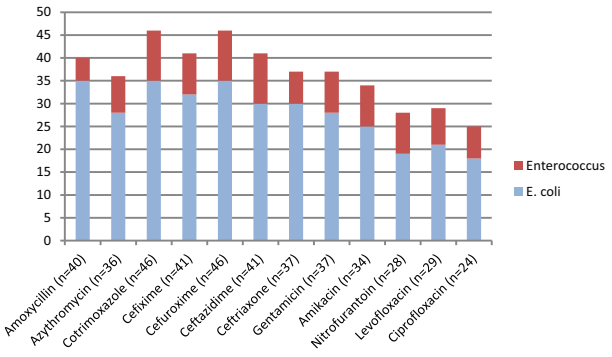

Fig-1: *Resistance of commonly used antibiotics against two common isolates (E. coli & Enterococcus) (n=47)*

Figure 1 shows the resistance pattern of commonly used antibiotics against two common isolates (E. coli & Enterococcus). There was a generally high level of resistance of isolates to Cotrimoxazole (98%), Amoxycillin (85%), Aminoglycosides (Gentamicin 79% and Amikacin 72%), Azythromycin (77%) and the Cephalosporins like Cefuroxime (98%), Ceftazidime (87%), Cefixime (87%) and Ceftriaxone (79%) compared to Ciprofloxacin (53%), Nitrofurantoin (60%) and Levofloxacin (62%).

Discussion:

In the present study, urine routine microscopy was done in all 180 cases of suspected UTI. Among all urine analysis 67% had significant pyuria (n=120) which was higher than another study done in the Philippines (35.2%)[14] and lower than two other studies done at Mymensigh Medical college, Bangladesh (91%) and Dhulikhal hospital, Nepal (95.8%).[9,14] Of the 120 urine samples processed for routine microscopy and culture, 58 samples were having culture positive accounting 48.3% of the total sample studied. In our present study culture positivity rate is

more than that of study done in two studies of Nepal (28% and 19.5% respectively)[2,15] and another study from India (39.6%)[16] which may be attributed to the sample size and urine collection method.

The first and most critical step in establishing the diagnosis of UTI is the method by which urine is collected. In young patients, care must be taken in preparing the perineum and periurethral area for placement of the sterile plastic receptacle, which will be used for collection of urine. In infants, the best way to obtain urine for culture aseptically is by urethral percutaneous suprapubic bladder aspiration or by catheterization. These procedures avoid the potential problem of contaminated urine cultures that often result from bag specimens. Older children and adolescents can be instructed to collect a midstream urine specimen after proper cleansing of the urethral area with plain water without soap.[17] The specimen should be transported to the laboratory within 30 minutes to two hours or stored at 4°C. Urine collected in this way is used for dipstick, microscopy and for culture and sensitivity test. [7] In this study, the culture negativity was may be due to non-compliance about aseptic urine collection in case of outdoor patients.

Majority of growth positive cases in our study were in the age group of less than five years (Table 1) which goes with the findings in other international studies. [11,12,14,] 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. [18]

The prevalence of UTI varies with the age and sex of children. Overall, in terms of gender distribution, our study showed that UTI was 1.7 times more frequent in girls (Table 2). The predominance of females in this study is consistent with many previous reports. [2,15,19,20] The reason of this disease being more common in female child is probably short urethra in female besides others factors. But this result is not consistent with the study done by Rekha et al. and GK Rai et al. where UTI was more prevalent in male children (53.3%). [16,21] The authors of that study depicted male preferences for physician's visit to be the cause of male predominance in UTI. UTI is generally more common in females than in males. 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.[11,12] In this study urine culture negative cases mostly were females (39.2%) which was statistically significant (P<0.05). It may be due to faulty collection of urine in female children.

The spectrum of etiologic agents causing UTI and the pattern of their antimicrobial resistance has been continuously changing over the years, both in community and in hospitals. In this study, E. coli was the most common organism isolated and constituted 62.1% of all positive samples. This is in complete agreement to the findings in two studies done in Nepal and another Bangladeshi study. [2,9,22] This was less than the finding observed by GK Rai et al (93.3%) among children of Nepal. [21] In different studies, the percentage of *Escherichia coli* (E. coli) was different ranging from 30.2% to 90% in collected urine samples.[2,10,11,12]

In this study, E. coli was followed by Enterococcus (19.2%), Klebsiella (10.2%) and others as shown in Table 3. This is in close agreement with a previous study reported by Ladhini and Grandsen. [23] 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,[12] it was followed by Proteus (20%), Klebsiella (5.4%) and Pseudomonas (1.8%) in a study of Nepal.[2] E. coli (54.80%)was followed by Klebsiella (16.0%), coagulase negative Staphylococci (11.2%), Enterobacter spp. (9.6%), Proteus 1.4% and Pseudomonas (1.4%) in a study of Iran.[24]

Antibiotic sensitivity patterns done in various centers in different times varied greatly some of which are similar to this study. Shrestha et al. reported E. coli as most sensitive to Nitrofurantoin (84.6%), Amikacin (80.7%), Gentamicin (73%) and Ofloxacin(53.8%). [2] In this study, Enterococcus was found to be most sensitive to Vancomycin, Amoxycillin, Ciprofloxacin and Ceftriaxone. (Table 5) Imipenem was the most effective antimicrobial agent against Entercoccus, described by Afsharpaiman et al.[25] Cephalosporins and Ciprofloxacin were the least active agents against Enterococcus found in different studies which contradicts the finding of ours.[26,27] In a study done in S.S.G hospital India, Klebsiella was the second most common organism and was found to be most sensitive to Ofloxacin, Amikacin and Piperacillin+Tazobactum. Acinetobacter constituted the third most common agent for UTI and was found to be most sensitive to Piperacillin+Tazobactum, Ofloxacin and Amikacin.[11]

Vancomycin was 100% sensitive to all organisms isolated in a study done at Dhulikhal hospital, Nepal. But in our study, only Enterococcus showed sensitivity to Vancomycin. [14]

There was a generally high level of resistance of E. coli and Enterococcus isolates to Cotrimoxazole, Amoxycillin, Aminoglycosides, Azythromycin and the Cephalosporins like Cefuroxime, Ceftazidime, Cefixime and Ceftriaxone compared to Ciprofloxacin, Nitrofurantoin and Levofloxacin in our study. Inspite of good sensitivity of uropathogens to Nitrofuratoin, it may not have good compliance in practice due to its bitterness.[5] Nevertheless, some studies recommended Nitrofurantoin as the first choice among oral antibiotics for prophylaxis and treatment of UTI in children due to higher sensitivity.[28] Third generation Cephalosporins were found to be having better coverage with relatively low reported resistance in different studies and were suggested for the empiric treatment of febrile UTI.[5,10] But in this study, Cephalosporins had higher resistance rates to E. coli and others. This reveals grave therapeutic implications for patient care, as many traditional antibiotics, which are affordable and easily available, are no longer useful. This high resistant profile confirms the observation of several authors. [2,11,24]

The level of high resistance to commonly practiced antibiotics underscores the importance of instituting a surveillance system to monitor the magnitude of the problem in different hospitals. This will also guide the

establishment of local antibiotic policy. Empiric treatment with a “best guess” antibiotic should be started in all cases of suspected UTI after an appropriate urine specimen is obtained. The use of an inappropriate antibiotic will delay effective treatment and increase the risk of renal scarring and chronic renal failure later in life. Therefore the current study presents the pattern of organisms isolated from the urinary tracts of children of CMH, Dhaka and their antimicrobial profiles to have a local antibiotic guideline.[29,30]

Recommendation:

Since the spectrum of causative organism for UTI may vary among geographical locations, hospitals and also in different age groups, each institution should carefully plan their empirical antibiotic selection based on the knowledge of local prevalence of bacterial organisms and antibiotic sensitivities rather than on universal guidelines.

Conclusion:

Based on our findings, Ciprofloxacin, Levofloxacin and Nitrofurantoin are appropriate for initial empirical therapy for UTI among Bangladeshi children. High prevalence of drug-resistant urinary tract pathogens to traditional antibiotics among Bangladeshi children suggests cautious use of antibiotic therapy for the treatment.

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