

Original Article

Urinary Tract Infection in Boys Less Than Five Years of Age: A General Pediatric Perspective

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ABSTRACT

Objectives: To examine the pattern of urinary tract infection (UTI) in boys < 5 years admitted to general pediatric wards and to identify the approach to imaging investigations.

Design: During the period from January 2002 through December 2002, 34 boys < 5 years of age were admitted to Farwania Hospital with UTI. Age at diagnosis, presenting features, urinalysis, pathogens, acute phase reactants and imaging procedures were reviewed for these patients.

Results: All 34 patients in this study were less than one year. Fever was the most common presenting feature and was seen in 70.6% of patients. Pyuria was found in 77%, positive leukocyte esterase (LE) test in 85.7% and positive nitrite test in 45.7% of patients. Significant leukocytosis was found in 39.3%, high C-reactive protein (CRP) in 46.8% and high erythrocyte sedimentation rate (ESR) in 50% of children. *Escherichia coli* (*E.coli*) were the most common pathogen affecting 77.1% patients. Radiological investigations were recommended as follows: ultrasound scan (US) for all patients (94.2% did

the test, 46.8% had normal scans and 43.7% had dilatation of pelvicalyceal system); Early-scheduled ^{99m}Tc dimercaptosuccinic scan (DMSA) was done in seven patients. Five or 71% had evidence of acute pyelonephritis; Late-scheduled DMSA was recommended for 25 patients. Only 52% did the test and out of those 46% had evidence of chronic involvement of the kidney(s); Micturating cystourethrogram (MCUG) was advised for 32 patients. 43.8% failed to carry out the procedure. Vesicoureteric reflux (VUR) was found in 38.8% of those who performed the test.

Conclusion: Unexplained fever in young boys should suggest UTI. Absence of fever does not exclude UTI, if other suggestive features exist particularly in the very young. UTI is commonly suggested by findings on urinalysis, on the other hand, negative urinalysis should not exclude the infection. Empiric antibiotics should cover gram-negative bacilli. Innovative strategies to ensure compliance to radiological investigations are needed.

KEYWORDS: dimercaptosuccinic (DMSA), Farwania hospital, micturating cystourethrogram (MCUG), urinalysis, 2002

INTRODUCTION

Urinary tract infection (UTI) is a condition that causes acute morbidity and may result in long-term complications including hypertension and reduced renal function^[1]. UTI is a relatively common condition in infants and young children. Age and gender are important factors influencing prevalence. As males are more likely to be born with structural abnormalities of the urinary tract, UTI is common in their first six months of life^[3]. Few infections are encountered in boys in the age range of 1 - 5 years. In preschool years symptomatic infections occur 10 to 20 times more frequently in girls than in boys^[2]. Since boys may be less suspected of having UTI than girls, it was our aim to profile the condition in Kuwait, highlighting the age of highest vulnerability, common presenting features and common pathogens.

Microorganisms reach the urinary tract by the way of ascending, hematogenous, or lymphatic

routes. The ascending route accounts for almost 95% of cases of UTI^[4]. This is particularly common for *Escherichia coli* (*E.coli*) and other Enterobacteriaceae. Compromised host's natural defenses (e.g., obstruction, catheterization) decrease the virulence requirements of the bacterial species. Certain bacterial strains are virulent enough to induce infection with no predisposing factors in the host^[4,5].

The clinical presentation of UTI in infants and children can be very subtle and atypical, and a high index of suspicion must be kept in order to diagnose UTI^[6]. Unexplained fever particularly should raise suspicion but very young infants may present without fever.

Accurate diagnosis of UTI is needed for two reasons: to permit identification, treatment, and evaluation of the children who are at risk for kidney damage and to avoid unnecessary treatment and evaluation of children who are not at

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risk^[1]. Urine specimen that is unlikely to be contaminated is needed for this purpose.

Although the outcome of UTI is usually benign, parenchymal scarring develops in 10 to 15%, with greater risk in those less than one year of age^[2]. On the other hand, some recent studies do not support age distinction and indicate that the risk of renal scarring may not decrease with age^[7]. Renal scarring is associated with complications such as hypertension, renal damage and end-stage renal failure^[8].

Renal scars can be detected by the use of imaging procedures. These are also essential for detection of anatomical abnormalities of the urinary tract, which increase the risk of renal scarring^[4].

The main imaging modalities include ultra sound scan (US), dimercaptosuccinic scan (DMSA), and Micturating cystourethrogram (MCUG). In this review the scheme of radiological investigations carried out in Farwania Hospital is outlined.

PATIENTS AND METHODS

The medical records of male patients five years and less diagnosed to have UTI and who were admitted to the general pediatric wards in Farwania Hospital from January 2002 through December 2002 were retrospectively reviewed. UTI was defined by the presence of two cultures of pure bacterial growth $> 10^5$ colony forming units/ml (CFU/ml) if the samples were collected by clean catch or midstream urine, one culture of pure bacterial growth $> 10^3$ (CFU/ml), if urine were collected by catheter. A total number of 34 boys were admitted during the study period with the diagnosis of UTI. The medical records of these boys were reviewed to determine age at presentation, main presenting feature, urinalysis, type of organism, acute phase reactants *i.e.*, blood white cell count, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) and type and results of radiological procedures.

The main presenting feature was the feature that led the treating physician to suspect UTI and carry out urine cultures. Urinalysis included dipstick testing in all patients and microscopic examination in 26 patients. Leukocyte esterase (LE) and nitrite test were selected from the dipstick criteria for review. On microscopic examination pyuria was defined by the presence of 10 or more white cells per seven high power field (7 hpf) and hematuria by the presence of 10 or more red cells per 7 hpf. Leukocytosis above $15 \times 10^9/l$ was considered significant. CRP was considered high, if above the cutoff point of 20 mg/l and ESR was considered high, if above 20 mm/hr.

The main radiological modalities were US, MCUG and DMSA. US was recommended for all

Table 1: Distribution of 34 cases of urinary tract infection according to presenting features, urinalysis, pathogen and acute phase reactants

| Variables | n | % |
|--------------------------|----|------|
| Presenting features: | | |
| Fever | 24 | 70.6 |
| Urinary symptoms | 11 | 32.4 |
| Vomiting | 7 | 20.5 |
| Neonatal jaundice | 3 | 8.8 |
| Nonspecific symptoms | 4 | 11.7 |
| Urinalysis | | |
| Pyuria | 26 | 77.1 |
| Hematuria | 14 | 40.0 |
| Positive LE test | 29 | 85.7 |
| Positive nitrite test | 16 | 45.7 |
| Pathogens | | |
| <i>E.coli</i> | 26 | 77.1 |
| <i>K.pneumoniae</i> | 7 | 20.0 |
| <i>P.aeruginosa</i> | 1 | 2.8 |
| Acute phase reactants | | |
| Significant leukocytosis | 13 | 39.3 |
| High CRP | 15 | 46.8 |
| High ESR | 16 | 50.0 |

patients during the actual infection, MCUG was recommended for all patients except two, 3-4 weeks following clearance of the infection. Early-scheduled DMSA (DMSA done during or shortly after the actual infection) was recommended for nine patients, late-scheduled DMSA (DMSA done 3-4 months following the infection) was recommended for patients with evidence of pyelonephritis on the initial DMSA. Late-scheduled DMSA was also recommended for a further 20 patients.

Data extracted were recorded using an Excel (Microsoft Corporation, Redmond, VA) spreadsheet and then subjected to descriptive statistical analysis.

RESULTS

The age of the boys enrolled in this study ranged from three days to 11 months. The median hospital stay was 10 days and the median duration of antibiotic treatment was 8.2 days.

The main presenting features included fever, urinary symptoms (these include difficulty in passing urine, crying on micturition, and frequency of urination, and change in the color or smell of urine), vomiting, neonatal jaundice and non-specific symptoms. Patients who presented with non-specific symptoms were suspected to have UTI because of abnormalities found on urinalysis. The number of patients and their percentage of total in relation to presenting features are shown in Table 1. Children who presented without fever were all less than three months of age. Vomiting was usually associated with other features. Infants who presented with jaundice were all less than one

Table 2: Number of patients for whom radiological investigations were recommended with percentage of failure to perform the procedures (n = 34)

| Radiological test | Number of patients for whom the test was recommended | | Number of patients who failed to perform the requested test | |
|-------------------------|--|------|---|------|
| | n | % | n | % |
| US* | 34 | 100 | 2 | 5.8 |
| MCUG** | 32 | 94.1 | 14 | 43.8 |
| DMSA ^s early | 9 | 26.4 | 2 | 22.2 |
| DMSA ^s late | 25 | 73.5 | 12 | 48 |

*Ultrasound, **Micturating cystourethrogram, ^s 99mTc dimercaptosuccinic scan

Table 4: Distribution of 32 urinary tract infection cases who performed US according to performance and results of DMSA

| US | DMSA* | | | | | Total |
|--------------------------|----------|--------|----------------------|--------------------------------------|---------------------|-------|
| | Not done | Normal | Acute pyelonephritis | Renal scar or chronic pyelonephritis | Other abnormalities | |
| Normal | 10 | 2 | 2 | 0 | 1 | 15 |
| Pelvicalyceal-dilatation | 5 | 4 | 3 | 1 | 0 | 13 |
| Other | 0 | 1 | 0 | 2 | 1 | 3 |
| Total | 15 | 7 | 5 | 3 | 2 | 32 |

*Not including those done for the second time in the same patient

month of age i.e., 20% of all infants under one month of age.

All patients had urinalysis (i.e., dipstick testing) in addition to microscopic examination of urine in 26 patients. The abnormal findings are shown in Table 1.

The pathogens were all gram negative Enterobacteriaceae, except one patient in whom the offending organism was gram-negative *Pseudomonas aeruginosa* (*P. aeruginosa*). The types of pathogens and the number and percentage of affected patients are shown in Table 1.

White blood cell count was estimated in 33 patients, CRP and ESR were measured in 32 patients. Number of patients with significantly elevated acute phase reactant is shown in Table 1.

The number and percentage of patients for whom radiological tests were recommended and those who failed to do the test are demonstrated in Table 2.

Thirty-two patients had an US examination and in 15 out of them there were no abnormalities found on the scans. Of those 15 patients with normal scans, seven had no further radiological investigation. Five had both MCUG and DMSA done, two had only MCUG done and one had only DMSA done. For the 17 patients with abnormalities

Table 3: Distribution of 32 urinary tract infection cases who performed US according to performance and results of MCUG

| US | MCUG | | | | Total |
|--------------------------|----------|--------|------|--------|-------|
| | Not done | Normal | VUR* | Others | |
| Normal | 9 | 4 | 1 | 1 | 15 |
| Pelvicalyceal-dilatation | 3 | 5 | 5 | 0 | 13 |
| Other abnormalities | 3 | 0 | 1 | 0 | 4 |
| Total | 15 | 9 | 7 | 1 | 32 |

*Vesicoureteric reflux

on ultrasound, seven had both DMSA and MCUG done, four only DMSA and four only MCUG. Two patients had neither of these investigations.

Most common abnormality found on US was a dilated pelvicalyceal system; gross hydronephrosis was found in six patients, mild to moderate dilatation was found in eight subjects. One patient had horseshoe kidney, an upper pole scar was detected in one patient and the left kidney was not visualized in one patient. MCUG results in relation to findings on the US are shown in Table 3. On the whole, 18 patients underwent MCUG and in 10 out of them the study was normal. VUR was detected in seven patients and posterior urethral valve in one patient.

Out of the seven patients who did an early-scheduled DMSA five were found to have evidence of pyelonephritis. Late-scheduled DMSA was recommended for those five patients; four of them performed the test plus further nine patients who did not have an early-scheduled DMSA. In those 13 patients three were found to have renal scars, three had evidence of chronic pyelonephritis, small kidney with decreased function, in one patient there was a horseshoe kidney demonstrated and in the remaining seven DMSA was normal. In nine patients DMSA was considered unnecessary because of normal radiological investigation (i.e. US and MCUG in two patients, normal US in three patients and normal early-scheduled DMSA in two patients). In the other two children other radiological investigations were preferred. Results of DMSA in relation to US findings are shown in Table 4.

All the patients were scheduled for follow-up in the general pediatric outpatient; however, in two patients urosurgical consultation was sought. One patient had posterior urethral valve, while the other was referred to exclude the possibility of pelviureteric junction obstruction.

DISCUSSION

In our study we attempted to examine the pattern of UTI in boys less than five years, since UTI is more common in younger boys than in later

age^[3]. In our group of patients we found that all affected boys were less than one year old and 47% were one month or younger. There was complete absence of cases in the age range of one to five years. We could not find a definite explanation for this finding but it may be related to the fact that almost all boys living in Kuwait would have been circumcised by one year of age. Vulnerability of uncircumcised boys to UTI has been suggested in many other studies^[9,10].

As UTI is a disease that seldom features physical signs^[5], we tried in this study to elucidate possible presenting features. Fever was the most common presenting feature, affecting 70.6%; it is prudent to keep a high index of suspicion for febrile young boys. However, 10 patients in this study had no fever at presentation; these were all infants three months of age or younger. UTI should not be automatically ruled out in the absence of fever particularly in young infants.

As urinary symptoms are difficult to evaluate in the very young, an observant mother is invaluable in this aspect and such observations must be taken into serious consideration. Jaundice was one of the features that led to the diagnosis of UTI. Infants less than eight weeks who present with jaundice should be screened for UTI^[11]. In our study 8.8% of all affected boys or 19% of those less than one month presented with jaundice. Similar findings were reported by Francisco *et al* who described diagnosing UTI in 7.5% of asymptomatic, afebrile, jaundiced infants (both boys and girls) younger than eight weeks^[11].

Abnormalities found on urine analysis may be the instigating factor in the diagnosis of UTI. Thus it is imperative that the test be sensitive enough not to miss cases. Both dipstick testing and microscopic examination of urine should probably be used. The dipstick findings had 81% sensitivity and 95% specificity^[3]. Urine microscopy was found to be less sensitive (60 and 70%)^[2,3]. In our group of patients, three or 8.8% had negative urine testing. Urinalysis should be performed in all suspected cases so that treatment can be started early and before the results of culture. However, the treating physician should proceed to urine culture if despite negative urinalysis the child presents with suggestive symptoms^[8], particularly in the very young. Urine culture should be done as a part of the septic workup.

In correlating elevated acute phase reactants (leukocytosis, high ESR and high CRP) with pyelonephritis as diagnosed by DMSA, there were five patients diagnosed to have pyelonephritis; in three out of them all acute phase reactants were not elevated, one patient had all acute phase reactants elevated and in one patient only ESR was elevated. The number of cases was small and yet it was

obvious that acute phase reactants were not helpful in predicting pyelonephritis. Ross *et al* had similar conclusions as they found that ESR, CRP, and peripheral WBC counts were not helpful in identifying UTI in febrile infants^[12]. Fretzayas *et al*, also concluded that CRP is not a very sensitive marker for localizing UTI site. They found that CRP was less sensitive than the other two inflammatory parameters (ESR and polymorphonuclear elastase-a1-antitrypsin complex or E-a1-Pi); its accuracy was only slightly inferior to that of E-a1-Pi. ESR was less sensitive than E-a1-Pi (90% vs. 96%) but the overall accuracy of these two markers was quite similar. They commented that their results were in agreement with other studies^[13]. Stokland *et al*, on the other hand, concluded that children with high levels of CRP, high fever, and dilating reflux had a risk of renal damage up to 10 times higher than children with normal or slightly elevated CRP levels, no or mild fever, and no reflux^[14].

The offending organisms in this study were exclusively of the gram negative Enterobacteriaceae family, the majority being *E.coli* and a significant minority being *Klebsiella pneumoniae* (*K.pneumoniae*). The knowledge of the possible offending pathogens is useful in the initial choice of antibiotics since there is evidence that early treatment before obtaining the results of culture and sensitivity may be associated with less chance of developing renal scarring^[15].

US has replaced intravenous pyelogram in the initial radiological evaluation of children with UTI. US can measure renal size and shape, identify hydronephrosis and structural or anatomical abnormalities of the kidneys and urinary tract and can diagnose renal calculi. It is convenient, relatively cheap and easy and has no radiation risk. However, US is not reliable for detection of VUR reflux, renal scarring or inflammatory changes; pyelonephritis cannot be reliably diagnosed on US. US is largely operator-dependent^[16]. In our study US was performed in most of the patients and proved to be reasonably reliable in detecting hydronephrosis and anatomical abnormalities and in indicating the possibility of VUR. It was not useful in the diagnosis of pyelonephritis. Contrary to the other radiological methods, there was a low rate of refusal or non-compliance. That low rate of refusal may call for more reliance on US through introducing techniques that may compensate for MCUG, like cystosonography enhanced with SH U 508A, a galactose-based echo-enhancing agent, which has as much a diagnostic value as traditional MCUG in diagnosing VUR^[17,18].

DMSA is the most reliable technique in the diagnosis of chronic renal cortical scarring as compared to other imaging modalities such as US

examination and intravenous urography^[19]. DMSA scintigraphy has also been used in the diagnosis of renal infarcts, horseshoe kidney, multicystic dysplastic kidney, and ectopic kidney. Acute pyelonephritis may cause residual scan abnormalities for at least three months after infection. In the detection of renal cortical scars, it is advocated to perform the DMSA study 3-6 months following the infection; however, these abnormalities may last for up to 12 months^[19]. In our group of patients DMSA was performed in seven patients during the acute stage to diagnose pyelonephritis and in five patients there was scintigraphic evidence of pyelonephritis. Follow-up scans in these patients showed renal scarring in two patients, reduced function of one kidney in one, was normal in one patient and one patient failed to do the follow-up study. Seven patients, out of thirteen had evidence of scarring and/or chronic pyelonephritis on late-scheduled DMSA.

In boys, initial work-up should include MCUG, which is needed for the diagnosis of VUR and for detection of urethral abnormalities such as urethral diverticulum or posterior urethral valves as normal US and/or DMSA do not exclude VUR^[13,20]. VUR was found in six of our patients who had undergone MCUG (42.9%). This is similar to findings in many other studies^[21]. One of the significant findings in this study is the high rate of failure to perform MCUG. Out of 30 boys for whom MCUG was recommended, 12 or 40% did not carry out the procedure. McDonald *et al* found in their study that in hospitalized children who underwent MCUG within a week after diagnosis of UTI, the presence of reflux was not significantly different from those studied later^[22]. They also had a high rate of failure (to perform the procedure) in those who were given late scheduled appointments. They concluded that the traditional recommendation to perform the MCUG at three to six weeks after the diagnosis of UTI should be reconsidered, especially for hospitalized children^[22]. MCUG remains essential in the evaluation of UTI, particularly to exclude VUR^[20].

CONCLUSION

Those who care for children should be aware that there is a high prevalence of UTI among children. He or she should have knowledge of the various presenting features, which are commonly atypical and be aware of the need to have a high index of suspicion. Medical care providers should keep track of the best ways to screen for and to diagnose UTI in children, particularly in infants. Early detection and treatment of the first infection in infants may be the only way to reduce the incidence of reflux nephropathy and to prevent

renal damage^[23]. However, diagnosis should be properly documented to avoid unnecessary investigation. Those with documented UTI should have radiological investigation to detect any structural abnormalities. These should include an US scan shortly after diagnosis to detect any anatomical abnormalities and MCUG after clearance of the infection, as it is the most reliable method to diagnose VUR. DMSA 3-6 months after the infection is important to diagnose renal scars. Early DMSA is valuable as the most accurate way to diagnose pyelonephritis as a definite diagnosis may be essential in some cases. Children who have structural abnormalities will need long term follow up^[10].

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