*HK J Paediatr (new series)* 2004;**9**:30-36

# Symptomatic Urinary Tract Infection in Children: Experience in a Regional Hospital in Hong Kong

KW ***Fong***, SN ***Wong***

**Abstract**

We performed a retrospective review of the demographic, clinical, imaging and outcome data of 94 children diagnosed in our hospital to have symptomatic urinary tract infection (UTI) between January 1994 to June 1996. Our findings were compared with previous local reports to look for changing epidemiology, and with overseas studies to look for ethnic differences. We found that in this local Chinese cohort, UTI mainly affected boys (78%) and infants (85% <1 year), in whom it presented with fever and non-specific symptoms. The diagnosis was established by demonstrating pyuria and significant positive bacterial culture from either suprapubic aspirated (42.5%), catheter (34%) or clean catch urine (14.9%) samples, but 8 patients required DMSA scan for retrospective diagnosis because of mixed growth in bag urine or no growth due to prior antibiotic therapy. The causative organisms were *E. coli* in 78% of cases, but could also be *Klebsiella*, Proteus and Enterococci. Complete imaging studies were performed in 86% of our patients and revealed hydronephrosis in 12%, VUR in 23%, persistent renal scarring in 16% of patients. No abnormalities were found in 56%. There was a strong association between VUR, recurrent UTI and renal scarring. On medium term follow up, 16% of patients had recurrence of UTI. The prognosis was favourable as 77% of the 31 refluxing units and 43% of hydronephrosis detected resolved spontaneously. One patient required partial nephrectomy and excision of ureterocele and two patients required circumcision. An overall of 21 patients (22%) had "complicated" UTI and they required long term follow up management, preferably by paediatric nephrologists in consultation with urologists.

**Key words** Children; Chinese; Renal scarring; Urinary tract infection; Vesicoureteral reflux

## Introduction

Urinary tract infection (UTI) is a common bacterial infection in children. Studies in Western countries suggested that it accounted for 5% of febrile illnesses in young children.[1] It is especially common in infants, female and the White race.[2] Imaging studies following UTI revealed a high incidence of abnormalities in the renal tract, with vesicoureteric reflux (VUR) in 30-50%[1] and obstructive uropathies in 1-4%.[3] Evidence of renal parenchymal damage was present in 1.6-15% as seen on intravenous urography[3] and 59% as seen on $^{99m}$Technetium-dimercaptosuccinic acids (DMSA) scans.[4] The risk of renal scarring was positively associated with the severity of VUR and number of recurrent febrile UTI. The relationship of such radiographic findings to long term sequalae such as hypertension and chronic renal failure have been challenged. Nevertheless four of the 52 patients with VUR reported by Smellie et al developed end stage renal failure after 10 years.[5] A review of the literature also found that end stage renal disease developed in 3-10% of patients with extensive scarring.[1] Ethnic difference has also been reported in the incidence of UTI and VUR.[6]

Despite controversies in its management, it is important to recognise UTI in young children and be familiar with its

**Department of Paediatrics & Adolescent Medicine, Tuen Mun Hospital, Tsing Chung Koon Road, Tuen Mun, N.T., Hong Kong, China**

KW **Fong** （方國華） *MBBS(HK), MRCP*
SN **Wong** （黃錫年） *MBBS(HK), FHKAM(Paed), FRCPCH*

**Correspondence to:** Dr SN **Wong**

*Received June 30, 2003*

clinical significance. In the local Chinese population, case series of childhood UTI were reported in the mid-1980's.[7,8] In the present study we aimed to review the epidemiology, clinical findings, imaging studies and outcome of a more recent cohort of UTI patients and highlight any secular changes by comparing with previous reports, or any significant differences from the Western populations.

## Patients and Methods

All children admitted to the Department of Paediatrics, Tuen Mun Hospital from 1st January 1994 to 30th June 1995, and diagnosed to have symptomatic UTI were included and their records were retrieved for analysis.

UTI was diagnosed by the following criteria: (1) presence of symptoms such as fever, irritability, vomiting or dysuria or frequency, and (2) any bacterial growth in the suprapubic aspirated urine, or a pure bacterial growth of $\geq 10^5$ in midstream, catheterised or clean catch urine samples, or (3) any inflammatory change demonstrated in the early DMSA scans. Treatment of the acute UTI consisted of 7-10 days of cefuroxime or netromycin depending on clinical responses. Follow up imaging studies (USG, VCUG and DMSA) were recommended for all patients below 5 years old.

The ultrasonographic (USG) examination was performed by the radiologists using adapted equipment with high-resolution curvilinear and linear transducers. Voiding cystourethrography (VCUG) was performed by filling the bladder by urethral catheterisation. VUR was graded according to the International Reflux Study Committee classification. DMSA scans were performed by intravenous injection of $^{99m}$Tc-DMSA. Images were acquired by a gamma camera with patients in supine position. The fractional left and right renal activity was calculated for each kidney after background correction.

Patients were given prophylactic antibiotics until imaging investigations were completed. Those found to have VUR or other urological abnormalities were given long term prophylactic antibiotics (usually trimethoprim, co-trimoxazole or nitrofurantoin), as were those who developed recurrent UTIs. Parents were advised that when their children developed unexplained fever, they should immediately consult medical advice to have UTI diagnosed or excluded. During follow-up visits, any recurrence of UTI was recorded. Patient's body weight and height, blood pressure, urinalysis and urine cultures were done. The age and sex, presenting symptoms, culture results, the investigation results, duration of follow up and outcome were analysed.

## Statistical Method

The data were analysed by Chi-square test or Fisher's exact test where appropriate. A $P$ value $<0.05$ was considered significant.

## Results

### *Demographic Characteristics (Table 1)*

Ninety-four patients were studied, including 73 boys

**Table 1** Clinical presentation of children of first symptomatic urinary tract infection.

| Age of patient on first presentation | <1 month of age | 1-12 months of age | 1-8 years of age |
|---|---|---|---|
| Number of patients (Total = 94) | 8 (8.5%) | 72 (76.6%) | 14 (14.9%) |
| Sex (Male / Female) | 7 / 1 | 57 / 15 | 9 / 5 |
| Presentation | | | |
| Fever | 7 (87.5%) | 68 (94.4%) | 7 (50%) |
| Vomiting | 1 (12.5%) | 4 (5.5%) | |
| Diarrhoea | | 8 (11.1%) | |
| Poor feeding | 1 (12.5%) | 10 (13.8%) | |
| Irritable | | 4 (5.5%) | 5 (35.7%) |
| Dullness | | 3 (4.2%) | |
| Haematuria | | 2 (2.8%) | 5 (35.7%) |
| Dysuria | | | 10 (71.4%) |
| Frequency | | | 8 (57.1%) |
| Seizure | 1 (12.5%) | 6 (8.3%) | |

(78%) and 21 girls (22%). The mean age of presentation was 9.5 months (median 3 months, range one day to 7.9 years). Eight patients (8.5%) were neonates (M:F = 7:1). Seventy-two (76.6%) were between 1-12 months old (M:F = 57:15), and 14 were older children (M:F = 9:5).

### *Symptoms and Signs (Table 1)*

Fever (≥38.0ºC) was the major symptom in 87.5% of the neonates (<1 month) and in 94.4% of infants. Other symptoms in these age groups were also non-specific. In older children, only 50% had fever, but 70% presented with dysuria. One neonate (12%) and 6 infants (8%) presented as febrile seizure. One patient had *Escherichia coli* septicemia secondary to UTI.

### *UTI Diagnosis*

UTI was documented by significant bacterial growth in the suprapubic aspirated urine in 40 patients (42.5%), catheterised urine in 32 patients (34%) and midstream urine in 14 (14.9%). In 8 patients UTI was diagnosed by significant growths in bag urine samples and confirmed by evidence of acute pyelonephritis in DMSA scan done within 2 months.

### *Microbiologic Findings (Table 2)*

*Escherichia coli* was obtained in 74 patients (78%), followed by Enterococci (6%) and *Klebsiella sp.* (4%). Mixed organisms or no growth were obtained in 4% of cases and diagnosis was confirmed by positive findings of acute pyelonephritis in the early DMSA scans.

### *Imaging Studies*

Only a minority of patients did not undergo full investigation either because of older age at presentation or parental refusal. Eighty-three of the 94 (86%) had undergone all 3 investigations (USG, VCUG & DMSA), with normal findings in 53 (56%).

USG was performed on 90 patients and showed abnormalities in 11 (12%): Six patients had unilateral hydronephrosis; two had bilateral hydronephrosis; and one had a duplex left kidney with ectopic ureterocele.

VCUG was performed in 87 patients. Twenty patients (23%) had VUR which was bilateral in 11 (8 boys and 3 girls) and unilateral in 9 (6 boys and 3 girls). Of the 31 refluxing kidneys in these 20 patients, 23 were mild (IRSC Grade I-III) while 8 were severe (Grade IV-V). Table 3 shows the relationship of the kidneys in relation to sex, laterality, VUR, grading of VUR and DMSA scan abnormalities.

Eighty-eight patients had undergone DMSA scan at a mean time of 2.7 months post-UTI (86 cases within 6 months post-UTI). Decreased isotope uptakes were found in 36 kidneys (20%) of 35 patients (40%). After second scan at a mean time of 12.1 months post-UTI (range: 2.3-27 months), 22 kidneys became normal (hence having transient acute pyelonephritic changes only). Persistent abnormalities were found in the 14 kidneys of 13 patients

**Table 2** Microorganisms causing symptomatic urinary tract infection in children

| Microorganism isolated | Numbers (Percentage) |
|---|---|
| *Escherichia coli* | 74 (78%) |
| Enterococci | 6 (6%) |
| *Klebsiella* | 4 (4%) |
| Proteus | 2 (2%) |
| Enterobacter | 1 (1%) |
| Mixed | 4 (4%)* |
| No growth | 2 (2%)* |
| Not done | 2 (2%)* |

*UTI were confirmed retrospectively by evidence of acute pyelonephritis in DMSA scan within 2 months.

**Table 3** Number of kidneys (number with persistent DMSA abnormalities) in relation to sex, laterality, VUR and grades of VUR

| | Male (Total 73 patients) | | Female (Total 21 patients) | |
|---|---|---|---|---|
| | Left kidneys | Right kidneys | Left kidneys | Right kidneys |
| Non-refluxing kidneys | 64 (1*) | 60 (1#, 4*) | 16 | 17 (1^) |
| Refluxing kidneys | 9 (1#) | 13 (2#, 1*) | 5 (1#, 1*) | 4 (1*) |
| Grade I-III units | 7 | 10 | 3 (1#) | 3 |
| Grade IV-V units | 2 (1#) | 3 (2#, 1*) | 2 (1*) | 1 (1*) |

# contracted kidneys with differential cortical mass <35%

* kidneys with focal cortical scars

^ renal agenesis

Assumption: all patients without VCUG and DMSA have no abnormalities

(16%). As shown in Table 3, 7 kidneys among the 67 patients without VUR had persistent abnormalities (1 renal agenesis, 1 small contracted or dysplastic kidney, 5 focal cortical scars), while 7 kidneys among the 20 patients with VUR had persistent abnormalities (4 small contracted kidneys and 3 focal renal scars). As shown in Table 4, renal scarring was significantly associated with presence of VUR especially high grade VUR, but not with sex or side of VUR, or infecting organism.

### *Outcome*

The mean duration of follow-up was 30.7 months (median 21 months, range 1-83 months). Most patients were either discharged or defaulted themselves after investigations showed no renal tract abnormalities and there were no UTI recurrences after 1-2 years. Only 3 patients had defaulted follow up despite significant renal abnormalities: small cortical scar (1), bilateral VUR (1) and right renal agenesis and left grade V VUR with focal scar (1).

Fifteen patients (16%) had recurrences of UTI despite prophylactic antibiotics therapy. The majority (80%) occurred within the first 3 months, even before full imaging studies could be arranged. Five patients had two or more relapses. Associated renal abnormalities were found in 11 of the 15 patients (73%). These included: 8 patients with VUR (with small contracted kidneys in 2, focal scar in one and renal agenesis in one), 2 with dilated renal pelvis, and one with no VUR but a small contracted kidney. *E. coli* was the commonest microorganism in the recurrent UTI being involved in half of the episodes. *Klebsiella* and Enterococci was the second and third common causative microorganism respectively. As shown in Table 5, there was strong association of UTI recurrence with VUR and persistent DMSA abnormalities.

Spontaneous resolution of VUR occurred in 24 kidneys of 16 patients (77% of the 31 refluxing units). This was detected at a mean of 31 months after the UTI. However, this was not the true time of resolution but just reflected the average interval we would repeat voiding cystograms.

**Table 4** Comparing potential risk factors for renal scarring

| | **Kidneys with no scarring N=174** | **Kidneys with scarring** N=14 | ***P*-value** |
|---|---|---|---|
| Mean age on presentation (month) | 9 | 17 | N/A |
| Male | 136 | 10 | N.S. |
| Female | 38 | 4 | |
| No VUR | 150 | 7 | P = 0.0026 |
| With VUR (any grade) | 24 | 7 | |
| No VUR | 150 | 7 | P = 0.0001 |
| With Grade I-III VUR | 21 | 2 | |
| With Grade IV-V VUR | 3 | 5 | |

N.S.= not significant, P>0.05

**Table 5** Comparing potential risk factors for UTI recurrences

| | **Recurrence of UTI (no. of patients)** | **No recurrence of UTI (no. of patients)** | ***P*-value** |
|---|---|---|---|
| Male | 10 | 63 | N.S. |
| Female | 5 | 16 | |
| Maximum grade of VUR | | | |
| Grade IV-V | 5 | 1 | <0.0001 |
| Grade I-III | 3 | 11 | |
| No VUR | 7 | 67 | |
| DMSA abnormalities | | | |
| Early scan +ve | 6 | 28 | N.S. |
| Early scan -ve | 9 | 51 | |
| Late scan +ve | 5 | 7 | 0.0215 |
| Late scan -ve | 10 | 72 | |

As shown in Table 6, there was no relationship to the sex, laterality, grading of VUR or presence of renal scarring.

Four out of the 7 hydronephrotic kidneys (43%) resolved spontaneously. Surgical operations were required for 3 patients: one patient with duplex left kidney and ectopic ureterocele underwent partial nephrectomy and ureterectomy, and two other patients underwent circumcision because of multiple recurrences of UTI.

No patients had hypertension and renal impairment. However the length of follow up was probably inadequate for such complications to develop.

## Discussion

This study describes the demographic, clinical and imaging features of an unselected cohort of children with first time UTI presenting to a regional hospital in Hong Kong in 1994-95. Compared with previous reports by Chow et al[7] (cohort from 1978-85) and So et al[8] (cohort from 1984-86), this is a more recent cohort with more comprehensive imaging studies performed, especially with the availability of DMSA scan. However we should be aware that this is a hospital based study and some patients with UTI may have been missed because they were treated by private practitioners and not referred to our hospital.

Our data showed that children with UTI commonly first presented in infancy (80% of our cases). This was in agreement with So and Davies[8] (86% of boys and 60% of girls presenting in the first year) but differed from the report by Chow et al[7] (only 45.5% in the first year). Since the inclusion criteria were similar, the difference may reflect genuine decrease in incidence of UTI in older children because they have been picked up at an earlier age or because of improvement in other risk factors such as constipation and poor toilet habits.

In contrast, Hoberman et al reported a female predominance (276 girls versus 33 boys) in their cohort of children in the USA who had UTI below 2 years of age.[9] Similar female predominance were also noted in the meta-analysis by Downs, which showed a prevalence of 3% and 2% in febrile boys below and above 1 year old respectively while the prevalence was 7% and 8% for febrile girls below and above 1 year old respectivley.[1] This is probably because neonatal circumcision was commonly practised in the USA while it is seldom performed in Hong Kong. Previous studies have shown that the prevalence of UTI could be increased 10 times in uncircumcised boys compared to circumcised boys.[10,11]

The presenting symptoms of our patients were similar to those of previous reports. Indeed they have not changed since the early description by Smellie[12] that young children presented with fever and non-specific symptoms while older children would have increasing symptoms of cystitis. Thus current guidelines mandates testing urine for all febrile children below 2 years of age.[13,14]

*Escherichia coli* accounted for 78% of UTI episodes in our study, followed much less commonly by *Klebsiella*, Proteus and Enterococci. In contrast to previous impression,[15] non-*E.coli* UTI were not significantly associated with complicated UTI such as the presence of VUR or renal scarring. However this may be due to the small sample size of our cohort.

Current guidelines recommend that young children with first symptomatic UTI should undergo USG and VCUG. The role of DMSA is more controversial.[13,16] Compared with previous local reports, our data provided a more accurate incidence of urological abnormalities that would be found

**Table 6** Comparing potential prognostic factors for resolution of VUR

| | **VUR resolved (no. of kidneys) 16 patients** | **VUR not resolved (no. of kidneys) 4 patients** | ***P*-value** |
|---|---|---|---|
| Male | 18 | 4 | N.S. |
| Female | 6 | 3 | |
| Left kidneys | 10 | 4 | N.S. |
| Right kidneys | 14 | 3 | |
| Grade I-III VUR | 17 | 6 | N.S. |
| Grade IV-V VUR | 7 | 1 | |
| Permanent DMSA abnormalities +ve | 6 | 1 | N.S. |
| Permanent DMSA abnormalities -ve | 18 | 6 | |

in children with first time UTI, because 86% of patients had undergone a "complete" investigation. We found that 44% of patients had abnormalities on either or all of USG, VCUG or DMSA. Twelve percent had abnormal USG findings, mostly being hydronephrosis but one patient having duplex left kidney with obstructed upper moiety and ectopic ureterocele. Twenty-three percent had VUR which was of severe grade (IV-V) in a quarter. This was lower than the incidence of 30-50% in Western studies.[1] Forty percent of patients had abnormalities on the first DMSA scan, though only 16% had persistent abnormalities (i.e. renal dysplasia or focal scars) as shown by repeated DMSA scans. Such information would be useful to counsel parents in the local scenario. We did not do second DMSA scan for patients who had normal first scan. However, from a previous study where all children had undergone both acute and follow up DMSA scans, no patients with normal initial scan had abnormalities on second scan and 15% of all patients had renal scars.[9]

Hoberman et al reported that in his cohort of 309 US children, USG detected renal tract dilatation in 12%, VCUG detected VUR in 39% but only 1.9% were of grade IV.[9] They concluded that USG was of limited value as they did not modify management. However their cohort was highly selective and children with known urological abnormalities were excluded. In their population, most urological abnormalities would have been detected by antenatal USG screening. This may not apply to our population where antenatal ultrasound screening was not a standard or universal practice. For our patients, a change in management plan was required in 21 patients as a result of the imaging studies: surgery in one, prophylactic antibiotic and monitoring VUR in 20 patients, monitoring renal tract dilatation in 8, long term follow up for the 13 patients with persistent DMSA abnormalities. We must point out that the long standing practice of prophylactic antibiotic for VUR was based on weak evidence from a few randomised trials and has become a controversial and undecided issue recently.[17,18]

Our study was limited by the short duration of follow up in most cases, and clinically important outcomes such as hypertension or renal impairment were not detected in our patients. Nevertheless concerning the prognosis of these patients, we showed that firstly, recurrence of UTI was an important problem. It recurred in 16% of our patients, most in the first 3 months. Recurrence was highly associated with VUR and renal scarring/dysplasia, and not with gender nor early DMSA abnormalities. We recommend that all young children with first UTI be closely observed for recurrence in the first 6 months and they should be covered with prophylactic antibiotics till results of imaging studies were available.

Secondly persistent DMSA abnormalities (renal scarring or dysplasia) were present in 14 kidneys (16%) of 13 patients (14%). It may be an important surrogate indicator for long term sequalae, though this is still controversial. We also showed significant associations between recurrence of UTI, VUR (especially high grade VUR) and renal scarring/dysplasia. This was in support of previous reports. A meta-analysis by AAP revealed that the risk of renal scarring in patients with high grade VUR was 8-10 times of those without VUR and 4-6 times of those with low grade VUR.[1] Also the risk of renal scarring rose exponentially as the number of recurrent UTI increases.[19] However VUR is not the only important factor for renal scarring/dysplasia. A separate meta-analysis by Gordon et al in 2003 showed that among seven studies involving 1062 kidneys, abnormal DMSA scan occurred in 44% of the kidneys with VUR and in 31% of kidneys without VUR. They concluded that a positive MCU only increased the likelihood ratio of abnormal DMSA scan by 2.34 times (CI 1.53 to 3.57), and a negative MCU reduced the likelihood ratio to 0.71 (CI 0.58 to 0.85).[4]

Thirdly VUR has a high chance of spontaneous resolution (77% in our patients), and can be managed medically. Previous reviews have shown that the chance of resolution decreases with advancing age, increased severity of VUR and bilateral VUR.[20] This was not seen in our patients, probably because of the small sample size and short duration of follow up.

Lastly surgical correction was indeed required in one patient and circumcision was performed in two patients to stop multiple recurrences of UTI. Thus management of the minority of patients with complicated UTI should involve a joint approach of nephrologists and urologists.

In conclusion our review provided useful local data on childhood UTI, in terms of demographic data, imaging abnormalities, and short term outcome. We showed that there was an increasing trend of infantile UTI compared with reports 10 years ago. In contrast to overseas reports which have female preponderance, local data suggested a strong male predominance. The bacteriology was not different from previous or overseas reports. Because almost all our patients had undergone USG, VCUG and DMSA scans, our data provided more accurate information than previous local studies on the urological abnormalities in children presenting with first time UTI. Also we found a lower incidence of VUR than overseas figures (23% versus

30-50%). The incidence of persistent renal scarring were similar. Sixteen percent of patients had UTI recurrences. One patient required partial nephrectomy and excision of ureterocele and two patients required circumcision for multiple recurrences. There were strong associations between VUR, recurrent UTI and renal scarring. An overall of 21 patients (22%) with these various abnormalities required long term follow up management, preferably by paediatric nephrologists in consultation with the urologists.

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