ORIGINAL ARTICLE

Prevalence, Etiology and Predictors of Urinary Tract Infections in Febrile Children under the Age of Five Years

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Abstract

Background
Urinary tract infections (UTI) represent a major burden of infections in children; early diagnosis and appropriate treatment are important to avoid long-term morbidity. In low-middle-income countries, UTI concomitantly presents with other infections. Therefore, this study was done to determine the burden of UTI among febrile children and identify common pathogens and their sensitivity pattern. We also constructed a model that predicts UTI in febrile children.

Material and Methods
This was a cross-sectional study conducted at the Pediatric unit, Civil hospital Sukkar from 1st August 2013 to 30th September 2014. Patients up to five years of age of either gender with fever for less than two weeks were enrolled after written consent. Demographic and clinical features were recorded in a proforma. Urine culture was sent within 30 minutes of its collection. Identification of isolates using in-house biochemical tests and susceptibility to commonly used antibiotics was performed using the disc diffusion method. The data was entered and analyzed using SPSS version 20.

Results
272 patients were enrolled in the study. The median age of enrolled children was 2.8 (Interquartile range 2) years. Male patients accounted for 53.3% cases with male to female ratio of 1:1.14. The majority of children presented with low-grade fever, 182 (66.9%) followed by diarrhea (19.5%), dysuria 37 (13.6%), ureteric colic 31 (11.4%) and flank pain 28 (10.3%). Out of them, 32 (11.8%) patients had UTI. *E. coli* was the most commonly isolated pathogen accounting for 12 cases. Most of the pathogens were sensitive to aminoglycosides, fluoroquinolones, and fosfomycin. Female gender (OR 5.7, 95% CI: 1.88-17.41), diarrhea (OR 7.7, 95% CI: 2.36-28.82) and flank pain (OR 3.67, 95% CI: 1.02-13.21) were independent predictors of urinary tract infection in febrile children.

Conclusion
UTI is common among febrile children. Gram negative organisms are common pathogens of UTI and most are still sensitive to conventional antibiotics.

Keywords
Febrile children, UTI, Pathogen, Predictors

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Introduction
Urinary tract infections (UTI) can be defined by the presence of a significant bacterial count in the urine along with signs and symptoms of infections.[1] UTI is a common diagnosis in childhood, particularly in the first three years of life.[2] The prevalence of UTI is 3-5% in girls compare to 1-3% in boys.[3] In infants, the incidence of UTI is more in males than females due to higher incidence of obstructive anomalies of the urinary tract in boys but after one year, UTI is more frequent in girls than boys because of small urethra in females and increase chances of vaginal contamination with fecal flora and beyond two years the male to female ratio with UTI is 1:10.[4] UTI is more common in uncircumcised boys.[4] Literature suggests that fever is a common clinical presentation of UTI in neonates, infants, and young children whereas older children present with urinary symptoms (dysuria, polyuria, increase frequency, urgency).[5-6] Eighty (80%) of the infants with culture-proven UTI in a study, presented with fever.[7] UTI in children can occur concomitantly with other infections. Clinical features are vague and non-specific in infants so the diagnosis of UTI is missed by most pediatricians. Diagnosis and management of UTI is a challenge for physicians and leads to misdiagnosis that is often followed by ill health and renal damage.[7]

In a study, 110 out of the 3625 children seen in the out-patient department had UTI accounting for prevalence of 3.0%. The majority of the patients (59, 53.6%) were less than 2 years of age with a male: female ratio of 1:1.3. Fever was the commonest presenting symptom and the commonest organisms isolated in urine were *Klebsiella* (27, 24.5%), and *Staphylococcus aureus* (24, 21.8%). The organisms were sensitive to gentamicin (50, 45.5%), ceftriaxone (49, 44.5%), and ciprofloxacin (36, 32.7%).[8]

In another study, the prevalence of UTI was 7.87% and E. *coli* was reported as the most common etiological agent of UTI

(65.2%), followed by *Klebsiella* spp. (26%), *Pseudomonas aeruginosa* (3.6%), and *Staphylococcus* coagulase positive (3.7%). Results of antimicrobial susceptibility analysis for *E. coli* to commonly used antibiotics were as follows: amikacin (79.7%), ofloxacin (78.3%), gentamicin (71.6%), ceftriaxone (41.8%), cefotaxime (41.4%), and cefixime (27.8%).[9]

In another study, The most common pathogens isolated were *E. coli* in 297 (64.41%) samples, *Klebsiella Spp* and *Enterobacter* each in 51 (11.31%) samples, *Proteus* in 36 (7.8%) samples, *Pseudomonas* in 15 (3.27%) samples and *Citrobacter* in 8 (1.74%) samples.[10]

Recognizing UTI is very important to prevent long-term sequelae like renal scarring, hypertension, and chronic renal failure. To ensure optimal treatment with antibiotics it is necessary to know the causative organisms and their sensitivity pattern in patients visiting Civil Hospital, Sukkar so that appropriate antibiotics can be prescribed to prevent these long-term sequelae. The study was done to establish the magnitude of UTI among febrile children and to determine common uropathogens and their sensitivity pattern.

Material and Methods

This cross-sectional study was conducted in the Pediatric unit Civil Hospital from 1st August 2013 to 30th September 2014. Children were included in the study through non-probability convenience sampling from both the outpatient and inpatient departments. Patients' up to five years of age of either gender with complaints of fever (defined as the axillary temperature of =101°F) for less than two weeks and parents willing to participate in the study were included. Patients who were very sick, chronically ill, received antibiotics within the last 48 hours, refused to give written consent or had structural anomalies of urinary tract were excluded from the study.

The study physician explained the purpose, procedure, risks and benefits of the study to the parents and written consent was taken from them. An interview along with complete physical examination was performed and a urine sample for microscopy and culture was sent for all enrolled patients. Urine was collected following standard aseptic measures and sent to the laboratory within an hour of its collection. Aseptic bags were used for urine collection. Urethera was washed before attaching urine bag. For males, the penis was placed in the bag and for females, the bag was placed over the two folds of skin on either side of the labia. The culture was considered positive if at least 50,000 colony-forming units (CFU) per mL of a uropathogen were identified from the quantitative culture.[11] High colony count with more than one species was considered as a contaminant; however, the clinical correlation was also done. In the case of contamination & clinically febrile children, the second culture was sent. Disc diffusion method was used to determine the susceptibility of isolates. The zone diameters of each drug are interpreted using the criteria published by the Clinical and Laboratory Standards Institute (CLSI, formerly the National Committee for Clinical Laboratory Standards or NCCLS).[12]

The sample size was calculated using WHO software for sample size calculation. Using the prevalence of urinary tract in febrile patients of 13%,[3] confidence level of 95% and degree of precision of 5% the total sample size was 272. Data was entered and analyzed on SPSS version 20.0. The mean + standard deviation is presented for age. Frequency and percentage are reported for categorical variables like sex, age group, circumcision, voiding habits, urinary tract infections and causative organisms. Univariable and multivariable logistic regression analyses were done to determine the independent predictors of UTI in children.

Results

A total of 272 children of less than 5 years of age were enrolled with fever. The median age of enrolled children was 2.8 (Interquartile range 2) years. Male patients accounted for 53.3% cases with male to female ratio of 1:1.14. The majority of children presented with low-grade fever, 182 (66.9%) followed by diarrhea (19.5%), dysuria 37 (13.6%), ureteric colic 31 (11.4%) and flank pain 28 (10.3%). The other symptoms like polyuria in 24 (8.8%) case, poor stream 17 (6.3%), vomiting in 16 (5.9%), refusal to feed in 24 (8.8%) cases and convulsions in 11 (4%) cases were observed. Of 272 febrile children, 32 (11.8%) had urinary tract infection confirmed by urine culture. None of the children had received any prior antibiotics.

Comparison of demographic and clinical features of patients with culture confirmed UTI and those without UTI is summarized in table 1. In the univariable analysis, the age of the child, female gender, flank pain, ureteric colic, diarrhea, vomiting and refusal to feed were found to be associated with urinary tract infection (Table 1). However, in multivariable analysis, female gender (OR 5.7, 95% CI: 1.88-17.41), diarrhea (OR 7.7, 95% CI: 2.36-28.82) and flank pain (OR 3.67, 95% CI: 1.02- 13.21) were independent predictors of urinary tract infection in febrile children. The sensitivity and specificity of the model were 100% and 90% respectively (Table 2).

Among patients with positive urine culture, 30 had a single pathogen; *E. coli* was most commonly isolated organism (Figure 1). Antimicrobial susceptibilities of the pathogens are given in table 3.

Discussion

UTI is a significant problem in children. The factors responsible for the consequences of UTI are the non-specific clinical presentation in children and lack of appreciation of high morbidity and mortality associated with UTI and the spectrum of microorganisms associated with it. Significant bacteriuria has been documented in febrile infants and children even with an alternative diagnosis of fever.[11, 12]

Table 1: Comparison of demographic and clinical characteristics between children with and without urinary tract infection

	Children with urinary tract infection (n=32)	Children without urinary tract infection (n=240)	Univariable analysis	
			*OR	CI†
Age *Median (IQR)*	2.3 (2.2)	2.7 (2)	1.37	(1.02-1.83)
Male	10 (31.3%)	135 (56.3%)	1	
Female	22 (68.8%)	105 (43.8%)	2.82	(1.28-6.23)
Low grade fever	17 (53.1%)	165 (68.8%)	1	
High grade fever	15 (46.9%)	75 (31.3%)	1.94	(0.92-4.09)
Dysuria	4 (12.5%)	33 (13.8%)	1.12	(0.36-3.38)
Polyuria	4 (12.5%)	20 (8.3%)	1.57	(0.50-4.93)
Flank pain	10 (31.3%)	18 (7.5%)	5.61	(2.31-13.63)
Ureteric colic	16 (50%)	15 (6.3%)	15	(6.29-35.73)
Poor stream	4 (12.5%)	13 (5.4%)	2.49	(0.76-8.17)
Diarrhea	26 (81.3%)	27 (11.3%)	34.18	(12.91-90.52)
Vomiting	7 (21.9%)	9 (3.8%)	7.87	(2.46-20.96)
Refusal to feed	7 (21.9%)	17 (7.1%)	3.67	(1.38-9.71)
Convulsions	2 (6.3%)	9 (3.8%)	1.71	(0.35-8.29)

**OR-Odds ratio, †CI-Confidence interval*

Table 2: Predictive model for diagnosis of children with febrile urinary tract infections

Predictors	OR	95% CI	
		Lower	Upper
Age	1.23	.846	1.80
Gender	5.72	1.88	17.41
Diarrhea	7.73	2.36	28.82
Flank pain	3.67	1.02	13.21

Sensitivity 100% Specificity 90%

Table 3: Antibiotic sensitivity pattern of causative organisms

Antibiotics	Organisms			
	E. coli *(n=12)*	*Klebsiella* **spp (n=8)**	*Pseudom- -onas* **spp** *(n=4)*	*Proteus* *(n=6)*
Amoxicillin/ clavulanic acid	8	6	1	2
Cefaclor	10	3	NT	2
Cefixime	4	2	2	2
Ciprofloxacin / ofloxacin	10	4	5	2
Nalidixic acid	2	4	1	2
Gentamicin	10	5	2	1
Amikacin	10	6	2	2
Fosfomycin	12	7	0	2

In our study children less than five years age and females were predominant. A study conducted in Yemen reported similar results.[13] A study in Lahore by Waqar *et al* reported UTI was common in patients between one to five years of age.[17] Among 272 febrile children 32 (11.8%) had UTI in this study. This finding is comparable to a study in India conducted in 2003, which concluded incidence of UTI in febrile children as 10%.[13] A quarter of the subjects had dysuria on presentation, a much

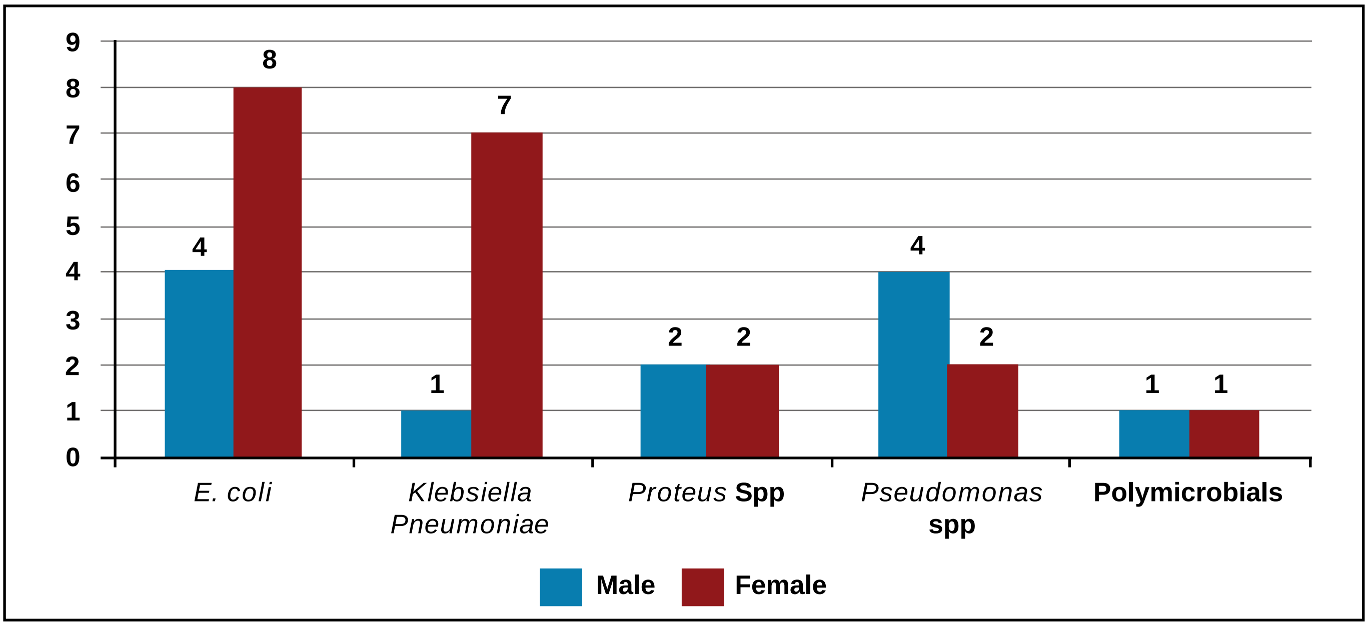

Fig 1. Frequency distribution of causative organisms isolated from urine culture

higher frequency (68%) has been reported in other studies. Female preponderance has been documented worldwide in all settings.[12, 13] This finding was due to the short urethra of females and perineal contamination. In our study febrile children with UTI presented with diarrhea and vomiting each accounting for 33.3%. Diarrhea has been significantly associated with UTI; reported by many studies conducted in India.[14, 15]

In our study UTI was common in uncircumcised males; similar findings have been reported by other investigators. This finding is due to colonization of bacteria in foreskin that may cause contamination of urine.[12, 13]

In the present study factors that predicted UTI in febrile children were female gender, diarrhea and flank pain. These factors can be used in developing countries to predict UTI in children in a place where urine culture is not routinely done. Diagnosis of UTI in children poses a significant challenge due to the fact that most of the clinical characteristics in children suspected to have UTI are not reliable, in the present study as in other studies[18] dysuria, flank pain, vomiting, failure to thrive, irritability were not statistically significantly associated with UTI. There is not a specific sign or symptom that can predict the presence of UTI in infants and children. Combinations of findings, including a prior history of UTI, should be taken into account when making a decision to evaluate for UTI.[19-20] The limitation of this study is that other causes of fever were not investigated. In our study *E. coli* was most commonly isolated organism followed by *Klebsiella pneumoniae*. *E. coli* was commonly reported organism in the study at Yemen[16] and a study conducted in Ayub teaching hospital reported similar results comparable to our study. However, a few studies have indicated a lower percentage of *E. coli* and higher infection with *Proteus* and *Klebsiella*.[17] *Proteus* was isolated from 2 male subjects. This has been explained by the ability of the *Proteus* species to swarm the long urethra of males and ascend to cause infection.[11]

E.coli was sensitive to Co-amoxiclauvulanic (66.6%), quinolones (83.3) and resistant to nalidixic acid and co-trimoxazole (83.3%). Unlike our study, in Yemen, *E. coli* were sensitive to nalidixic acid (70%).

In conclusion, a high prevalence of UTI is observed among febrile children in our setting and is predicted by female gender, diarrhea, and flank pain. Gram negative organisms are common pathogens of UTI and most are still sensitive to conventional antibiotics.

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