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Study of clinical etiological and radiological profile of UTI cases

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ABSTRACT

Background: Fever and significant bacteriuria and pyuria in children with undocumented sources of infections must be presumed to be symptoms of pyelonephritis, an invasive infection of the renal parenchyma requiring prompt treatment. The present study is undertaken to study of clinical, etiological and radiological profile of children with culture positive UTI.
Methods: This study is being performed on children with culture positive Urinary tract infection admitted or attending OPD at department of Paediatrics during the study duration were included in the present study.
Results: The highest incidence of UTI in present study was found to be 52.25% in the age group of children below 2 years. E-coli (75%) was the commonest organism found in urine culture in all age groups. Sensitivity, negative predictive value and positive predictive value of renal ultrasonography in detecting VUR was very poor, supporting the impression that renal USG is deficient in accurately excluding VUR. VUR are common in Culture positive UTI, milder grade are more common which are more likely to be missed by renal USG, thus stressing the need of MCU in children of culture positive UTI.
Conclusions: Urine examination and culture and sensitivity must be a part and partial in evaluating child with fever without focus. As the scope of USG in detecting VUR is low, MCU must be done in all cases of UTI -5years irrespective of USG finding.

Keywords: MCU, UTI, USG, VUR

INTRODUCTION

Children with fever comprise a substantial proportion of the practice in Out Patient Department and Emergency Medicine, unlike occult bacteraemia or severe bacterial illness (in infants and children), little attention has been focused on the identification of urinary tract infections in febrile children in the emergency department , despite recent information that suggests a high prevalence of urinary tract infections and significant associated morbidity in these patients. Quite often, child receives antibiotics empirically, without adequate evaluation for urinary tract infection. Fever, however, is often the only symptom in children with urinary tract infections.

Fever and significant bacteriuria and pyuria in children with undocumented sources of infections must be presumed to be symptoms of pyelonephritis, an invasive infection of the renal parenchyma requiring prompt treatment. Recent studies using renal parenchyma - avid nuclear scans to determine the presence of urinary tract infection have revealed that more than 75% of children under 5 years of age with febrile urinary tract infection have pyelonephritis.[1-3]

Pyelonephritis leads to renal scarring in 27% to 64% of children with urinary tract infections in this age group, even in the absence of underlying urinary tract abnormalities.[4,5] Most urinary tract infections that lead to scarring or diminished kidney growth occur in children younger than 4 years of age especially among infants in the first year of life those with gross vesico ureteric reflux or obstruction and those who have a delay in therapy for urinary tract infection.[2,5] Among children under 3 years of age with recurrent urinary infections, putting them at higher risk for renal scarring, as many as one-third being asymptomatic.[6]

It is essential to identify urinary tract infections in febrile children and institute prompt treatment to reduce the potential for life long morbidity. Progressive renal damage from unrecognised pyelonephritis in childhood may lead to hypertension and chronic renal failure in later life.

A study from Sweden showed that focal renal scarring caused by pyelonephritis in children cared a 23% risk for hypertension, a 10% nsk for end-stage renal disease, and a 15% nsk for toxemia during pregnancy as an adult.[7] Approximately 13% to 15% of end-stage renal disease is thought to be related to urinary tract infection in childhood that was often unrecognised and therefore, under treated.

The present study is undertaken to study of clinical, etiological and radiological profile of children with culture positive UTI.

METHODS

This study is being performed on children with culture positive Urinary tract infection admitted or attending OPD at department of Paediatrics during the study duration were included in the present study.

Selection criteria

- Case admitted or attending OPD, symptomatic or asymptomatic with culture positive UTI,
- Within age group of 1 month to 12years were included in the study.

Clinical evaluation

Detailed records were maintained on a proforma containing symptoms, signs and investigation check list. Detailed history of chief complaints in a chronologic order was taken.

Patients were examined in detail with special attention to temperature, blood pressure, palpable kidney or bladder and renal angle tenderness. Genitals were examined in detail to uncover meatal stenosis, phimosis, circumcision or labial adhesion. Detailed neurological examination with special attention to lumbosacral area was examined to look for any of the skin markers of the occult spinal Dysraphism.

Further investigation and evaluation was done as follow:

Relevant base line investigation like

- CBC-done by using SYSMAX auto analyser.
- Urea and Sr. creatine
- Urine examination

Collection of bag sample

In children below 2 years of age the genitalia was cleaned with soap and water and person collecting sample washed hands before touching the bottle or bag for collecting urine sample. In males prepuce retracted if possible, in females below 2 years labia was split apart and washed. Urine was collected in bag, around 10 ml of urine was transferred into sterile bottle and sent for culture and sensitivity in children above 2years, midstream sample was collected.

Method of collection of mid stream sample

After taking the above precautions child was allowed to pass urine, mid stream sample was collected in sterile bottle and was sent for culture and sensitivity.

Urine routine: aseptically collected fresh urine was examined for protein, RBC pus cells by using DIIUI H-100 autoanalyser and centrifuged urine was examined Microscopically

Urine culture: Urine collected aseptically in sterile test tube was sent immediately for urine culture. Culture was done by the standard loop method on blood agar and MacConkey medium and sensitivity to various antibiotics tested. An organism with zone of inhibition measuring 15 mm or more in diameter was considered to be sensitive to the particular antibiotics.

Radiological investigations

Renal ultrasonography (USG) was done in all the patient. Further imaging was done depending on the initial USG report as follow-If initial USG abnormal, patient underwent MCU and DMSA scan. If initial USG normal; 1) if child <2years - both MCU and DMSA scan was done , 2) if chil 2-5 years –DMSA scan (MCU if scar on DMSA or DMSA not available), 3) child >5 years- no further evaluation. MCU was done once the acute inflammation has resolved (4-6 weeks after the episode of UTI).

Statistical analysis

Descriptive statistics such as mean, SD and percentage were used. Sensitivity, Specificity, PPV, NPV were also calculated.

RESULTS

Table 1: Age and sex distribution.

Age	Sex		Total	Percentage
	Male	Female		
< 2year	17	4	21	52.5
2-5 year	7	2	9	22.5
>5year	5	5	10	25
	29	11	40	100

Table 2: Distribution of children according to presenting features.

Presenting complaints	Total numbers	Percentage
Fever	40	100
Straining during micturation	28	70
Burning micturation	22	55
Vomiting	16	40
Failure to thrive	9	22.4
Dribbling	7	17.5
Poor urinary stream	5	12.5
Constipation	5	12.5
Urgency	4	10
Foul smelling urine	3	7.5
Suprapubic pain	2	5
Incontinence	2	5
Convulsion	1	2.5

Out of 40 children with UTI, 29 were males and 11 were females with male to female ratio of 2:6:1 Highest (52.25%) includes of UTI in present study was in age group of children below 2 years.

Table 3: Distribution of cases as per the organisms in urine culture.

Organisms	Total number	Percentage
E. coli	30	75
Klebsiella pneumonia	5	12.5
Proteus mirabilis	3	7.5
Pseudomonas aeruginosa	1	2.5
Staphylococcus aureus	1	2.5

In the present study predominant organism osolated in urine culture was *E. coli* 30 (75%) Children, followed by *Klebsiella pneumonia* 5 (12.5%), *Proteus mirabilis* 3 (7.5%), *Pseudomonas aeruginosa* 1 (2.5%) and *Staphylococcus aureus* 1 (2.5%).

All (100%) the tested isolates were sensitive to gatifloxacin, ceftriaxone, meropenam. imipenam, ceftazidime, cefoperazone, cefixime, cefepime, while 91.3% sensitive to cefuroxime, 86% sensitive to amikacin, 66.6% sensitive to gentamycin, 40% sensitive to netimycin, 19% sensitive to ciprofloxacin. All (100%) the tested isolate were resistant to cotnmaxazole amoxy-clavulinic acid, while 91.3% resistant to norfloxacin, 80% to ciprofloxacin, 60% to netilmycin, 33.3% to gentamycin. 13% to amikacin.

Table 4: Antibiotic and sensitivity pattern of organism *E. coli* in UTI.

Drugs	Total no tested	Sensitive	Resistance	Sensitive %	Resistance %
Ceftriaxone	25	25	0	100	0
Cefixime	21	21	0	100	0
Ceftazidime	21	21	0	100	0
Cefotaxime	25	25	0	100	0
Meropenam	23	23	0	100	0
Imipenam	14	14	0	100	0
Cefoperazone	20	20	0	100	0
Gatifloxacin	19	19	0	100	0
Cefepime	6	6	0	100	0
Cefuroxime	23	21	2	91.3	8.6
Amikacin	27	25	4	86	13
Gentamycin	9	6	3	66.6	33.3
Netilmycin	15	6	9	40	60
Ciprofloxacin	21	4	17	19	80
Norfloxacin	23	2	21	8.6	91.3
Contrimaxazole	7	0	7	0	100
Amoxyclavulinic acid	23	0	23	0	100

Table 5: Sonographic findings in children with UTI.

USG finding			Total	Percentage
Hydronephrosis	RT	2	6	15
	LT	2		
	Bilateral	2		
Pylonephritis	RT	2	3	7.5
	LT	0		
	Bilateral	1		
Dilated ureter	RT	0	3	7.5
	LT	3		
	Bilateral	1		
Small kidney	RT	0	1	2.5
	LT	1		
	Bilateral			
Cystitis		9	9	22.5
Normal		20	20	50

Ultrasound examination of abdomen was done in all the children of which 20 (50%) had normal USG, 9 (22.5%) Children had cystitis, 6 (15%) children had hydronephrosis, 3 (7.5%) had pylonephritis and dilated ureter and 1 (2.5%) child had small kidney.

Table 6: MCU findings in children with UTI.

VUR			Total	Percentage
Grade 1	RT	1	3	7.8
	LT	2		
	Bilateral	0		
Grade 2	RT	4	6	15.7
	LT	2		
	Bilateral	2		
Grade 3	RT	2	5	13.15
	LT	3		
	Bilateral	1		
Grade 4	RT	1	3	7.8
	LT	1		
	Bilateral	1		
Grade 5	RT	0	00	00
	LT	0		
	Bilateral	0		
Normal		21	21	55.2

MCU was done in 38 children as per protocol. It was normal in 21 (55.2%) children and abnormal in 17 (44.7%) children of which 4 (10.5%) children had bilateral VUR and 13 (34.2%) children had unilateral VUR, 3 (7.8%) children had grade 1 MUR, 6 (15.7%) children had grade 2 VUR : 5 (13.15) children had grade 3 VUR and 3 (7.8%) children had grade 4 VUR.

Sensitivity of USG in detecting VUR = 55%. Specificity of USG in detecting VUR = 72%. Positive predictive value of USG in Detecting VUR = 68%. Negative predictive value of USG for detecting VUR = 59%.

Table 7: Comparison of USG and MCU in detecting VUR.

Imaging modality		USG		Total
		Abnormal	Normal	
MCU	Abnormal	11	5	16
	Normal	9	13	22
Total		20	18	

DMSA was done in 26 (65%) children as per the protocol, 1 9 (73%) children had normal DMSA scan, 7 (26.9%) had abnormal DMSA scan.

Table 8: Distribution of patients according to the DMSA scintigraphy (99m Tc dimercaptosuccinic acid).

DMSA	Total	%
Normal	19	73
Abnormal	7	27
Total	26	100
Not done	14	65

DISCUSSION

Urinary Tract Infections (UTI) are common, potentially serious infections of childhood. They cause acute morbidity as well as long term sequele including hypertension and impaired renal function. Accurate diagnosis of UTI is important to facilitate appropriate management of acute illness, and to ensure appropriate evaluation and follow-up. A total of 40 children with urine culture positive UTI were included in the study, of which 29 children were males and 11 children were females with M:F ratio 2.6:1 . Highest (52.25%) incidences of UTI in the present study were in children below 2 years of age.

In Biggi A et al report of 101 with acute pyelonephritis, 60 were females and 41 were males.[8] In consensus statement of Indian Pediatric Nephrology Group it has been mentioned that during the first year of life, male to female ratio is 3-5: 1, beyond 1-2years, there is female preponderance with male to female ratio of 1: 10. Alia EMA et al, of 100 patients (45.2%) had significant growth on urine culture and fulfilled the criteria for the diagnosis of acute UTI.[9] Children confirmed to have UTI had a mean age of 3.4 years (SD 3.6, range 15 days-14 years) and infants constituted 35% of them. The majority of children with were males (53%), the majority of whom were below 5 years of age (74%). The male-female ratio of affected children was 2.1 1 among infants, and 1:1.2 among older children.

Symptoms

Most common presenting complaint in our study was fever 40 (100%) followed by, straining during micturation 28 (70%), burning micturation 22 (55%),

vomiting 16 (40%), failure to thrive 9 (22.5%), dribbling 7 (17.5%), poor urinary stream 5 (12.5%), constipation s (12.5%) and urgency 4 (10%).

In study of Anis-ur- Rehaman et al on 375 children with culture positive fever was present in 91% cases, dysuria in 65%, failure to thrive 40%, poor urinary stream 15%, discharge through urethra 10%(59), Altered colour of urine 12%, pain in abdomen 22%, and vomiting in 28% of the patient.[10]

Rushton et al had mentioned constipation as an important risk factor for Recurrent UTI and improvement in bowel habits reduces the incidence of UTI.[11]

Organisms on urine culture

In present study *E. coli*was the predominant organism isolated in urine Of 30 (75%) children. followed by *Klebsiella pneumonia* 5 (12.5%), *Proteus mirabilis* 3 (75%), *Pseudomonas aeruginosa* l (2.5%) and *Staphylococcus aureus* I (25%) In all age group. *E. coli*was commonest isolate.

Brayan CS et al reported *E. coli* as the common urinary pathogen in 85% of cases.[12] According to Bagga A et al 90% of first symptomatic urinary tract infection and 70% reccurence infections were due to *E. coli*.[13] Hoberman et al reported as *E. coli* as the most common bacterium isolated in his study.[14]

Organisms and their antibiotic sensitivity pattern

E. coli

All (100%) the tested isolates were sensitive to gatifloxacin, ceftriaxone, meropenam, imipenam, ceftazidime cefoperazone, cefotaxime cefixime, cefepime while 91.3% sensitive to cefuroxime, 86% sensitive to amikacin, 66.6% sensitive to gentamycin, 40% sensitive to netilmycin and 19% sensitive to ciprofloxacin.

Klebsiella

All (100%) the tested isolate were resistant to cotrimoxazole, amoxy-clavulinic acid, while 91.3% resistaht to norfloxacin, 80% to ciprofloxacin, 60% to netilmycin, 33.3% to gentamycin, 13% to amikacin. All (100%) the tested isolates were sensitive to gatifloxacin, ceftriaxone, meropenam, imipenam, ceftazidime, cefoperazone, cefotaxime, cefixime, cefuroxime, cefepime. while 80% sensitive to amikacin, 50% sensitive to netilmycin, 25% sensitive to ciprofloxacin. all (100%) the tested isolates were resistant to norfloxacin, 75% to ciprofloxacin, 50% to netilmycin, 20% to amikacin.

In study of Mortazavi et al the most frequently isolated germs were *E. coli*, Klebsiella, Enterobacter, *Pseudomonas aeroginosa* and Proteus in descending order.[15] Among the oral agent nitrofurantoin and ciprofloxacin, and among the parenteral agents, amikacin and gentamycin had the highest activity against *E. coli*. The highest sensitivity of Klebsiella was to ciprofloxacin, nalidixic acid, cefixime and Amikacin in the descending order. The activity of ceftriaxone, ceftizoxime, nalidixic acid and cephalexin againt *E. coli* has decreased significantly over six years ($p<0.05$).

Also activity of ceftriaxone, ceftizoxime, nalidixicacid, gentamycin, amikacin against Klebsiella has decreased in comparison with result of six year ago ($p<0.05$). There was not any significant difference in sensitivity of Enterobacter and Pseudomonas with result of six year ago.

In large study of Anbumani N et al on 1500 urine specimen with significant bacteruria of which 106 (7.1%) were from children of 10 years or less, of which *E. coli*were 29.6%, *Klebsiella pneumonia* 17.6%, *Pseudomonas aeruginosa* 10.1%, *Staphylococcus aureus* 7.5%, *Enterococcus faecalis* 7%, Acinetobacter species 6.1%, *Proteus mirabilis* 2%, *Proteus vulgaris* 1.5%, Enterobacter species 3%, Citrobacter species 2.4%, coagulase negative staphylococci 1.4%, enterococcus faecium 1%, *Morganella morgani* 0.5%, polymicrobial aetiology 9%, and candida Species 1.3%.[16] Among the isolates from inpatient *E. coli* (33%) was the commonest isolated organism.

80% of isolated *E. coli* was resistant to cotrimoxazole, while the first generation cephalosporin was still effective against *E. coli*. The newer aminoglycoside like amikacin and third generation cephalosporin were found to be effective against *Klebsiella pneumonia* and *Pseudomonas aeruginosa* but ineffective against acinetobacter species. Among the out patients, more than 50% patients showed *E. coli* as the commonest isolate which were 70-80% resistant to cotrimoxazole and aminopenicillin. However, first generation cephalosporin, nitrofurantoin and nortloxacin were effective. However, in cases of UTI with organism other than *E. coli*, amikacin and third - generation cephalosporins were found to be effective.

Renal function test

In the present study maximum patients had normal renal functions, indicating that renal function is essentially preserved in uncomplicated first febrile UTI.

Berg et al reported decreased concentrating capacity of the kidneys during UTI, which comes to the normal after 4-6 weeks of treatment.[17]

Renal ultrasonography

It has completely replaced intravenous pyelography for assessing the gross anatomy of urinary tract and it is routinely performed after the diagnosis of a first urinary tract infection. It is a noninvasive test that can

demonstrate the size and shape of the kidneys. The presence of duplication and dilation of the ureters, the presence of ureteroceles, and the existences of gross anatomical abnormalities, such as a horseshoe kidney.[18]

The identification of a nonrefluxing megaureter or ureteropelvic-junction obstruction, may lead to surgery, identification of a solitary or dysplastic kidney results in more aggressive management of vesicoureteral reflux. However, ultrasonography is not sensitive enough to detect the presence of hydronephrosis, hydroureter, acute pyelonephritis, or renal scarring consistently. In addition, because of its dynamic nature, vesicoureteral reflux cannot be consistently detected by ultrasonography.

In our study, Ultrasound examination of abdomen was done in all the children, of which 20 (50%) children had normal USG, 9 (22.5%) children had cystitis, 6 (15%) children had hydronephrosis, 3 (7.5%) children had pyelonephritis and dilated ureter, 1 (2.5%) child had small kidney.

In 40 children who had their USG and 38 children had MCU done, probability of detecting VUR by USG was poor (sensitivity of USG in detecting VUR-55%, positive predictive value of USG in Detecting VUR-, 68%) MCU and VUR, VUR which affects approximately 30-40% of young children and has been associated with renal scarring, has been an important consideration in the treatment of children with UTI.

MCU were done in 38 children as per protocol. It was normal in 21(55.2%) children 17 (44 7%) children had abnormal MCU of which 3 (7.8%) children had grade 1 VUR, 6 (15.7%) children had grade 2 VUR-5(13.15) children had grade 3 VUR, 3 (7.8%) children had grade 4 VUR 4 (10.5%) children had bilateral VUR, and 13 (34.2%) children had unilateral VUR.

In comparative study of Tan and Chee et al, 55 children with culture positive UTI were studied by both USG and MCU, 32 had normal USG and MCU; of remaining 23 children, 14 had normal and 9 abnormal USG.[19]All 14 patients who had normal USG, subsequently proven by MCU to have either unilateral or bilateral VUR, of the remaining 9 patients with abnormal USG, only 3 patient were subsequently proven To have VUR, conversely of the 17 patients with reflux on MCU only 3 were reported to have abnormal USG and supported the impression that at present renal USG is deficient in accurately excluding VUR.

In study of Smellie JM et al, comparing 4 methods of investigations (USG, MCU, DMSA. IVU), all four investigations were normal in 12 children 36 with VUR on MCU dilatation was reported on USG in eight children, radiological renal scaring was seen in 20 children, it was suspected on USG in nine with dilatation alone in four, and normal report in seven.[20] Duplex kidneys identified on IVU were unrecognized on USG or DMSA studies; USG showed no change corresponding to presume acute defect on DMSA studies that later resolved. Disparities were observed at all age. This study suggests that USG is unreliable in detecting VUR, renal scarring, or inflammatory changes and alone, is inadequate for investigating UTI children's.

In study by Jothilakshmi et al, about the study of the association of structural abnormalities of the urinary tract in children with UTI using Ultrasound examination, 262 children with culture proven UTI were studied.[21] Fifty four (16.7%) patients had an underlying urinary tract anomaly, 42 (77.7%) were picked up by Ultrasound and 12 (22.2%) by MCU. 22.9% of male and 15.9% of female had anomaly of the urinary tract Children less than 2 years had the highest incidence of anomalies 20% of children with urinary tract infection had an underlying structural abnormality of the urinary tract, 75% of which were picked up on ultrasound. Ultrasound abdomen is recommended in all children after the first UTI. In addition MCU is also indicated in all below 2 years age with UTI, since one third of anomalies will be missed if only Ultrasound is done.

DMSA

Role of renal cortical scintigraphy in the treatment of young children with urinary tract infection has not been evaluated systematically. In the present study criteria for doing DMSA is as per the guidelines of IAP. Although renal scintigraphy with technetium 99m-labeled dimercaptosuccinic acid is a valid diagnostic tool for confirming the presence of acute pyelonephritis and for documenting the presence of renal scarring (36,59,60 p), routine use of this imaging method during the acute illness does not alter treatment in the majority of the cases.

In present study, DMSA was done in 26 (65%) children as per the protocol, 19 (73%) children had normal DMSA scan, 7 (26.9%) had abnormal DMSA scan. Out of 17 children with abnormal MCU only 7 (41 1%) children had abnormal DMSA. Incidence of scarring in the present study was 41 1%.

In study by Nammalwar et al, 42 children with positive urine culture and 26 children with negative urine culture who had supportive evidence of UTI as determined by the predetermined criteria and diagnosed to have acute pyelonephritis (APN) by DMSA.[22]All of them had USG, DMSA and MCU. They were followed up for a minimum period of 6 months. Out of the 42 children with positive urine culture 92.9% had features of APN in DMSA of whom 82.1% had VUR. The DMSA was abnormal in 26 children with negative urine culture, of whom 65.5% had VUR.

Ultrasound suggestive of parenchymal change was observed in 47.6% in culture positive groups and 65.4% in the culture negative group. In conclusion, it is

suggested, that DMSA is useful investigation for diagnosis of APN in febrile UTI. DMSA is indicated in febrile children with negative urine culture but with supportive evidence of UTI and in FUO. An abnormal DMSA is a strong indication for work up for VUR (54). In the comment of above article, Mukta M has questioned the utility of DMSA in pediatric UTI, as DMSA in acute stage does not change the management of individual case, not easily available, costly and increases the radiation exposure.[23]

In cross-sectional study of DMSA in pediatric UTI by Clark et al, they concluded, that infective renal change may be superimposed on underlying congenital lesions (perhaps detectable antenataly) or may be acquired following UTI in presence of reflux and are thus potentially preventable.[24] This study also suggests that VUR is almost certain to have occurred (98%) in child who has bilateral abnormal 99tc DMSA image following UTI and is also commonly present in those with definite unilateral defect.

CONCLUSION

Sensitivity, negative predictive value and positive predictive value of renal ultrasonography in detecting VUR was very poor, supporting the impression that renal USG is deficient in accurately excluding VUR. VUR are common in culture positive UTI, milder grade are more common which are more likely to be missed by renal USG, thus stressing the need of MCU in children of culture positive UTI. In present study DMSA showed scaring and abnormality in 41.1%. Because of its cost, not easily available and do not provide information that modifies the management in acute stage. Urine examination and culture and sensitivity must be a part and partial in evaluating child with fever without focus. As the scope of USG in detecting VUR is low, MCU must be done in all cases of UTI -5years irrespective of USG finding.

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