

Urinary Tract Infection and Predisposing Factors in Children

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Abstract

Objective: This study was designed to determine the predisposing factors in children with symptomatic urinary tract infection (UTI) according to age and gender.

Material & Methods: We reviewed prospectively 183 pediatric patients with symptomatic UTI admitted to emergency department or referred to nephrology clinic from November 2002 through July 2005. All patients underwent renal ultrasonography and voiding-cystourethrography or radionuclide cystography. Diuretic renal scan or intravenous pyelography (IVP) was performed in those with urinary system dilatation. Urodynamic studies were done in patients with normal radiologic findings and recurrent infections or urinary-intestinal symptoms.

Findings: Of 183 patients, 130 cases (71%) were female and 53 patients (29%) male. Most of the patients (61.9%) were between 2-24 months old ($P=0/001$). Vesicoureteral reflux (VUR) was the most common predisposing factor in both genders (46.9% in girls and 48.9% in boys). Voiding dysfunction in girls and urinary obstruction in boys were found with a significant difference ($P=0/03$ for both). In all age groups, except patients ≤ 1 month, the most common predisposing factor was reflux. Reflux, urinary obstruction and nephrolithiasis were found with a significant difference in 2-24 months age group ($P=0/001$ for all).

Conclusion: In our study vesicoureteral reflux (VUR) was as common in boys as in girls, and suggested urolithiasis as a significant UTI predisposing factor. This study showed that voiding dysfunction in girls and urinary obstruction in boys are as significant predisposing factors. We suggest urodynamic studies in patients with normal radiologic findings and recurrent infections or urinary-intestinal symptoms.

Key Words: Urinary tract infection, Children, Predisposing factors, Vesico-ureteral reflux, Urinary obstruction, Voiding dysfunction, Urolithiasis

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Introduction

Urinary tract infection (UTI) is one of the most common bacterial infections in children. In one study of 7-year-old school entrants, 7.8% of the girls and 1.6% of the boys had symptomatic UTI verified by urine culture^[1]. The goal should be to diagnose the very first UTI, especially in infants, and to identify risk factors and high risk patients.

Imaging studies have been done to diagnose congenital anomalies such as vesicoureteral reflux (VUR), obstruction, ureterocele; that predispose for recurrent infections^[2]. Practice guidelines from American Academy of Pediatrics recommend voiding cystourethrogram (VCUG) and renal ultrasonogram after a first UTI in children between 2-24 months of age^[3].

Most pediatric urologists would agree that all children under 5 years of age, boys of any age, all children with febrile UTI, and school aged girls who have had two or more UTI's, need to perform VCUG^[4,5]. Mingin study showed that in children with febrile UTI and normal radiologic findings (VCUG and renal ultrasonogram), recurrence was more common in girls and uncircumcised boys during the first year of life^[6]. In children without congenital anomalies, bladder dysfunction and residual urine are probably the major factors for recurring UTI. Those with more than 5ml of residual urine had a recurrence rate of 75% within a year^[1].

Bachelard study with purpose of evaluating VCUG as a method for identifying bladder instability in infants showed that the more signs noted on a film (irregularity of bladder wall, elongation of bladder shape, and filling of posterior urethra), the stronger the indication of instability^[7]. Epidemiological studies have shown that diurnal enuresis or a combination of diurnal and nocturnal enuresis is associated with pediatric UTI's, and urodynamic testing of otherwise radiologically normal children with recurrent UTI's and incontinence has shown abnormal cystometry and voiding patterns^[8].

Urinary stones can cause UTI by urinary stasis or obstruction. Joul study on 769 patients with nephrolithiasis which were followed for 10 years showed infectious complications in 20% including chronic pyelonephritis in 82 patients, pyonephrosis in 60 patients and perinephric

abscess in 10 patients^[9].

The purpose of this study was to determine UTI predisposing factors according to age and gender.

Material & Methods

We reviewed prospectively 183 children with symptomatic UTI which were admitted to emergency department or referred to nephrology clinic of Dr. Sheikh Children's Hospital between November 2002 and July 2005. The patients were divided into four age groups including; less than month, 2-24 months, 25 months to 5 years and more than 6 years.

UTI was diagnosed as clinical symptoms and positive urine culture (colony count more than 10^5 CFU/ml) and in older children with specific symptoms (fever, dysuria, frequency, etc) with colony count more than 10^4 CFU/ml. Samples were obtained by urine-bags in infants and small children and by midstream method in toilet trained children.

Colony count $\geq 10^5$ CFU/ml in samples obtained by urine bags were considered positive if there was pyuria (urine leukocyte ≥ 5 /hpf).

Renal ultrasonogram and VCUG or direct radionuclide cystogram (DRC) were obtained for all patients with symptomatic UTI except for first episode of cystitis in girls over 5 years of age with normal renal ultrasonogram. Girls older than 5 years with one episode of cystitis and normal renal ultrasonogram were excluded from study. Diuretic renogram (TC^{99m} -DTPA scan) or intravenous pyelography was performed in patients with dilatation of pyelocalycial system or dilated ureter.

Urodynamic studies including uroflowmetry, electromyography, cystometrography and, in infants, measurement of leak point pressure were performed in patients with normal radiographic findings (VCUG and renal ultrasonogram) and recurrent infections or urinary-intestinal symptoms in the absence of infection including daytime incontinence, nocturnal enuresis, constipation or encopresis. Flowchart presents method of evaluation of patients.

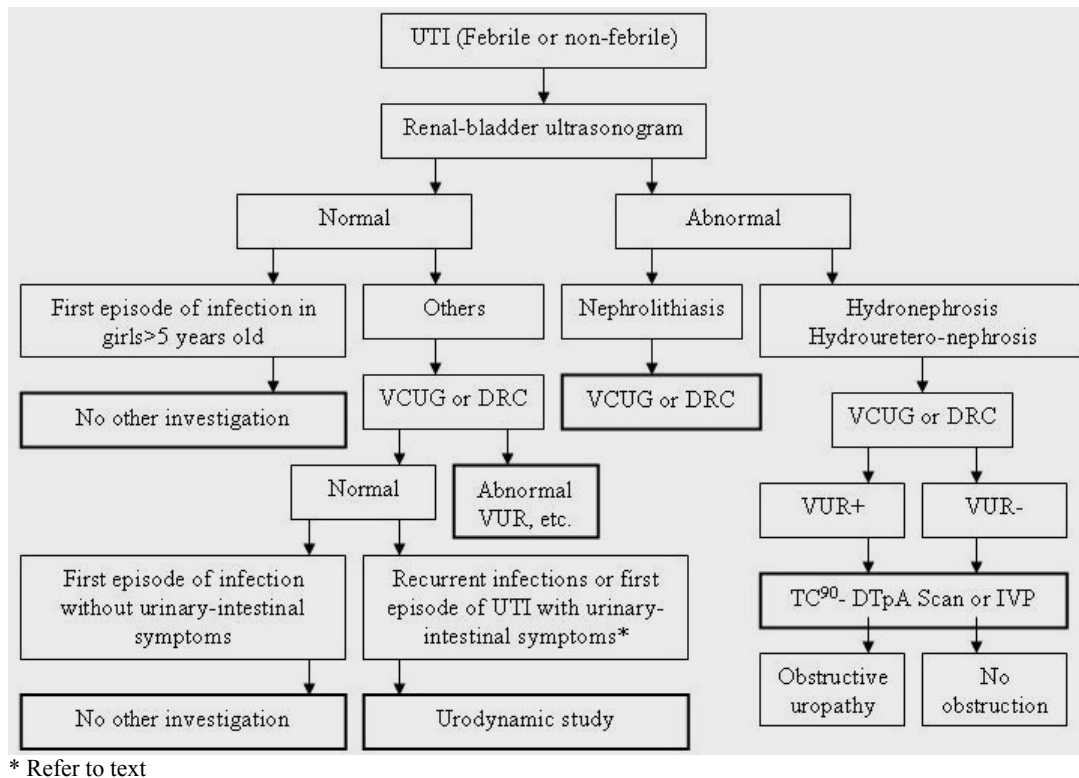


Fig 1- Flowchart for evaluation of patients with UTI

The data were analyzed using Chi-square and non-parametric Chi². A *P*-value of <0.05 was considered significant. Different steps of the study were fully described for patients' parents and their consent for inclusion in the study was obtained.

Findings

Of the 183 patients, 130 patients (71%) were female and 53 cases (29%) male (F/M=2.5). UTI was found in a significantly higher proportion of girls (*P*=0.002). Age at first infection was between 3 days and 11 years with a mean age of 12.25 months. In all patients and in each genders, most of the patients were 2-24 months old (*P*=0.001). In boys, age less than one month and in girls age more than 6 years showed a significant difference (*P*=0.001 for both). Distribution of patients according to age and gender is presented in fig 2.

The most common clinical symptoms were fever and irritability (*P*=0.014) which were found in 120 cases (65%); other clinical symptoms are presented in table 1.

Seventy four patients (40.4%) had normal renal-bladder ultrasonogram, in 20 cases (10.9%) renal ultrasonogram was normal but there were abnormalities in bladder ultrasonogram, including bladder wall thickness, irregularity of bladder wall, and residual urine. Frequency of ultrasonogram findings is presented in table 2.

VUR was found in 87 (47.5%) patients; 77 patients had VUR alone, 6 patients in association with urinary stone, and 4 patients with urinary obstruction. Nephrolithiasis was reported in 18(9.7%) patients, of whom 6 patients had VUR. Urinary tract obstruction was found in 10 (5.5%) patients consisting of 7 cases ureteropelvic junction obstruction (UPJO), 2 cases of ureterovesical junction obstruction (UVJO) and one case of posterior urethral valve (PUV). Four patients (40%) of urinary tract obstruction had urinary tract obstruction. Diagnosis in 13 (7.1%)

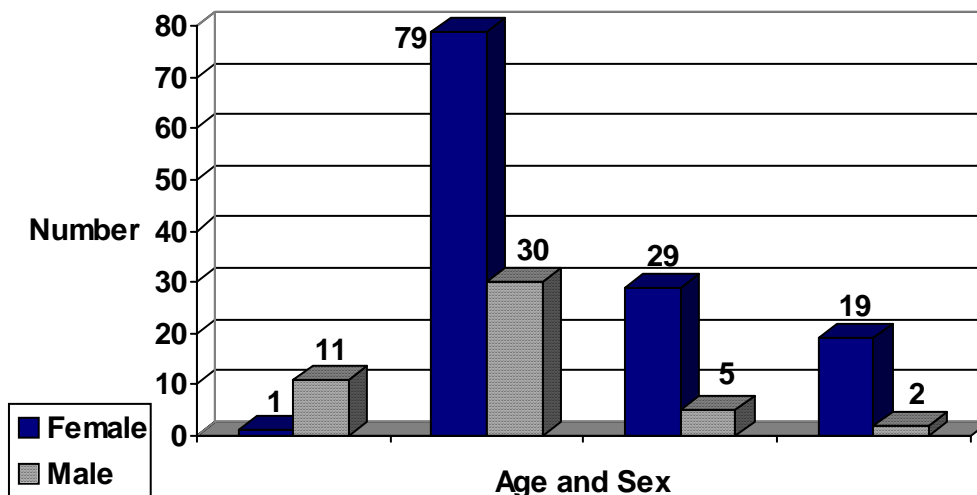


Fig 2- Distribution of UTI patients according to age and gender

Table 1- Frequency of symptoms in patients

Symptoms	Number of Patients (%)
Fever and irritability	120 (65%)
Dysuria	43 (23.5%)
Urinary frequency	34 (18.6%)
Abdominal or flank pain	27 (14.7%)
Vomiting	26 (14.2%)
Failure to thrive	17 (9.3%)
Diarrhea	12 (6.5%)
Fever and convulsion	12 (6.5%)
Bad odour urine	9 (4.9%)
Gross hematuria	8 (4.4%)
Poor feeding	5 (2.7%)
Urinary incontinence	5 (2.7%)
Dribbling	4 (2.2%)
Malaise	2 (1.1%)
Respiratory distress and sepsis	2 (1.1%)
Genital burning	2 (1.1%)

Table 2- Frequency of ultrasonogram findings of our patients

Ultra-sonogram findings	Number of Patients (%)
Normal renal-bladder Ultra-sonogram	74 (40.4%)
Increased bladder wall thickness	34 (18.5%)
Unilateral or bilateral Hydronephrosis	22 (12%)
Urinary stone	18 (9.8%)
Unilateral or bilateral hydroureteronephrosis	12 (6.5%)
Residual urine	11 (6%)
Decrease kidney size	5 (2.7%)
Fullness of pyelocalyial system	5 (2.7%)
Single kidney	3 (1.5%)
Changed ecogenecity (Hypo or Hyper)	3 (1.6%)
Decreased cortical thickness	2 (1.1%)
Dilated ureter	2 (1.1%)
Ectopic kidney	1 (0.5%)

patients was neurogenic bladder including 11 patients with myelomeningocele and 2 patients with spastic cerebral palsy. Prevalence of other predisposing factors is presented in table 3.

Of 65 patients with normal radiologic findings, 41 patients had recurrent infections (19 cases two, and 22 cases had three or more episodes of UTI). Thirty one patients (16.9%) had urinary or intestinal symptoms in the absence of infection, including daytime incontinence in 16 patients, nocturnal enuresis in 10 patients, interrupted urine stream in one patient, constipation in 16 patients and encopresis in 4 patients.

Urodynamic study was performed in 17 of them that showed abnormal findings in 15 including low compliance bladder, hypertonic bladder or detrusor-sphincter dyssynergia (DSD pattern). In one patient, bladder dysfunction was diagnosed on the basis of VCUG findings (spinning top deformity) and clinical symptoms. Of the 16 patients with diagnosis of voiding dysfunction, 15 were girls and one was boy.

The most common predisposing factor was VUR, reported in 87 patients (47.5%). VUR was the most common predisposing factor in both genders and all age groups except patients less than one month. VUR was found in 41.7% patients of less than one month, 47.3% of patients aged 2-24 months, 40% of patients 25 months to 5 years old, and 40.9% of patients aged more than 6 years.

Table 3- Prevalence of predisposing factors in our patients

Predisposing factor	Number (%)
Vesicoureteral reflux	87 (47.5%)
Undetermined predisposing factor	49 (26.7%)
Urinary stone (nephrolithiasis)	18 (9.7%)
Voiding (bladder) dysfunction	16 (8.7%)
Neurogenic bladder	13 (7.1%)
Urinary obstruction	10 (5.5%)

VUR, nephrolithiasis and urinary tract obstruction were found with a significant difference in patients of 2-24 months ($P=0.001$ for all). Sixty three percent of VUR, 94% of urinary stones and 60% of urinary tract obstructions were found in patients of 2-24 months (table 4 and 5).

In other age groups, there was no significant difference between different predisposing factors ($P>0.05$). VUR was the most common predisposing factor in both genders. In girls voiding dysfunction and in boys urinary tract obstruction were found with a significant difference ($P=0.007$, $P=0.026$) and normal radiologic findings were reported in a significantly higher proportion of girls ($P=0.026$). Frequency of predisposing factors according to gender is presented in table 6 and 7.

Table 4- Prevalence of predisposing factors according to age

Predisposing factors	≤1 month	2-24 month	25 month – 5 years	≥6 years
	N0 (%)	N0 (%)	N0 (%)	N0 (%)
VUR	5 (41.7%)	52 (47.3%)	16 (40%)	9 (43%)
Nephrolithiasis	0	16 (14.5%)	1 (2.5%)	0
Urinary tract obstruction	1 (8.3%)	6 (5.5%)	2 (5%)	0
Neurogenic bladder	0	6 (5.5%)	4 (10%)	0
Voiding dysfunction	0	3 (2.7%)	7 (17.5%)	6 (28.5%)
Undetermined	6 (50%)	27 (24.5%)	10 (25%)	6 (28.5%)
Total	12 (100%)	110 (100%)	40 (100%)	21 (100%)

Table 5- Correlation between age and predisposing factors

Age group	VUR	Nephro-lithiasis	Urinary tract obstruction	Neurogenic bladder	Voiding dysfunction	Undertermined predisposing factor
	No (%)	No (%)	No (%)	No (%)	No (%)	No (%)
≤1 month	5 (6.1%)	0	1 (10%)	0	0	6 (12.2%)
2-24 month	52 (63.4%)	16 (94%)	6 (60%)	6 (60%)	3 (18.7%)	27 (55.1%)
25 month – 5 years	16 (19.5%)	1 (6%)	2 (20%)	4 (40%)	7 (43.8%)	10 (20.4%)
≥6 years	9 (11%)	0	1 (10%)	0	6 (37.5%)	6 (12.3%)
Total	82 (100%)	17 (100%)	10 (100%)	10 (100%)	16 (100%)	49 (100%)

Discussion

We analyzed the data of a group of children with symptomatic UTI, in whom imaging studies were systematically performed. The diagnostic imaging methods that are usually performed to determine the UTI predisposing factors include: renal ultrasonogram, VCUG or direct radio-nuclide cystogram and intravenous pyelography or diuretic renogram. A Swedish UTI study (1993-1995) revealed that most of infections in neonates occurred among males, but after six months of age, most of infections were seen in females^[10,11]. In our study, UTI was found in a significantly higher proportion of girls. In Burbige study, 75% of UTI patients had anatomical abnormalities, most commonly VUR, and more than 25% had obstructive lesions^[12].

Swedish UTI study revealed that 36% of girls and 24% of boys with UTI had reflux^[10], Hoberman study on 309 children with UTI, revealed VUR in 39%^[3], Honkinen study on 76 children with UTI, demonstrated reflux in 28 and obstruction in 12 of the patients^[8]. In our study the major predisposing factor in both genders was VUR with similar frequency (46.9% in females and 48.9% in males). Winberg et al reported obstructive lesions in 2% of girls and 10% of boys with UTI^[13]. Other studies reported VUR in 26% to 53%^[14-17] and significant obstructive uropathy in fewer than 1% of children with urinary tract infection^[18].

A new prospective study by Hoberman revealed severe obstructive lesions in less than 1% of children with first febrile UTI and Burbige

Table 6- Correlation between predisposing factors and gender

Predisposing factor	Female	Male	Total
	Number (%)	Number (%)	
VUR (alone)	57 (74%)	20 (26%)	77
Unidentified	38 (77.5%)	11 (22.5%)	49
Nephrolithiasis	6 (50%)	6 (50%)	12
Neurogenic bladder	7 (53.8%)	6 (46.2%)	13
Voiding dysfunction	15 (93.7%)	1 (3.3%)	16
Urinary tract obstruction	3 (50%)	3 (50%)	6
VUR+Obstruction	0	4 (100%)	4
VUR+Nephrolithiasis	4 (66.7%)	2 (33.3%)	6

Table 7- Predisposing factors according to gender

Predisposing factor	Female	Male
	Number (%)	Number (%)
Vesicoureteral reflux (alone)	57 (43.9%)	20 (37.7%)
Undetermined predisposing factor	38 (29.2%)	11 (20.8%)
Voiding (bladder) dysfunction	15 (11.5%)	1 (1.9%)
Neurogenic bladder	7 (5.4%)	6 (11.3%)
Nephrolithiasis (alone)	6 (4.6%)	6 (11.3%)
VUR + nephrolithiasis	4 (3.1%)	2 (3.7%)
Urinary obstruction	3 (2.3%)	3 (5.7%)
VUR + Urinary obstruction	0	4 (7.6%)
Total	130 (100%)	53 (100%)

Notice: Age related tables are designed according to 176 patients whose age at the first episode of infection was known

study showed urinary tract obstruction in 25% of boys with UTI^[3, 12]. In our study, 10 (5.5%) patients had obstructive lesions including 3 girls (2.3% of the female patients) and 7 boys (13.2% of the male patients).

In a review of literature, it was noted that in patients without congenital anomalies (VUR, obstruction), non-organic causes including neurogenic bladder and voiding dysfunction may be the predisposing factor^[2,7,8]. In Chen study, aimed to quantify the relationship between dysfunctional elimination syndrome (DES), gender, UTI and VUR in children, girls had a significantly higher rate of DES than boys in all UTI and VUR subgroups^[10]. In our study, predisposing factor in 13 (7.1%) patients was neurogenic bladder. We performed urodynamic studies for 17 patients with normal radiologic findings and recurrent UTIs or urinary-intestinal symptoms suggestive of bladder dysfunction, and revealed abnormal findings in 15 patients including DSD pattern, low compliance bladder or hypertonic bladder (14 girls and 1 boy). Joul et al reported infectious complications in 20% of patients with nephrolithiasis which were followed for 10 years. In our study, of the 183 patients, 9.7% patients had urinary stone and in 6.5% patients the only predisposing factor was nephrolithiasis^[11].

In our country, unfortunately prenatal renal ultrasonography is not performed routinely, and

relatively high incidence of VUR and obstructive lesions in our patients may be related to the absence of prenatal diagnosis. Therefore, we suggest applying prenatal renal ultrasonography as a routine approach. We also suggest undertaking urodynamic studies in patients with normal radiologic findings and recurrent infections or intestinal-urinary symptoms (like day time incontinence or constipation).

For an exact judgment about predisposing factors in neonatal period, we need to study higher number of patients. We suggest nephrolithiasis in both genders, obstructive lesions in boys and voiding dysfunction in girls as important UTI predisposing factors.

Conclusion

This study showed that in neonatal period, UTI is more common in boys, but with increasing age, female patients increase, and in children ≥ 6 years, most of patients are girls and we clearly saw that UTI is more common in 2-24 months age group. This study revealed that VUR is the major predisposing factor in both genders (46.9% of girls and 48.9% of boys had VUR), with equal incidence and it is the most common predisposing factor in all age groups except in neonatal period.

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