Original Article

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# Paediatric Urinary Tract Infection: A Hospital Based Experience

Paediatrics Section

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## ABSTRACT

**Introduction:** Paediatric Urinary Tract Infection (UTI) is one of the commonly encountered entities by paediatricians. Studies have shown easy vulnerability of paediatric urinary tract in any acute febrile illness and a miss in diagnosis could have long term consequences like renal scaring with its adverse effects. Bearing these evidence based preludes in view we designed our study to know the prevalence of UTI in Kashmir province.

**Aim:** Aim of the present study was to know the prevalence of UTI in febrile children and to know the sensitivity of different imaging modalities like Renal and Urinary Bladder Ultrasonography (RUS), Voiding Cystourethrography (VCUG) and Dimercaptosuccinic Acid (DMSA) scan in diagnosing UTI.

**Materials and Methods:** A total of 304 patients, between 2 months to 10 years, with axillary temperature of ≥ 100.4°F (38°C), who did not have a definite source for their fever and who were not on antibiotics were included in the study. Detailed history and through clinical examination was done to rule out any potential or definite focus of infection as per the predesigned proforma. Routine urine examination with culture and sensitivity, followed by RUS and VCUG was done in all patients where routine urine examination was suggestive of UTI. DMSA was done in only culture proven cases after 6 months to document the renal scarring.

**Results:** Out of 304 children, 140 were males and 164 were females, UTI was present in 40 patients who had fever without any apparent cause giving a prevalence of 13.2%. *Escherichia coli (E. coli)* were the commonest isolated organism, followed by *Klebsiella* and *Citrobacter* species. Renal and Urinary Bladder Ultrasonography (RUS) detected Vesicoureteral Reflux (VUR) in 25% (10/40) while VCUG showed VUR in 55% (22/40) giving a RUS sensitivity of 45% for detecting VUR. DMSA done only after 6 months in UTI diagnosed patients showed a renal scarring in 25% (10/40) patients.

**Conclusion:** Missing a febrile paediatric UTI, can prove a future catastrophe if not timely diagnosed and treated.

**Keywords:** *E.coli,* Urine culture, Vesicoureteral reflux, Voiding cystourethrography

## INTRODUCTION

Paediatric Urinary Tract Infection (UTI) is a microbial inflammation of lower (cystitis and urethritis) and upper urinary tract (ureteritis and pyelonephritis), or both. Untreated pyelonephritis is associated with devastating consequences in the form of renal scarring, hypertension, toxemia of pregnancy and end stage renal disease [1-3]. It is estimated that approximately 7% of children between 2 months to 2 years of age with undifferentiated febrile illness and 8% of children between 2-19 years of age presenting with possible urinary symptoms were suffering from UTI [4]. Prevalence rates of UTI were highest in uncircumcised boys (20.1%) compared with circumcised boys (2.4 %) under the age of 3 months and dropped significantly there after [5]. In one of the recent studies from USA, most common uropathogens remain *Escherichia coli* (*E. coli*) accounting about 70% of total cases followed by *Proteus mirabilis*, *Klebsiella*, *Enterobacter*, *Pseudomonas aeruginosa* and *Enterococcus* while *Proteus* species are common causes of UTI in uncircumcised boys and *Staphylococcus saprophyticus* causes acute UTI in adolescent girls [6]. *Serratia marcescens*, *Citrobacter* species, and *Staphylococcus epidermidis* may cause low-virulence infections in patients with malformation or dysfunction of the urinary tract [7,8].

Serial radiological and nuclear medicine workup is critical in determining appropriate therapy. Most of the time diagnostic modalities utilized are Renal and Bladder Ultrasonography (RUS) and Voiding Cystourethrogram (VCUG), followed by Dimercaptosuccinic Acid (DMSA) scan [1] i.e., "bottom up approach" while "top down" approach is starting from DMSA to RUS, is also a viable option for research purposes. This sequential evaluation of children with febrile UTIs must be weighted with evidence based risk benefit ratio rather than a blanket recommendation regarding the managing of febrile UTI [9].

Latest imaging modalities include Magnetic Resonance Urography (MRU) and Interactive Voiding Cystourethrography (iMRVC) both offering exquisite anatomic detail in conjunction with dynamic, functional information without the need for radiation.

## AIM

Aim of the present study was to know the prevalence of UTI in febrile children and to know the sensitivity of different imaging modalities like RUS, VCUG and DMSA scan in diagnosing UTI.

## MATERIALS AND METHODS

The present hospital based observational study was conducted between 2013-2014 after approval by Institution's Ethics Committee. Children aged 2 month to 10 years presenting with undifferentiated fever with axillary temperature ≥38°C without any localizing sign (s) were recruited consecutively. All those children who have received antibiotics during last 7 days, immunosuppressive drugs, has had transuretheral catheterization, possess urinary tract anomalies, or suffer from immunocompromised states like severe Protein Energy Malnutrition (PEM), sickle cell disease, malignancies, nephrotic syndrome, chronic renal failure, and human immunodeficiency virus/acquired immunodeficiency syndrome) were excluded.

With detailed history and physical examination a clinical diagnosis of suspected UTI was made in these patients. The urine samples were collected in sterile, boric acid containing bottles and used for urine microscopy, culture and sensitivity within 1 hour of collection according to standard methods [10]. In the age group of 2 months to 2 years: urine was collected by supra-pubic aspiration; >2

years to 5 years, urine was collected by urinary catheterization or clean catch midstream urine; while in > 5 years to 10 years urine was collected by clean catch mid stream urine. For routine urine examination 10-15ml was taken and for urine culture 5ml was taken. Urine was refrigerated, if not plated within one hour of receipt. A volume of 5-10 ml of urine was centrifuged at 2000 rpm for 5 min and a wet preparation of the sediment was examined using ×40 objective microscope. Presence of any bacteria per High Power Field (HPF) and pyuria (more than 5 white blood cells (WBCs) per HPF) was regarded as significant and suggestive of UTI. Urine culture was done employing the standard quantitative method [11]. Each uncentrifuged urine sample was well mixed and inoculated on plates of cystine lactose electrolyte deficient medium and blood agar as described by Urquhart and Gould [12].

The culture plates were incubated aerobically at 37°C for 24 hour after which the colonies were counted with a colony counter. All plates were incubated at 30°C and examined daily for growth for two days as per microbiological protocols. A positive result was taken as per the criteria for diagnosis of UTI as shown in [Table/Fig-1] [13].

**RUS:** RUS was performed in all febrile patients where routine urine examination was suggestive of UTI using an ATL HDI 5000™ with sector or linear 7 and 7.5 MHZ to know the kidney size, parenchymal outline, echogenicity, outlet obstruction, and draining channel anatomy.

Scanning of the right kidney was performed with patient supine by putting probe at midclavicular line in right upper quadrant, moving through mid sagittal plane to have an anterior and posterior view. The probe was rotated to have a better view for renal vasculature, hilum and upper and lower poles [14].

The technique and documentation for left renal ultrasonography is identical to that of the right side. However, the left kidney is slightly more cephaled than the right kidney. Ultrasound imaging of the left kidney lacks the liver as an aquastic window, and it is sometimes more difficult to image the left kidney in a true saggital plan. Renal pelvic and ureteral dilatations were graded as per the standardized criteria [15]. Similarly, urinary bladder was scanned in sagittal and transverse manner angling the probe into the pelvis to know the dilatation of the distal ureters, hypertrophy of the bladder wall, presence of ureteroceles and diverticuli.

**VCUG:** All those patients with undifferentiated fever with urinalysis suggestive of UTI underwent VCUG to know anatomy of the urinary bladder, urethra, dilatation of ureters, VUR, any diverticula or ureterocele. The parents of our studied cases were explained first about the procedure and risks involved. We prepared the contrast first by diluting equal amount of contrast medium (300mg iodine/ml) and normal saline. The contrast solution was warmed to body temperature to reduce the discomfort experienced by children undergoing VCUG [16]. Amount premixed contrast was instilled as per age standardized bladder capacity formula; < 1 year of age: Bladder capacity (ml) = Wt in kg X 7 and > 1 year of age: Bladder capacity (ml) = (Age in years + 2) X 30. We used tube 5-F feeding tube in infants, and for older children 6-8 F feeding tube was used with 2% lignocaine jelly as lubricant. Contrast solution was instilled via the gravity drip [17]. Routine images were taken including bladder view, voiding urethra view and post-void bladder view. Right oblique and left oblique views were also taken for ureteral visualization. All VCUGs were performed within 2-6 months after the infection, and Vesicoureteral Reflux (VUR) was classified according to the international VUR classifications [18]. All imaging studies were read by experienced paediatric radiologist who was unaware of this study.

**DMSA:** This procedure was done in all culture positive patients after 6 months of initial diagnosis. The procedure was helpful to have knowledge about renal scars. After explaining parents about the procedure and the risks involved, patients were asked to void prior to procedure or the same was done by catheterization. Then IV Line was secured through which Tc-99m DMSA @ 50 micro curie/kg was administered as per the standardized method [19]. After 2 hours of drug injection, different images like anterior, posterior and oblique views were taken by planar camera. All DMSA Scans were read by experienced Nuclear medicine expert who was unaware of the study.

## STATISTICAL ANALYSIS

Statistical Package for the Social Sciences (SPSS) software version 15.0 for Windows® (SPSS Inc. 2006 Chicago, Illinois, USA) was used for data analysis, which included patients' history, physical findings and laboratory results. Descriptive statistics was used to describe the frequency, mean, median and standard deviation of continuous variables. Chi-Square test, or a Fisher's-Exact test, which ever appropriate, was employed for qualitative data. Sensitivity of different imaging modalities was also calculated. A p-value of <0.05 was taken as significant.

## RESULTS

A total of 304 children were recruited, among whom 140 were males and 164 were females. UTI was present in 40 patients who had fever without any apparent cause giving a prevalence of 13.2%. On urine culuture, *E. Coli* (E) was the commonest isolated organism, followed by *Klebsilla* and *Citrobacter*. RUS detected VUR in 25% (10/40) while VCUG showed VUR in 55% (22/40) giving a RUS sensitivity of 45% for detecting VUR. DMSA done only after 6 months in UTI diagnosed patients showed a renal scarring in 25% (10/40) patients. Significant results observed along with its corresponding reference numeral are shown in [Table/Fig-2-7].

| Collection method | Colony count (CFU/ml) | Probability of infection (%) |
|---|---|---|
| 1. Supra Pubic Aspiration (SPA) | Any growth | > 99% |
| 2. Trans-urethral Catheterization | $>10^5$<br>$10^4 – 10^5$ | 95%<br>Infection likely |
| 3. Clean-catch midstream void | $>10^4$ (boy)<br>$\geq 10^5$ (girl) (3 specimens)<br>$\geq 10^5$ (girl) (2 specimens)<br>$\geq 10^5$ (girl) (1 specimen) | Infection likely<br>95%<br>90%<br>80% |

**[Table/Fig-1]:** Criteria for diagnosis of urinary tract infection [13].
CFU colony-forming units

| Age | Males | Females | Total | Culture Positive |
|---|---|---|---|---|
| 2months – 12months | 40 | 30 | 70 | 10 (14.2%) |
| >1Year - 2Years | 28 | 36 | 64 | 8(12.5%) |
| >2 Years – 5 Years | 38 | 56 | 94 | 12 (12.8%) |
| >5 Years – 10 Years | 34 | 42 | 76 | 10 (13.2%) |
| Total | 140 | 164 | 304 | 40 (13.2%) |

**[Table/Fig-2]:** Age, gender and urine culture positivity distribution of studied patients.

| Sex | Total Patients | UTI (%) | p-value |
|---|---|---|---|
| Male | 140 | 10 (7.1%) | 0.043(Sig.) |
| Female | 164 | 30 (18.3%) | |

**[Table/Fig-3]:** Gender-wise distribution of patients with UTI.

| Organism | Number | Percentage | p-value |
|---|---|---|---|
| *E. coli* (E) | 34 | 85% | E vs K<br>p-value<0.001<br>K vs C<br>p-value=0.562<br>C vs E<br>p-value<0.001 |
| *Klebsiella* (K) | 4 | 10% | |
| *Citrobacter* (C) | 2 | 5% | |

**[Table/Fig-4]:** Organisms isolated among the studied patients.

## DISCUSSION

The relevance of UTI to childhood morbidity is more marked in under-fives, amongst whom the risk of renal damage is more

| Age Group | Total No. | Culture Positive | Abnormal USG Abd. | Abnormal VCUG |
|---|---|---|---|---|
| 2months– 12months | 70 | 10 | 4 | 8 |
| >1Year - 2Years | 64 | 8 | 2 | 4 |
| >2 Years – 5 Years | 94 | 12 | 2 | 6 |
| >5 Years – 10 Years | 76 | 10 | 2 | 4 |
| Total | 304 | 40 | 10 | 22 |

**[Table/Fig-5]:** Distribution of patients by culture and imaging results.

| Age group | RUS Suggestive of VUR | VUR on VCUG | Sensitivity of RUS for VUR |
|---|---|---|---|
| 2months – 12months | 4 | 8 | 50% |
| >1Year - 2Years | 2 | 4 | 50% |
| >2 Years – 5 Years | 2 | 6 | 33.33% |
| >5 Years – 10 Years | 2 | 4 | 50% |
| Total | 10 | 22 | 45.45% |

**[Table/Fig-6]:** Sensitivity of RUS for Detecting VUR.

| Age Group | Total Culture Positive | DMSA Positive | Sensitivity |
|---|---|---|---|
| 2months – 12months | 10 | 4 | 40% |
| >1Year - 2Years | 8 | 2 | 25% |
| >2 Years – 5 Years | 12 | 2 | 16.66% |
| >5 Years – 10 Years | 10 | 2 | 20% |
| Total | 40 | 10 | 25% |

**[Table/Fig-7]:** DMSA after 6 months in culture proven UTI patients.

and diagnosis is often missed as the clinical features are seldom overt and in most cases not referable to the urinary tract [20]. In present study UTI was present in 40 patients giving a prevalence of 13.2% [Table/Fig-2], a finding which is quite comparable with other studies [21-23].

Our findings show a statistically significant female preponderance of febrile UTI as shown in [Table/Fig-3] (with a female male ratio of 3:1, p<.05%) a finding which is similar to the earlier studies [4,24]. Age-wise break-up show that undifferentiated fever with UTI were mostly seen between 2 months to 24 months a consistent finding with earlier studies [4,8,25].

Pertaining to urinary microbiology among the febrile UTI patients, *E. coli* was isolated in 34 (85%), *Klebsilla* in 4 (10%), *Citrobacter* in 2 (5%); p-<0.001 [Table/Fig-4], which is in conformity with the earlier studies [26,27]. Our study showed that the frequencies of positive cultures were 25% for males and 75% for females (ratio 1:3) while Farajnia et al., reported this ratio 1:2 and Farrell et al., reported this ratio 1:4.1 [28,29].

RUS of genitourinary system is indicated in children with febrile UTI to distinguish between complicated and uncomplicated UTI [30]. RUS detects VUR in 10-45% of patients with VUR on VCUG [31] which is comparable to our findings (25%) as shown in [Table/Fig-6]. In 22/40 (55%) patients with febrile UTI, VUR were detected on VCUG implying RUS sensitivity of 45% for detecting VUR., a result which is quite comparable with the study done by Zamir et al., [32]. Although RUS is less sensitive at diagnosing grades I to III VUR, many experts question the importance of VUR at these grades because most low-grade VUR resolves spontaneously [32]. Out of 70 infants, 10 were culture proven febrile UTI among whom RUS was abnormal in 4 and VCUG revealed VUR in 8, giving RUS sensitively of 50% for VUR in infants [Table/Fig-5]. However, sensitivity of RUS, and VCUG for detecting the abnormalities of genitourinary system decreased with the increase in age, which can be explained by resolution of VUR with the advancing age. Present study favors the recommendations of American Academy of Paediatrics in the USA (AAP), and Italian Society of Paediatric Nephrology (ISPN), that all infants aged 2–24 months with febrile UTIs should undergo renal and bladder ultrasounds [33].

Although VCUG is rewarding tool for diagnosing regurgitation of urine to ureters, assessing the degree of VUR and the anatomy of the male urethra; but child discomfort, expensiveness of procedure, exposure to radiation and the risk of causing a UTI are its drawbacks. Our study showed 22/40 (55%) patients with febrile UTI had VUR on VCUG which is higher than the reported (20-40%) frequency of VUR in children with UTI [34,35]. This could be explained by probably higher VUR in febrile UTI due to bacterial toxin mediated ureterectasis. Present study favors the use of VCUG in all febrile UTIs despite AAP, NICE and ISPN recommends VCUG should not be performed routinely after first febrile UTI. However, European Association of Urology (EUA) recommends all under one year with UTI should undergo VCUG and /or DMSA scan to exclude VUR [36].

DMSA scintigraphy is the gold standard for detecting renal parenchymal defects by using a radio-pharmaceutical such as technetium 99m. The isotope is concentrated in the proximal renal tubules, and its distribution correlates with functioning renal tissue [36]. DMSA scan can be used to diagnose acute pyelonephritis when performed during acute illness and to identify renal scars when performed months following the acute illness [37]. Although this method requires exposure to radiation and is not likely to alter management; but is primarily useful when the diagnosis of acute UTI or of repeated UTI is in doubt [38]. DMSA was done after 6 months in UTI diagnosed patients in our study, which showed a renal scarring in 10/40 (25%) patients which is consistent with other studies which revealed renal scaring between 10-40% [39,40].

## LIMITATION

The study did not recruit the accurate target sample because of variability in the prevalence while considering age and sex. However, the prevalence of UTI was higher in the study sample than the 7% used for the sample size calculation, which mitigated loss of precision. The study was not powered to accurately determine the predictive value of symptoms and signs, and this resulted in large confidence intervals for the odds ratios and probabilities in the multivariable model.

## CONCLUSION

Paediatric UTI at times remains a diagnostic dilemma, and a miss in diagnosis can prove a future catastrophe for an affected child. A prevalence of 13.2% of paediatric UTI among the hospital visiting children favors to have a heightened awareness among the treating paediatricians and general public about this otherwise easily manageable entity.

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