Causative agents of urinary tract infections in children and their antibiotic sensitivity pattern: a hospital based study

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ABSTRACT

A retrospective study was conducted to find out the causative agents of urinary tract infection (UTI) in children and their antibiotic sensitivity pattern among Nepalese children. This was done at Kanti Children's Hospital in Kathmandu (Nepal) by analyzing the records of urine samples collected for culture and sensitivity tests over a period of six months (April to November, 2007). Of the total 1878 mid-stream urine samples collected from suspected cases of UTI, 538 (28.6%) were positive for pathogenic organisms. There was no significant difference in growth positive rate in two genders (M: 51.7% and F: 48.3%). Of the various pathogenic organisms isolated, *Escherichia coli* constituted for 93.3% followed by *Proteus* sp, *Klebsiella* sp, *Citrobacter* sp, *Staphylococcus aureus* and others. *E. coli* was found to be most sensitive to amikacin, chloramphenicol, nitrofurantoin and ofloxacin and least sensitive to most commonly used drugs like cephalexin, nalidixic acid, cotrimoxazole and norfloxacin.

Keywords: UTI, causative agents, antibiogram, children, Nepal.

INTRODUCTION

Urinary tract infection (UTI) is a common problem in children.[1] The incidence varies according to age, race and sex of children.[2,3] UTI occurs in about 1% of boys and 3-5% of girls.[4] It affects male children more than females in the first year of life and females after 1 year of age.[5] Three to five percent of febrile children are found to have UTI.[6] Symptoms of UTI may be minimal and non-specific in infants and small children.[7] Febrile children not suspected of having UTI are as likely to have UTI as those who are suspected of having UTI.[8] Therefore, diagnosis of UTI can not be made on symptomatology alone and urine examination is advocated in children with minimal suspicion of UTI.[9,10]

UTI may lead to life threatening complications like sepsis and renal scaring. Renal scaring is the most common cause of hypertension in later childhood and renal failure in adulthood.[2,7] Recognition of UTI in children should be made as early as possible to prevent these complications.[7] Therefore, investigations for early diagnosis of UTI are of outmost importance.[5]

At least 80.0% of UTI in children is caused by *Escherichia coli* followed by other organisms like *Proteus, Enterococcus, Pseudomonas, Klebsiella, Citrobacter* and *Staphylococcus* species.[5]

Selection of antibiotics should be based on antibiotic susceptibility pattern. Periodic evaluation of antimicrobial activity of different antibiotics is essential as the pattern of antibiotic sensitivity may vary over short periods.[11] Increasing antibiotic resistance among urinary pathogens, especially *E coli,* to commonly prescribed drugs like cotrimoxazole has become a global reality.[12] Use of antibiotics by medical practitioners is rampant resulting in increase in resistance to available antibiotics. Isolation of organisms causing UTI and their antibiotic susceptibility is very essential for their appropriate management.[13] The reported positive rate of UTI among Nepalese patients attending general hospitals ranged from 23.1% to 37.4%.[14-16] Urinary tract disorders in Nepal are estimated to be about seven percent and UTI constitutes majority of these disorders.[17] Therefore, this study was conducted to find out the organisms responsible for UTI and their sensitivity pattern in Kanti Children's Hospital, Kathmandu, Nepal.

MATERIALS AND METHODS

A retrospective study was conducted to find out the causative agents of urinary tract infections in children and their antibiotic sensitivity pattern among Nepalese children aged less than 15 years. This was done at Kanti Children's Hospital in Kathmandu (Nepal) by analyzing the records of urine samples collected for culture and sensitivity tests for a period of six months (April to November, 2007).

Urine samples collected from children from birth to 14 years of age were included in the study. Clean catch mid-stream urine samples collected into a wide mouthed

sterile container was inoculated on MacConkey and Blood Agar media using calibrated platinum loop following standard bacteriological technique and incubated at 37^0C overnight. Pure bacterial colony counting 100,000 or more was considered as significant and was subjected to identification based on colony characters and biochemical tests.

Antibiotic sensitivity test was performed by disc diffusion method (Kirby-Bauer's technique) using commercially available discs (HiMedia, India) and the results were recorded following the instruction of manufacturer. These test disks used included nitrofurantoin (300 mcg), nalidixic acid (30 mcg), amikacin (30 mcg), ofloxacin (5 mcg), ciprofloxacin (5 mcg), cotrimoxazole (1.25/23.75 mcg), ceftriaxone (30 mcg), cefotaxime (30 mcg), cephalexin (30 mcg), norfloxacin (10 mcg), chloramphenicol (30 mcg), gentamycin (10 mcg), tobramycin (10 mcg), kanamycin (30 mcg) and cloxacilin (5 mcg).

RESULTS

A total of 1878 urine samples were collected from children with suspicion of UTI. The age and sex distribution of children from whom the urine samples were collected is shown in Table-1. Majority of the cases were in the age group of less than 6 years. Relatively more number of samples was obtained from male children compared with females (p = 0.39). Of the total 1878, 538 (28.6%) were positive for pathogenic organisms (Table-2). Mixed growth seen in 8.1% samples were not considered. There was no significant difference in growth positive rate in two genders (M: 51.7% and F: 48.3%). The distribution pattern of culture positive samples in different age groups and sexes of children is shown in Table-3. Majority of growth positive cases were in the age group of less than six years. The types of organisms isolated are shown in Table-4. *Escherichia coli* was isolated in 93.3% of the positive samples. This was followed by *Proteus* sp and others.

Table 1: Age and sex distribution of children included in the study

Age group (yr)	Sex					
	Male		Female		Total	
	n	%	n	%	n	%
<1	153	56.5	118	43.5	271	14.4
1-5	384	55.1	313	44.9	697	37.1
6-10	287	51.4	271	48.6	558	29.8
11-15	177	50.3	175	49.7	352	18.7
Total	**1001**	**53.3**	**877**	**46.7**	**1878**	**100.0**

Table-2: Bacterial growth positive rate in urine samples collected.

Culture results	Samples n	%
Positive	538	28.6
Negative	1187	63.2
Mixed	153	8.1
Total	**1878**	**100.0**

E. coli was found to be most sensitive to amikacin, chloramphenicol, nitrofurantoin and ofloxacin and resistant to most commonly used drugs like cephalexin, nalidixic acid, cotrimoxazole and norfloxacin (Table-5). *Proteus sp* was found to be most sensitive to ceftriaxone, cefotaxime, ciprofloxacin and ofloxacin and least sensitive to cephalexin (Table-6). *Klebsiella sp* was most sensitive to ofloxacin followed by ceftriaxone and least sensitive to amikacin and nitrofurantoin (Table-7).

Pseudomonas sp was found to be most sensitive to ceftriaxone (100.0%) followed by amikacin (75.0%), ciprofloxacin (75.0%), ofloxacin (50.0%), nitrofurantoin (25.0%), nalidixic acid (25.0%) and cotrimoxazole (25.0%) and resistant to cephalexin. *Citrobacter sp* was also most sensitive to ceftriaxone (100.0%) followed by ofloxacin (75.0%), cefotaxime (66.7%), ciprofloxacin (50.0%), nalidixic acid (50.0%), cotrimoxazole (50.0%) and amikacin (25.0%). All isolates of *Citrobacter sp* tested were resistant to nitrofurantoin, norfloxacin and cephalexin. However, *Staphylococcus aureus* was most sensitive to chloramphenicol (100.0%) followed by ofloxacin (75.0%), cefotaxime (75.0%), amikacin (50.0%), cloxacillin (50.0%), cotrimoxazole (50.0%), ceftriaxone (33.3%) and ciprofloxacin (33.3%). It was found resistant to nitrofurantoin and nalidixic acid. *Enterobacter sp* made only 0.6% (3) of the positive isolates. It was sensitive to ofloxacin (100.0%), cefotaxime (100.0%), ciprofloxacin (66.7%), ceftriaxone (50.0%), nitrofurantoin (33.3%), nalidixic acid (33.3%),

Table-3: Distribution pattern of growth positive cases by age and sex

Age group (yr)	Sex					
	Male		Female		Total	
	n	%	n	%	n	%
<1	43	46.7	49	53.3	92	17.1
1-5	118	54.9	97	45.1	215	40.0
6-10	71	48	77	52	148	27.5
11-15	46	55.4	37	44.6	83	15.4
Total	**278**	**51.7**	**260**	**48.3**	**538**	**100.0**

Table-4: Pattern of organisms isolated from urine samples

Isolated organisms	Isolates n	%
E.coli	502	93.3
Proteus sp	12	2.3
Klebsiella sp	8	1.5
Citrobacter sp	4	0.7
Staph. aureus	4	0.7
Pseudomonas sp	4	0.7
Enterobacter sp	3	0.6
Salmonella typhi	1	0.2
Total	**538**	**100.0**

amikacin (33.3%) and resistant to cotrimoxazole and tobramycin. *Salmonella typhi* was isolated in only one positive urine sample and was sensitive to ofloxacin (100.0%) cefotaxime (100.0%) and ciprofloxacin (100.0%). It was resistant to cholramphenicol, nitrofurantoin, amikacin and cotrimoxazole.

DISCUSSION

The antibiotic sensitivity pattern of organisms changes rapidly over a short period. It is especially true for developing countries where antibiotics are prescribed irrationally not only by the medical practitioners but the antibiotics are also purchased directly from the chemists (medicine shop keepers) without prescription.[18] It has been advised that pediatricians should be aware of the rising resistance of urinary pathogens to commonly prescribed antibiotics as well as the profile of antibiotic resistance within their community.[19] Therefore, periodic evaluation of sensitivity pattern is essential for rational and appropriate use of antibiotics.[11]

The overall growth positive rate (28.6%) in our study was in agreement with previous reports (27.7%) from Nepal.[20] However, the age group of the febrile children included in their study ranged between 2 months to 2 years only. A slightly lower positive rate (23.1%) has also been reported in patients of all age groups.[14] In the contrary, Shrestha *et al*[21]observed bacterial growth in 35.7% of the urine samples collected from female patients of all age groups. This appeared to be due to the inclusion of only female patients. The reported significant growth positive rate among subjects of all age groups ranged from 21.8% to 25.7%.[14-16,22]

UTI is a common problem in children[1] but the prevalence varies with the age and sex of children.[2] It occurs in about one percent of boys and three to five percent of girls.[4] However, in contrast to this, present study showed marginally higher positive rate among male children compared with female children. This could be due to the relatively more number of male children coming to the hospital (Male 53.3% vs. Female 46.7%) and might have been attributed to the preference given to the male children in the Nepalese society.[23]

Majority of growth positive cases were in the age group of less than six years. This was in agreement with previous report from Iran.[24] This could be because younger children are not well toilet trained and likelihood of ascending infection with fecal flora is more common in this age group.[4,7] Eighty nine percent of the UTI in children was constituted by the age group of less than 6

Table-5: Antibiotic sensitivity pattern of *E. coli*

Antibiotics	Isolates tested	Sensitive	Intermediate	Resistance
Nitrofurantoin	494	232 (47.0%)	93 (18.8%)	169 (34.2%)
Nalidixic acid	494	102 (20.6%)	6 (1.2%)	386 (78.2%)
Amikacin	492	306 (62.2%)	100 (20.3%)	86 (17.5%)
Ofloxacin	477	217 (45.5%)	10 (2.1%)	250 (52.4%)
Ciprofloxacin	477	140 (29.4%)	52 (10.9%)	285 (59.7%)
Cotrimoxazole	299	64 (21.4%)	5 (1.7%)	230 (76.9%)
Ceftriaxone	237	86 (36.3%)	5 (2.1%)	146 (61.6%)
Cefotaxime	235	90 (38.3%)	1 (0.4%)	144 (61.3%)
Cephalexin	132	1 (0.8)	3 (2.3%)	128 (96.9%)
Norfloxacin	83	20 (24.1%)	10 (12.0%)	53 (63.9)
Chloramphenicol	28	14 (50.0%)	1 (3.6%)	13 (46.4%)
Gentamycin	23	7 (30.4%)	4 (17.4%)	12 (52.2%)

Table-6: Antibiotic sensitivity pattern of Proteus sp

Antibiotics	Isolates	Sensitive	Intermediate	Resistance
Ciprofloxacin	12	9 (75.0%)	2 (16.7)	1 (8.3%)
Ofloxacin	12	9 (75.0%)	1(8.3%)	2 (16.7)
Nalidixic acid	12	7 (58.3)	0	5 (41.7%)
Amikacin	12	5 (41.7%)	3 (25.0%)	4 (33.3%)
Nitrofurantoin	12	0	0	12 (100.0%)
Ceftriaxone	10	8 (80.0%)	0	2 (20.0%)
Cotrimoxazole	8	5 (62.5%)	0	3 (37.5%)
Cefotaxime	5	4 (80.0%)	0	1 (20.0%)
Cephalexin	3	0	0	3 (100.0%)

years in one of the studies.[25] Recent study on prevalence rates of febrile UTIs in children of 0-19 years of age found UTI almost four times less frequent in female children aged > 12 months as compared to children up to 12 months of age.[26]

E. coli was the most common organism isolated and constituted 93.3% of all positive samples. This is the common finding in UTI. This was followed by *Proteus* sp. and others. This was in agreement with previous report (93.0%) in young children from elsewhere,[3] but slightly more than the finding observed by Rimal *et al* (89.2%) among children of up to two years of age.[20] In one study conducted in children aged 3 months to 14 years E coli has been found to be 80.0% (Sharma, unpublished finding). On the other hand, this was much higher than the findings among adults as have been reported by Rajbhandari *et al* (73.8%),[14] Rai *et al* (61.8%),[15] Shrestha *et al* (60.2%)[21] and Chhetri *et al* (77.5%).[22] This discrepancy could be because of the age of the subjects included in the studies. *E. coli* constituted 59.4% of the nosocomial UTI in hospitalized patients as reported by Das et al. [27] Another study in children observed E coli in the urine isolates even higher (96.4%) than our study.[25] The pattern of bacterial isolates observed in our study was close to agreement with finding reported in another report.[28]

With regard to the antibiotic sensitivity pattern of isolates, *E coli* was found to be most sensitive to amikacin, chloramphenicol, nitrofurantoin and ofloxacin. Rajbhandari *et al* earlier have reported nitrofurantoin as most sensitive antibiotic (68.8%) followed by gentamycin, norfloxacin and ciprofloxacin.[14] Other reports have also shown nitrofurantoin as the most effective drug. However, there may be non-compliance to nitrofurantoin due to its bitterness. Cephalexin, nalidixic acid, cotrimoxazole and norfloxacin were found to be most ineffective. Rajbhandari *et al* also found cephalexin as least effective followed by ampicillin, nalidixic acid and cotrimoxazole.[14] *E. coli* was found to be resistant to ampicillin and ciprofloxacin in eastern part of Nepal in a study conducted by Kumari *et al*.[16] Another study done by Das *et al*[27] in western part of Nepal found *E. coli* to be most sensitive to amikacin (98.0%) followed by gentamycin (87.9%), ceftazidime (80.8%), norfloxacin (78.4%) and cotrimoxazole (77.9%).

Proteus sp was identified as a causative agent for UTI only in a small number of cases (2.3%) in this study. This was in agreement with the finding (2.4%) by Shrestha *et al*[21] but is much lower than the finding by Moderres *et al*[24] (male children: 24.8%). However, the finding in female children was similar (2.8%). One study in Nepal found *Proteus sp* only in 1.6% of the positive isolates.[15] *Proteus sp.* was found to be most sensitive to ceftriaxone, cefotaxime, ofloxacin and ciprofloxacin in our study. It was resistant to cephalexin, gentamycin and nitrofurantoin. Previously, *Proteus* sp. has been reported to be sensitive to norfloxacin, ampicillin, nalidixic acid and cotrimoxazole but not cephalexin and nitrofurantoin as observed in this study.[14]

Klebsiella sp. constituted the third most common agent for UTI. However, it was identified only in a few cases (1.5%). In the contrary, Moderres *et al*[24] found *Klebsiella* sp in 10.5% of children with culture positive UTI. Kumari *et al*[16] also observed similar finding (12.6%) in a referral hospital of eastern Nepal in patients of all ages. Das *et al*[27] found *Klebsiella* sp in even higher number of patients (15.7%), however, it was identified in hospitalized patients of all ages as a nosocomial infection. It was most sensitive to ofloxacin but least sensitive to amikacin, nitrofurantoin and cotrimoxazole in our study. The quinolone group like norfloxacin, nalidixic acid followed by nitrofurantoin was observed to be most effective and cephalexin and ampicillin followed by cotrimoxazole were least effective by another study.[14] *Klebsiella* sp was found to be resistant to ampcillin and ciprofloxacin in a study.[16]

Table-7: Antibiotic sensitivity pattern of *Klebsiella* sp

Antibiotics	Isolates	Sensitive	Intermediate	Resistance
Ofloxacin	8	7 (87.5%)	0	1 (12.5%)
Ciprofloxacin	8	3 (37.5%)	2 (25.0%)	3 (37.5%)
Nalidixic acid	8	3 (37.5%)	1 (12.5%)	4 (50.0%)
Cotrimoxazole	8	2 (25.0%)	0	6 (75.0%)
Amikacin	8	1 (12.5%)	3 (37.5%)	4 (50.0%)
Nitrofurantoin	8	1 (12.5%)	1 (12.5%)	6 (75.0%)
Ceftriaxone	5	2 (40.0%)	0	3 (60.0%)
Cefotaxime	3	1 (33.3%)	0	2 (66.7%)

The only gram-positive organism isolated in our study was *S. aureus* and constituted only 0.7% of the isolates. This was in contrast to previous reports ranging from 2.7 to 12.2% of the positive isolates from Nepal by different studies.[14,15,21,28]

Nearly one-third of urine samples collected showed significant bacterial growth with *E. coli* as predominant isolate followed by *Proteus* sp., *Klebsiella* sp., *Citrobacter* sp., *S. aureus* and others. *E coli* was found to be most sensitive to amikacin, chloramphenicol, nitrofurantoin and ofloxacin but least sensitive to most commonly used drugs like cephalexin, nalidixic acid, cotrimoxazole and norfloxacin. This appears to be due to over use and/or misuse of antibiotics. Present findings together with previous ones are suggestive of need of periodic monitoring of antibiotic sensitivity pattern of the bacterial isolates to provide effective treatment and thereby to make it more cost effective particularly in the impoverished countries like elsewhere and ours.

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