Print ISSN: 2321-6379
Online ISSN: 2321-595X
DOI: 10.17354/ijss/2018/133

Original Article

Outcome of Children with First Episode of Urinary Tract Infection

M S Vinodkumar, M Vishnu Mohan

[1]Assistant Professor, Department of Paediatrics, Government Medical College, Kozhikode, Kerala, India, [2]Assistant Professor, Department of Paediatrics, Malabar Medical College, Atholi, Kozhikode, Kerala, India

Abstract

Background: Urinary tract infection (UTI) is one of the most common childhood infections. UTI occurs in 1–3% of girls and 1% of boys of the pediatric population. In the former, it occurs by the age of 5 years which peaks during infancy and toilet training and in the later during the 1st year of life. UTIs are much more common in uncircumcised boys, especially in the 1st year of life. The prevalence of UTI during the 1st year of life is more in males with a male:female ratio of 2.8–5.4:1. Beyond 1–2 years, female preponderance with a male:female ratio of 1:10 is observed.

Aim of the Study: The aim is to study the outcome of first episode of UTI in children in terms of treatment response, recurrence, need for surgical intervention, renal scarring, growth retardation, hypertension, and renal function abnormalities.

Materials and Methods: A total of 120 children between 1 month and 12 years of age with the first episode of confirmed diagnosis of UTI were included in this prospective cross-sectional study. All the children were thoroughly investigated after elicitation of history. Culture of urine, ultrasonogram, micturating cystourethrogram (MCU), and technetium 99m-labeled dimercaptosuccinic acid investigations were done in addition to routine investigations before and during follow-up of treatment. Children were treated standard UTI treatment protocols recommended by the International Pediatric Society. All the data were analyzed using standard statistical methods.

Observations and Results: A total of 120 children with the first episode culture positive UTI between the age group 1 month and 12 years were taken; 63.4% were male children and 36.6% were female children. Of 120 cases studied, 28 (23.3%) cases were below 1 year, 60 (50%) cases were between 1 and 5 years, and 32 (26.6%) cases were between 5 and 12 years. 88 (73.3%) *Escherichia coli*, 21 (17.5%) *Klebsiella*, 3 each of CONS, *Enterobacter*, and *Staphylococcal aureus,* and 2 *Acinetobacter* species were isolated. Most common organism isolated was *E. coli* followed by *Klebsiella*. MCU was done in 40 cases (31 males and 9 females) and was abnormal in 12 (30%) cases. 4 (10%) and 2 (5%) of 40 cases had grade 1–2 vesicoureteral reflux (VUR) and grade 3–4 VUR, respectively. 6 (7.9%) of 76 males studied had posterior urethral valve. All children with posterior urethral valves (PUV) had undergone cystoscopic fulguration, and 4 of these 6 children had undergone pyeloplasty after fulguration.

Conclusions: The recurrence chance of UTI is present in 7.5% of children within 6 months of first episode of UTI. Majority of children with recurrent UTI had their second episode within 6 months and that too, with the same organism suggesting an unresolved or persistent bacteriuria. The presence of VUR is a risk for recurrence of UTI and renal scarring. The relative risk of recurrence of UTI is 14 times in the presence of renal scarring than in children without renal scar formation, and thus, renal scarring is a good predictor of recurrence.

Key words: children, Urinary tract Infections, Bacteriuria, Cystourethrogram

INTRODUCTION

Urinary tract infection (UTI) is defined as growth of a significant number of organisms of a single species in urine culture with the presence of symptoms of UTI. According to IAP, the diagnosis of UTI should be made only in children with a positive urine culture. The incidence of UTI reported from various epidemiologic studies is 1.1–1.8% of boys and 3.3–7.8% of girls.[1,2] UTI is 2–5 times more common in males than in females in the first few months of life; beyond this, male-female ratio is 1:10.[3] Sobel *et al.* reported bacteria as the most common etiological agents of UTI and may occasionally be caused by viruses and fungi.[4] Infection can reach the urinary tract in two ways: (1) The ascending route and (2) the hematogenous route; UTI in most of the cases

Access this article online

www.ijss-sn.com

Month of Submission : 02-2018
Month of Peer Review : 03-2018
Month of Acceptance : 03-2018
Month of Publishing : 04-2018

Corresponding Author: Dr. M Vishnu Mohan, Department of Paediatrics, Malabar Medical College, Atholi, Kozhikode, Kerala, India. Phone: +91-9809219037. E-mail: vishnumohanm007@gmail.com

results from an ascending infection; bacteria arise from the fecal flora, colonize the perineum, and enter the bladder through the urethra. In uncircumcised boys, the bacterial pathogens usually arise from the flora beneath the prepuce. These organisms ascend through the urethra to invade the urinary tract and cause asymptomatic bacteriuria, acute cystitis, or acute pyelonephritis in the host. Hematogenous spread of infection to the urinary tract accounts for <1% of UTIs. *Escherichia coli* adheres to uroepithelium with the help of adhesions or fimbriae which binds to specific receptors in the uroepithelium.[5,6] The organism is then internalized into epithelial cells which lead to apoptosis, hyperinfection, and invasion of the surrounding epithelial cells or an establishment of bacterial focus which forms a base for recurrent UTI where drugs cannot reach the focus.[5,6] UTI can be grouped into three clinically distinct presentations: (1) Cystitis, (2) acute pyelonephritis, and (3) asymptomatic bacteriuria. Cystitis occurs when infection is limited to the bladder and urethra, and it is mostly seen among girls who are more than 2 years old. Patients often present with localizing symptoms that include pain on urination (dysuria), frequency, urgency, cloudy urine, and lower abdominal discomfort. Acute pyelonephritis is an infection of the kidney and is the most severe form of UTI in children. Systemic features such as high fever, vomiting, abdominal pain or tenderness, malaise, poor feeding, or irritability in infants constitute the characteristic features of acute pyelonephritis. Diagnosis can be assisted by technetium 99m-labeled dimercaptosuccinic acid (DMSA) scan of the kidneys and inflammatory markers in the blood (e.g., C-reactive protein and erythrocyte sedimentation rate).[7,8] Manifestations of UTI vary with age, site of infection within the urinary tract, and the severity of infection. From a clinical perspective, infection of the urinary tract may be discussed either as a non-febrile UTI (acute cystitis) or a febrile UTI (acute pyelonephritis). Urine analysis enables only a provisional diagnosis of UTI and so a specimen has to be taken for urine culture before therapy with antibiotics.[9,10] Rapid tests include dipstick analysis for leukocyte esterase and nitrites which will be positive in infected urine although false negatives can occur in dilute urine. This test can be used as a screening for UTI. In a study of a cohort with 18% prevalence of UTI, a negative result on dipstick analysis had a negative predictive value of 96% which is more accurate than analysis of pyuria by microscopy in children.[11,12] Significant pyuria is defined as >10 leukocytes/cu.mm in a fresh uncentrifuged sample or >5 leukocytes/hpf in a centrifuged sample. UTI can occur without pyuria, and pyuria can occur without infection of urinary tract. Sterile pyuria is defined as leukocytes in urine with a negative urine culture and can occur in partially treated UTI, viral infections, renal tuberculosis, and renal abscess, urinary infection with obstruction in urinary tract, interstitial nephritis, any fever, glomerulonephritis, renal stones, and foreign body in urinary tract. White blood cell casts may also be seen. The accuracy of positive findings in the above said tests are as follows.[13] General measures include adequate fluid intake, frequent voiding, and treating constipation.[14] Double voiding should be encouraged as it ensures adequate emptying of the bladder of post-void residual urine. "Drink plenty and don't hold on" was propagated by the National Institute for Health and Clinical Excellence (NICE). Children are also advised to take sufficient fluids in frequent small amounts.[15] Imaging studies are done in children to detect any anatomical abnormality, VUR, and renal parenchymal damage that is predisposing to urinary infection.

MATERIALS AND METHODS

Study Design

This was a cross-sectional prospective observational study.

Institute of Study

This study was conducted at the Department of Paediatrics, IMCH, Government Medical College, Kozhikode, Kerala, India

Period of Study

The study duration was from March 2014 to August 2015.

Study Group

Inclusion criteria

The following criteria were included in the study:

1. Children between 1 month and 12 years of age with the first episode of confirmed diagnosis of UTI during the study period.
2. Children who are followed up for a minimum period of 6 months after diagnosis and starting the treatment.

Exclusion criteria

The following criteria were excluded from the study:

1. Children with previously known urinary tract anomalies.
2. Children with comorbid medical renal diseases.

Diagnostic criteria

First episode of UTI: A diagnosis of first episode of UTI is considered in a child with a positive urine culture and symptoms of UTI with no previous history of UTI. All the children included in the study were with the first episode of UTI and evaluated on admission, and a semi-structured pro forma was used to record data regarding history, risk factors, clinical examination findings, investigations, treatment response, and any surgical procedures done. All children were started on empirical antibiotic guided by sensitivity pattern of prevailing organisms in our locality and then changed according to the culture sensitivity

pattern of isolated organism in urine culture. Children who were toxic and who were not able to tolerate oral intake were given parenteral antibiotics. Advice regarding the need for further imaging studies as per guidelines of the Indian Society of Pediatric Nephrology was given. All children in the study group were screened by ultrasonography within 1–2 weeks. 40 children underwent micturating cystourethrogram (MCU) 2–3 weeks after treatment completion and 57 children underwent DMSA scan DMSA 2–3 months after treatment completion. Children were followed up regularly by clinical visits and telephone calls and assessed outcomes in terms of recurrence, renal scarring, growth retardation, hypertension, and renal function abnormalities at 3 months' interval by necessary examination and investigations and recorded in pro forma. Antibiotic prophylaxis was given to children in the study population as and when indicated. The routine performance of urinalysis and urine culture was done during subsequent febrile illnesses in all children with the firstepisode UTI. Any second episode of UTI was considered as recurrent UTI. It is defined as recurrence of symptoms and signs of urinary infection with significant bacteriuria in patients who have recovered clinically following treatment of an episode of UTI. Blood pressure, weight, height, mid-arm circumference, serum creatinine, and blood urea levels were recorded at every 3 months' interval during the follow-up period.

Statistical Analysis

The data obtained were coded and entered into Microsoft Excel spreadsheet and master chart was prepared. Categorical data were expressed in terms of rates, ratios, and percentages or graphically represented as pie diagrams or bar diagrams. The comparison for categorical data was done using Pearson's Chi-square test to determine the association between continuous variables. A probability value (*P* value) of ≤0.050 at 95% confidence interval was considered as statistically significant. All the statistical operations were done through IBM SPSS for Windows (version 20).

OBSERVATIONS AND RESULTS

Observations and analysis of 120 children with UTI who met inclusion criteria were made. Children entered the study population at different times and had different lengths of follow-up.

Of these 120 cases with a minimum follow-up of 6 months, 13 cases were followed up to maximum 18 months, 21 cases were followed for maximum 15 months, 66 cases were followed for maximum 12 months, and 93 cases were followed for maximum 9 months [Figure 1].

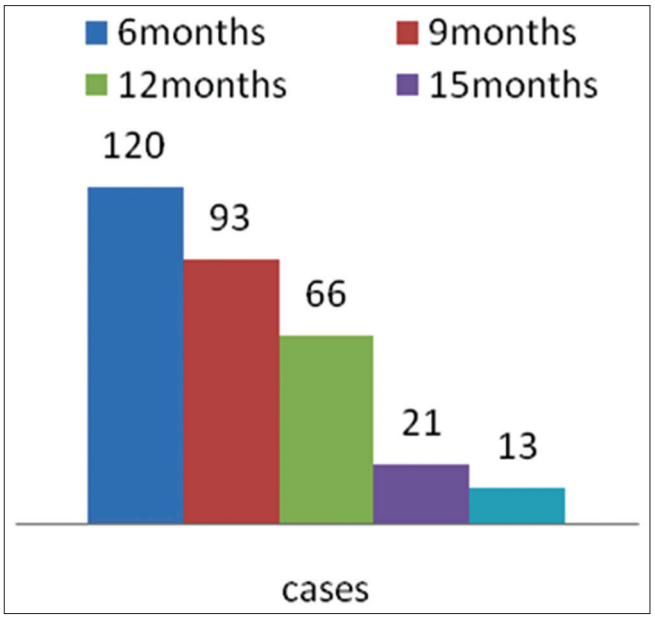


Figure 1: The follow-up periods in the study (*n* = 120)

Age and Gender Distribution

Of 120 cases studied, 28 (23.3%) cases were below 1 year, 60 (50%) cases were between 1 and 5 years, and 32 (26.6%) cases were between 5 and 12 years [Figure 2].

Gender Distribution

In the study population, 76 (63.4%) were males and 44 (36.6%) were females. Males outnumber females in children below 5 years (71.4% in children between 1 and 12 months and 73.3% in children between 12 and 59 months). Females (62.5%) outnumber males above 5 years [Figure 3].

Spectrum of Isolated Organisms

88 (73.3%) *E. coli,* 21 (17.5%) *Klebsiella*, 3 each of CONS, *Enterobacter*, and *Staphylococcal aureus,* and 2 *Acinetobacter* species were isolated. Most common organism isolated was *E. coli* followed by *Klebsiella* [Figure 4].

Ultrasonogram (USG)

USG was done in 120 cases and 14 (11.66%) cases had abnormal findings. Hydroureteronephrosis is seen in 8 cases (7%), cystitis in 4 cases (3%), and pelviureteric junction obstruction in 2 cases (1.8%) [Figure 5].

All the hydroureteronephrosis (8 cases) was detected in children below 5 years. Of 8 cases with hydroureteronephrosis, 7 (87.5%) were males, and 5 (71.4%) of these 7 males with hydroureteronephrosis had PUV [Figure 6].

MCU

MCU was done in 40 cases (31 males and 9 females) and was abnormal in 12 (30%) cases. 4 (10%) and

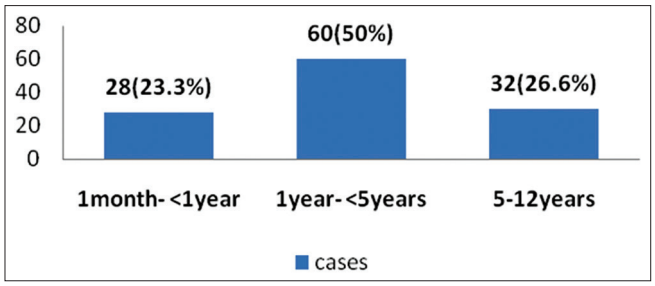


Figure 2: The age incidence in the study group (*n* = 120)

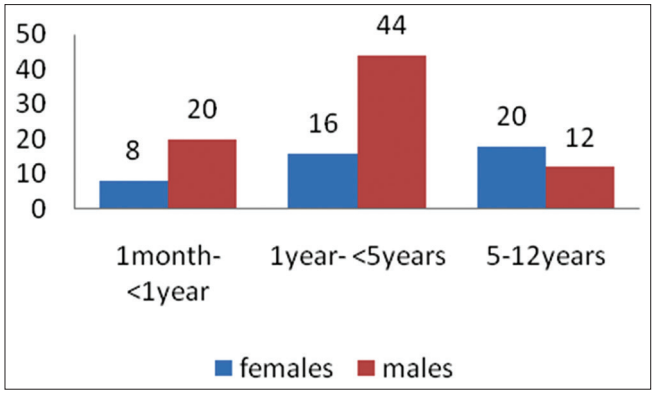


Figure 3: The gender incidence in the study (*n* = 120)

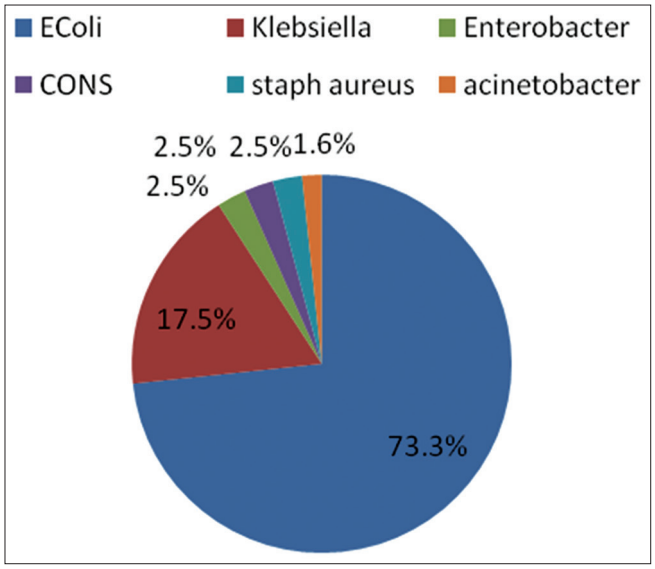


Figure 4: The distribution of organism cultured in the study (*n* = 120)

2 (5%) of 40 cases had grade 1–2 VUR and grade 3–4 VUR, respectively. 4 (13%) of 31 males and 2 (22%) of 9 females who underwent MCU had evidence of VUR; this female-to-male ratio of 1.7:1 found was not significant statistically ($P = 0.49$). In 31 males who underwent MCU, 6 (19.35%) had PUV. Of 6 PUV cases, 4 cases (66.7%) were detected before 12 months of age; 2 (33.3%) cases of PUV were detected after the age of 12 months [Figure 7].

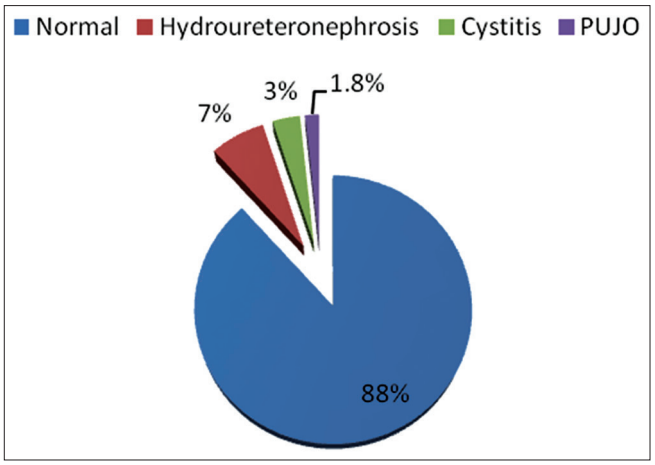
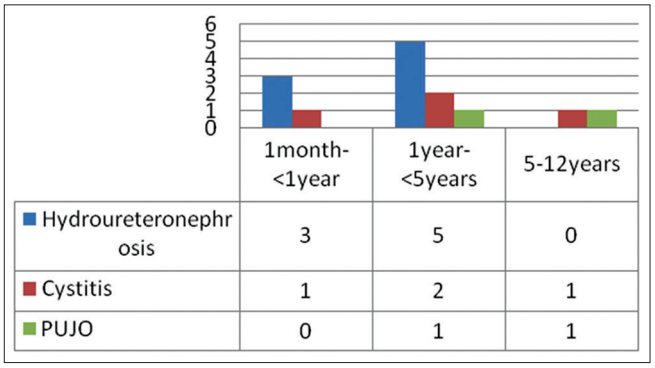


Figure 5: The incidence of abnormal ultrasonogram findings (*n* = 120)



	1month- <1year	1year- <5years	5-12years
Hydroureteronephrosis	3	5	0
Cystitis	1	2	1
PUJO	0	1	1

Figure 6: The age incidence of the abnormalities diagnosed on ultrasonogram (*n* = 14)

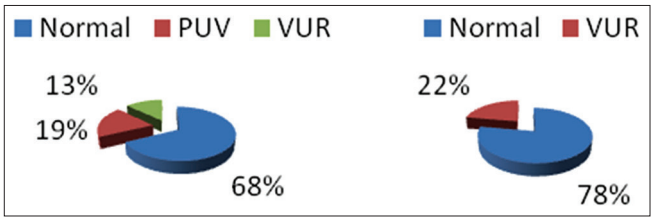


Figure 7: The incidence of micturating cystourethrogram findings (*n* = 12)

DMSA Renal Scan

DMSA was done in 57 cases and detected abnormality in 21 cases (37%). All children with abnormal DMSA renal scan (21 cases) had renal scarring at 2–3 months after first episode UTI. None of the children had renal function impairment which was assessed by split renal function on DMSA renal scan [Figure 8].

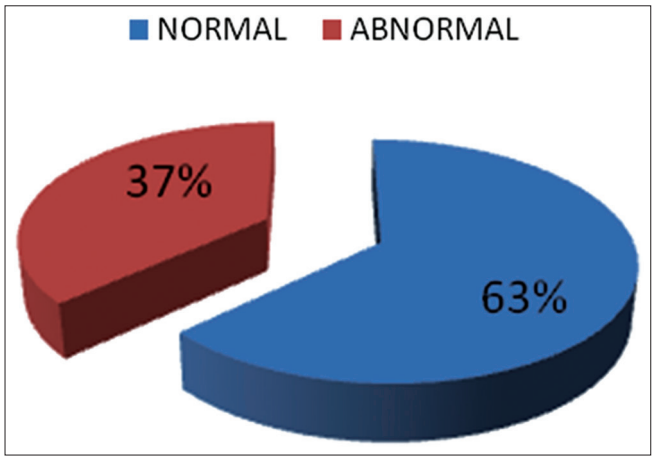
Treatment Outcome

Of 120 cases, 48 (40%) cases responded (became non-toxic and devoid of urinary symptoms) within 5–7 days of antibiotics. 47 cases needed antibiotics for 7–10 days and 25 cases needed antibiotics for 10–14 days for complete clinical recovery [Figure 9].

Surgical interventions: 6 (7.9%) of 76 males studied had posterior urethral valve. All children with PUV had undergone cystoscopic fulguration and 4 of these 6 children had undergone pyeloplasty after fulguration [Figure 10].

Recurrence

9 (7.5%) of 120 cases had second episode of UTI (with the same organism) within 6 months. 2 (3%) cases had second episode UTI (with different organism) after 6 months of first episode (n = 66). None of 120 cases had more than one recurrence during the study period [Figure 11].



Figurer 8: The incidence of abnormal technetium 99m-labeled dimercaptosuccinic acid results (n = 120)

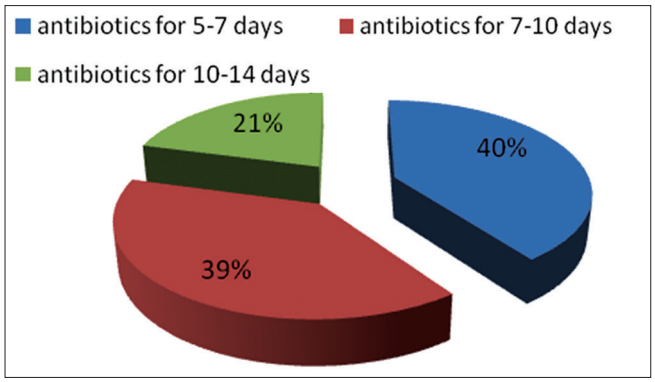


Figure 9: The treatment outcome in the study (n = 120)

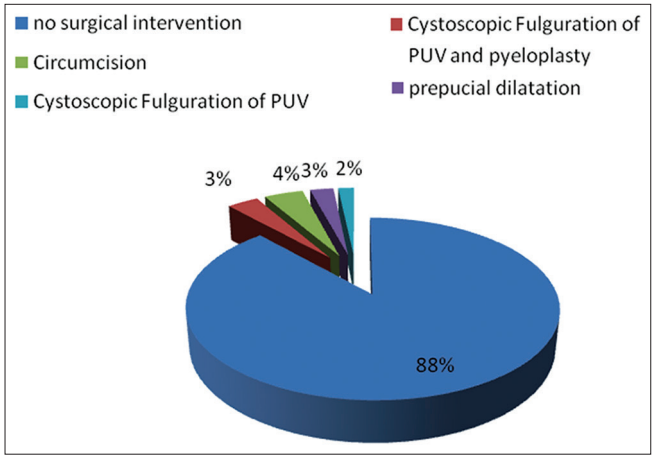


Figure 10: Types of surgical interventions undertake in the study (n = 120)

Recurrence of UTI in Relation to Age

3 (10.7%) of 28 cases under 12 months, 5(8.3%) out of 60 cases in age group 12–59 months, and 1 (3.1%) of 32 cases above 5 years had recurrent UTI within 6 months of first episode UTI; this difference is not statistically significant: P value (0.54) [Table 1].

Recurrence of UTI in males and females under different age groups is observed as follows:

Overall 6 of 76 (7.9%) males and 3 of 44 (6.8%) females had recurrence within 6 months of first episode UTI; P value is 0.8) and hence not statistically significant [Table 2].

Recurrence in Children with VUR

3 (50%) of 6 cases with VUR had a recurrence of UTI.

Renal Scarring: Renal Scarring in Relation to Age Group

Renal scarring is detected in 28.6% of cases under 12 months and 35% of cases in the age group of 12–59 months who underwent DMSA renal scan, and the difference is not statistically significant (P = 0.66). Renal scarring is detected in all 3 cases in the age group of 5–12 years who underwent DMSA scanning for which it is indicated (abnormal USG finding) [Figure 12].

Renal Scarring in Relation to Gender

39% of males (16 out of 41) and 31.2% of females (5 out of 16) who underwent DMSA renal scan had renal scarring; this difference in renal scarring percentage in relation to gender is not statistically significant: P value (0.58) [Table 3].

Renal Scarring in Relation to Isolated Organism

17 (39.5%) cases of 43 *E. coli*-positive UTI and 6 (33.3%) of 9 cases of *Klebsiella*-positive UTI had renal scarring, P value (0.72) [Figure 13].

Renal Scarring and Recurrence

Renal scarring is found in 6 of 7 (85.7%) cases that had recurrence within 6 months of first episode UTI. Renal scarring is found in 15 of 50 (30%) cases that does not have recurrence within 6 months of first episode UTI. Relative

Table 1: The incidence of recurrence according to the age groups (n=120)

Age group	% of recurrence within 6 months
1 month–<1 year	3 (10.7)
1 year–<5 years	5 (8.3)
5–12 years	1 (3.1)

risk of recurrence was 14 times (95% confidence interval: 1.5–126) more in cases with renal scarring than cases without renal scarring; (85.7% vs. 30%; *P* value 0.04) [Figure 14].

Renal Scarring in Cases with VUR

Renal scarring is found in all 6 cases with VUR (4 cases of grade 3–4 VUR and 2 cases of grade 1–2 VUR) in the present study.

Hypertension, Growth, and Altered Renal Function Tests

Hypertension, growth retardation, or altered renal function tests due to UTI alone were not observed on follow-up of total of 120 cases for 6 months, and of these, 13 cases were followed up to maximum 18 months, 21 cases were followed for maximum 15 months, 66 cases were followed for maximum 12 months, and 93 cases were followed for maximum 9 months.

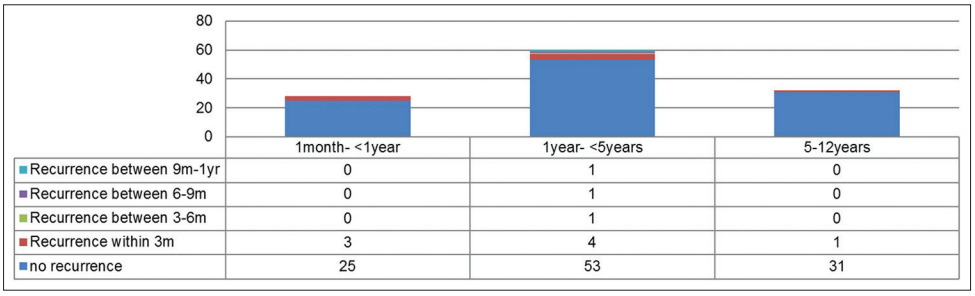


Figure 11: The incidence of recurrence in the study (*n* = 120)

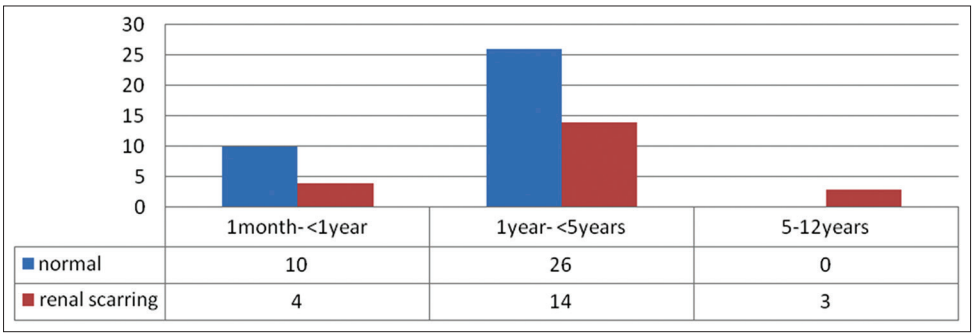


Figure 12: The incidence of renal scarring according to the age (*n* = 120)

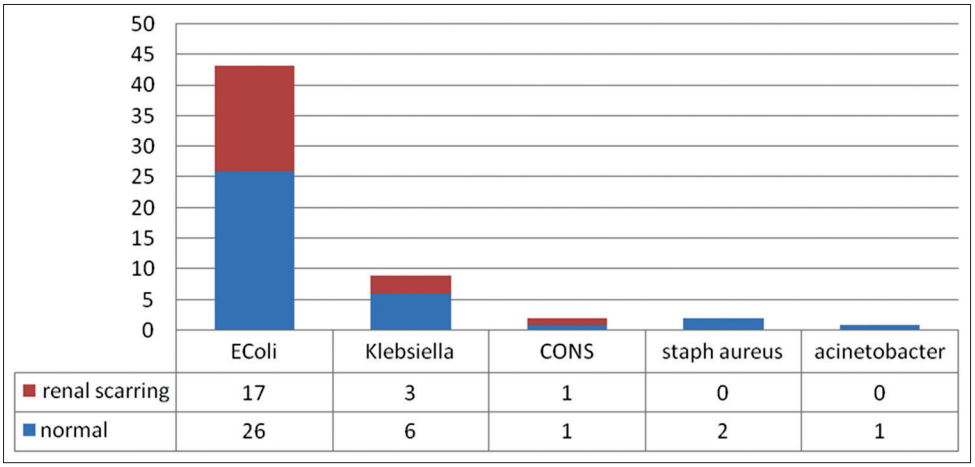


Figure 13: The relation between renal scarring and type off organism (*n* = 120)

Table 2: The recurrence of UTI according to the gender in the study (*n*=120)

Recurrence of UTI within 6 months	1 month–<1 year	1 year–<5 years	5–12 years	Overall %
Males	1 (5.3%)	4 (9%)	1 (8.3%)	6 (7.9%)
Females	2 (25%)	1 (6.2%)	0 (0%)	3 (6.8%)
P value	0.12	0.72	0.21	0.88

UTI: Urinary tract infection

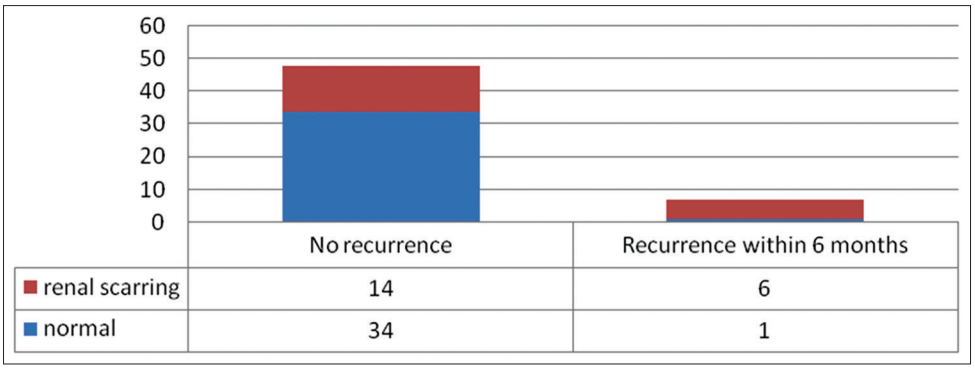


Figure 14: The relation between renal scarring and recurrence (*n* = 120)

DISCUSSION

Age and Gender Distribution

In the observation study of 120 children with first episode culture positive UTI between the age group 1 month and 12 years, male children (63.4%) were more than female children (36.6%) which is not comparable with the literature as the total number of male and female children who came to our hospital during the study period is not known. In a similar hospital-based study conducted by Singh *et al.*[16,17] of 135 patients, 32.5% were males and 67.4% were females forming a ratio of 1:2. Males outnumber females in children below 5 years (71.4% in children between 1 and 12 months and 73.3% in children between 12 and 59 months) and females (62.5%) outnumber males above 5 years in the study. Age and sex distribution obtained in the current study was similar to other hospital based studies done by Ali *et al.*[18] in UAE, Raghubanshi et al.[19] in Lalitpur, Nepal, April Bay and Anacleto[20] in Philippines [Table 4].

In majority of these hospital-based studies including the current study, it is noted that males are more affected in infancy than females, and as age increases, the gender ratio is reversed.

Etiology

Most common causative organism isolated was *E. coli* (73.3%) followed by *Klebsiella* (17.5%). This is comparable with the study by Sharma *et al.*[21] from Nepal and Akram *et al.*[22] from Aligarh, India [Table 5].

Bryan *et al.*[25] reported *E. coli* as the most common urinary pathogen accounting for 85% of community-acquired UTI. Bagga *et al.*[26] reported that about 90% of first symptomatic UTI and 70% recurrent infections were due to *E. coli*. The studies by Mantadakis *et al.*[27] and Islam *et al.*[28] showed *E. coli* as most common organism but with varying proportions. Gulati and Kher reported Gram-negative bacteria as the most common etiologic agents, among which *E. coli* was the most common.[29]

Table 3: The incidence of scarring after UTI according to the gender in the study (*n*=120)

Renal scarring	1–11 months	1 year–< 5 years	5–12 years	Overall
Males	3	11	2	39%
Females	1	3	1	31.2%
P value	0.46	0.27	-	0.58

UTI: Urinary tract infection

Table 4: Age and sex distribution

Male to female ratio	Infancy	Older children
Present study	2.5:1	1:1.5
Ali *et al.*[18]	2.1:1	1:1.2
Bay and Anacleto[20]	1.9:1	1:1.6
Raghubanshi *et al.*[19]	1.4:1	1.05:1

Table 5: Comparison of common organisms isolated

Organism	*Escherichia coli*	*Klebsiella*
Present study	73.3%	17.5%
Sharma *et al.*[21]	67.5%	20%
Akram *et al.*[22]	61%	22%
Waisman *et al.*[23]	76%	6%
Zamir *et al.*[24]	85%	7.1%

Imaging Studies

USG

Among imaging studies, 12% of children with UTI had abnormality in RUSG. This is similar to a study conducted by Hoberman et al.,[30] in his prospective study involving 309 children with UTI. USG findings were abnormal in 12%. This is low when compared with the study by Singh *et al.*[17] from Nepal and Ali *et al.*[18] from Sudan in which abnormal USG findings were found in 25% and 32.6%, respectively. The lower number of abnormal USG finding in the present study may be due to the resolution of cystitis/pyelonephritis at 1–2 weeks after treatment. Doing an USG before or on the day of starting treatment may be more sensitive.

MCU

MCU was normal in 70% of children who underwent this imaging and 15% of children had VUR. Grade 1–2 refluxes were shown by 10% of children who underwent this imaging and 5% showed Grade 3–4 reflux. In the study by Singh *et al*.[17] and Ali *et al*.,[18] VUR was found in 33.3% of children. Studies done by Pennressi *et al*.[31] and Ismali *et al*.[32] also showed similar findings. Among children with VUR in the present study, female-to-male ratio of 1.7:1 found is not significant statistically. This can be explained by very low number of children with VUR. In a study by Tekgul *et al*., VUR was found to be more in boys than girls among children with UTI,[33] whereas in IAP guidelines on UTI 2011, VUR is found common in females than males.[34]

Posterior urethral valve

Of 6 PUV cases detected by MCU, 4 cases (66.7%) were detected before 12 months of age; 2 (33.3%) cases of PUV were detected after age of 12 months [Table 6].

7.9% of males studied here had posterior urethral valve. This observation was high compared to a similar study done by Gupta *et al*. in JIPMER, Puducherry (2013), where 3 (2.3%) of 129 males with culture-proven UTI had PUV.[38] There is a significant difference in male infant sample size (66 children) in the compared study, and as the age of presentation of PUV is mostly in infancy, this may be a insignificant finding because a number of PUV cases presented in infancy is not mentioned in the JIPMER study.

DMSA

DMSA renal scan done was normal in 63% of cases, and 37% of cases had renal scarring. In a similar study of 186 children with culture-proven UTI done by Gupta *et al*. in JIPMER puducherry (2013), renal scarring was noted in 33 (47.8%) of the 69 children who underwent DMSA scan.[38] Sheikh *et al*. (2010)[39] in their meta-analysis of similar studies found 15% chance of renal scarring.

Outcome

Treatment response

Of 120 children, 40% of cases responded to 5–7 days antibiotics. 39% needed 7–10 days of antibiotics and 21% needed 10–14 days of antibiotics. Michael *et al*. in a comparison study of short (2–4 days) course versus standard long course (7–14 days) concluded that there was no significant difference in the frequency of positive urine cultures at 0–7 days after treatment in children with UTI.[40] Schroeder *et al*. (2014) found that relapse was not associated with treatment duration.[41] Hoberman *et al*. in their control trial comparing oral and parenteral treatment in children with febrile UTI found that there was no difference and recommended oral cefixime for decreasing expenditure.[42] Neuhaus *et al*. (2008) concluded in their study of children aged 6 months–16 years with DMSA-documented acute pyelonephritis that once-daily oral ceftibuten for 14 days yielded comparable results to sequential ceftriaxone/ceftibuten.[43] Bocquet *et al*. in 2012 found no significant difference between two treatment groups, who received either oral cefixime for 10 days or intravenous ceftriaxone for 4 days followed by oral cefixime for 6 days in relation to renal scarring and time to apyrexia.[44] In the present study, it was not able to compare the efficacy of oral versus intravenous antibiotics in the treatment of UTI in children as treatment was started with oral antibiotics for uncomplicated UTI and intravenous antibiotics for complicated UTI and non-responders to oral antibiotics. The study population should be randomized and given oral or intravenous antibiotics randomly to avoid selection bias.

Table 6: Age of presentation - posterior urethral valve

Age of presentation of PUV	NICE[35]	Uthup *et al*.[36]	Parkhouse *et al*.[37]
Between 0 and 1 month	9.5%	46.6%	33.3%
Between 1 month and 1 year	38%	36.6%	
Between 1 and 6 years	33%	16.8%	33.3%
More than 5 years	19%		33.3%

NICE: National Institute for Health and Clinical Excellence

Surgical intervention

All children with PUV had undergone cystoscopic fulguration followed by pyeloplasty for unresolved hydroureteronephrosis in 4 of these 6 children. The definitive treatment of PUV was cystoscopic fulguration of PUV which is supported by Warren *et al*.[45] Five male children underwent circumcision and 3 males underwent preputial dilatation. Shaikh *et al*.[46] in their study shown that circumcision was associated with a significantly reduced risk of UTI. Ginsberg *et al*. noted that 75% of boys with febrile UTI in the first 8 weeks of life were non-circumcised.[47] Studies suggest a 20–29-fold increase in febrile UTI in uncircumcised males in comparison to circumcised infants. The mechanism by which the intact prepuce predisposes to UTI is unclear. One of the possible explanations is that the prepuce allows the enteropathogenic bacteria to harbor and multiply in an uncircumcised male. However, the AAP taskforce on circumcision reports that the existing scientific evidence does not support a recommendation for routine neonatal circumcision.[9]

Recurrence

Recurrent UTI was present in 7.5% of children with first episode of UTI on a 6-month follow-up. This is supported by a meta-analysis of various studies under UTI done by Sheikh *et al*. 2010[39] in which recurrent UTI was found in 8% of cases. All nine children who had recurrence within 6 months had the same organism grown in their urine

culture suggesting unresolved or persistent bacteriuria. This is in correlation with Pewit *et al.* stating unresolved bacteriuria as the most common type of recurrent UTI.[48] The most common cause for unresolved bacteriuria is inadequate antibiotic therapy, and other causes include noncompliance, malabsorption, and suboptimal drug metabolism and resistant organism.

VUR and recurrence

50% of the children with vesicoureteric reflux had recurrent UTI in the study. In a study by Keren *et al.* (2015), 25.4% of children with VUR had recurrent UTI compared with 17.3% of children with no VUR.[49]

Recurrence in relation to age and gender

Association of the incidence of recurrence of UTI following UTI in relation to age and gender was inconclusive ($P > 0.05$). The NICE: 2007[12] states that recurrence was not associated with gender.

Renal scarring

Renal scarring is found in all 6 cases with VUR (4 cases of grade 3–4 VUR and 2 cases of grade 1–2 VUR) in this study. Sheikh *et al.* (2010) in their study found that children with VUR were significantly more (2.6 times) likely to develop renal scarring compared with children with no VUR.[39] Children with VUR grades III or higher were 2.1 times likely to develop scarring than children with lower grades of VUR. However, in a recent study by Keren *et al.* (2015), no significance was found in children with VUR and children with any VUR in relation to renal scarring.[49]

Renal scarring in relation to age and gender

Association of renal scarring following UTI in relation to age and gender was inconclusive in the present study. Park *et al.* (2012), Blumenthal *et al.* (2006), Mingin *et al.* in 2004, and Najib *et al.* in 2009 concluded that the age of presentation of the first UTI was not predictive of scar formation.[51-54] Piepsz *et al.* in a 5-year study showed that children younger than 2 years were at greater risk (1.8 times) for renal scarring than older children regardless of treatment.[55] Benador *et al.* (1997) in a study observed that the rate of renal scarring after pyelonephritis was high between 1 and 5 years of age.[56]

Renal scarring in relation to isolated organism

Association between organism isolated in urine culture and renal scarring was inconclusive ($P > 0.05$). Ronald *et al.* and Zmysłowska *et al.* in their studies found *E. coli* as the common uropathogen and no difference between the scar forming and non-scar forming groups.[57,58] Orellana *et al.*[59] found a significant higher incidence of renal scarring in children with non-*E. coli* infection.

Renal scarring and recurrence

Relative risk of recurrence was 14 times (95% CI: 1.5–126) more in cases with renal scarring than cases without renal scarring (85.7% vs. 30%; $P = 0.04$). Renal scarring is a predictor of recurrence of UTI which is also supported by NICE (2007).[50]

Growth retardation, renal function tests, and blood pressure

Hypertension, growth retardation, or altered renal function tests due to UTI alone were not observed in this study. This may be due to the short period of follow-up compared to other studies which had a long-term follow-up to observe these parameters. Salo *et al.* (2011) observed that a child with normal kidneys is not at significant risk of developing CKD because of UTIs.[60] Jacobson *et al.* in a 27-year follow-up study found that children with focal renal scarring due to pyelonephritis are at high risk of serious long-term consequences.[61,62] Hannula et al. in a 6–17-year follow-up study of 193 patients with childhood UTI observed no significant difference in BP, renal function and somatic growth in different groups with or without renal scars and/or VUR; and the risk of long-term consequences from childhood UTI in their studies were very low.

CONCLUSIONS

The recurrence chance of UTI is present in 7.5% of children within 6 months of first episode of UTI. Majority of children with recurrent UTI had their second episode within 6 months and that too, with the same organism suggesting an unresolved or persistent bacteriuria. The presence of VUR is a risk for recurrence of UTI and renal scarring. The relative risk of recurrence of UTI is 14 times in the presence of renal scarring than in children without renal scar formation, and thus, renal scarring is a good predictor of recurrence. Hypertension, growth retardation, and renal function abnormalities were not found in children with an episode of UTI on a 6–18-month follow-up and may need a long-term follow-up to observe these complications.

REFERENCES

1. Winberg J, Andersen HJ, Bergström T, Jacobsson B, Larson H, Lincoln K, *et al.* Epidemiology of symptomatic urinary tract infection in childhood. Acta Paediatr Scand Suppl 1974;252:1-20.
2. Larcombe J. Urinary tract infection. In: Clinical Evidence. Issue 7. London: BMJ Publishing; 2002. p. 377-85.
3. Wettergren B, Jodal U, Jonasson G. Epidemiology of bacteriuria during the first year of life. Acta Paediatr Scand 1985;74:925-33.
4. Sobel JD. Bacterial etiologic agents in pathogenesis of urinary tract infection. Med Clin North Am 1991;75:253-69.
5. Bower JM, Eto DS, Mulvey MA. Covert operations of uropathogenic *Escherichia coli* within the urinary tract. Traffic 2005;6:18-31.

6. Wullt B, Bergsten G, Connell H, Röllano P, Gebretsadik N, Hull R, *et al.* P fimbriae enhance the early establishment of *Escherichia coli* in the human urinary tract. Mol Microbiol 2000;38:456-64.
7. Zamir G, Sakran W, Horowitz Y, Koren A, Miron D. Urinary tract infection: Is there a need for routine renal ultrasonography? Arch Dis Child 2004;89:466-8.
8. Jacobsen SM, Stickler DJ, Mobley HL, Shirtliff ME. Complicated catheter-associated UTI due to *Escherichia coli* and *Proteus mirabilis*. Clin Microbiol Rev 2008;21:26-59.
9. American academy of Pediatrics Task Force on Circumcision. Circumcision policy statement. Paediatrics 1999;103:686-93.
10. Loening-Baucke V. Urinary incontinence and urinary tract infection and their resolution with treatment of chronic constipation of childhood. Pediatrics 1997;100:228-32.
11. Gochman RF, Karasic RB, Heller MB. Use of portable ultrasound to assist urine collection by suprapubic aspiration. Ann Emerg Med 1991;20:631-5.
12. Gorelick MH, Shaw KN. Screening tests for urinary tract infection in children: A meta-analysis. Pediatrics 1999;104:e54.
13. Downs SM. Technical report: Urinary tract infections in febrile infants and young children. The urinary tract subcommittee of the American academy of pediatrics committee on quality improvement. Pediatrics 1999;103:e54.
14. Roberts K, Downs S, Hellerstein S, Holmes M, Leibowitz R, Lohr J. American academy of pediatrics, committee on quality improvement, subcommittee on urinary tract infections. Practice parameters: The diagnosis, treatment and evaluation of the initial urinary tract infections in febrile infants and young children. Pediatrics 1999;103:843-52.
15. Indian Pediatric Nephrology Group. Consensus statement on management of urinary tract infections. Indian Pediatr 2001;38:1106-15.
16. Gauthier M, Chevalier I, Sterescu A, Bergeron S, Brunet S, Taddeo D, *et al.* Treatment of urinary tract infections among febrile young children with daily intravenous antibiotic therapy at a day treatment center. Pediatrics 2004;114:e469-76.
17. Singh SD, Madhup SK. Clinical profile and antibiotics sensitivity in childhood urinary tract infection at dhulikhel hospital. Kathmandu Univ Med J (KUMJ) 2013;11:319-24.
18. Ali E, Osman A. Acute urinary tract infections in children in Khartoum State: Pathogens, antimicrobial susceptibility and associated risk factors. Arab J Nephrol Transplant 2009;2:11-5.
19. Raghubanshi BR, Shrestha D, Chaudhary M, Karki BM, Dhakal AK. Bacteriology of urinary tract infection in paediatric patients. At KIST medical college teaching hospital. J Kathmandu Med Coll 2014;3:21-5.
20. Bay AG, Anacleto, F Jr. University of the Philippines college of medicine–Philippines general hospital. Clinical profile of UTI among children at the outpatient clinic of tertiary hospital. PIDSP J 2010;11:10-6.
21. Sharma A, Shrestha S, Upadhyay S, Rijal P. Clinical and biological profile of urinary tract infection in children at Nepal medical college teaching hospital. Nepal Med Coll J 2011;13:24-6.
22. Akram M, Shahid M, Khan AU. Etiology and antibiotic resistence pattern of community acquired UTI in JNMC hospital Aligarh, India. Ann Clin Microbial Antimicrob 2007;6:4.
23. Waisman Y, Zerem E, Amir L, Mimouni M. The validity of the uriscreen test for early detection of urinary tract infection in children. Pediatrics 1999;104:e41.
24. Bryan CS, Reynolds KL. Hospital acquired bacteremic urinary tract infection: Epidemiology and outcome. J Urol 1984;132:494.
25. Bagga A, Sharma J. UTI clinical features, evaluation and treatment. Pediatr Today 2000;3:395-401.
26. Mantadakis E, Tsalkidis A, Panopoulou M. Antimicrobial susceptibility to pediatric uropathogens in Thrace, Greece. Int Urol Nephrol 2010;43:549-55.
27. Islam MN, Khaleque MA, Siddika M, Hossain MA. UTI in children in tertiary level hospital in Bangladesh. Mymensingh Med J 2010;19:482-6.
28. Sanjeev G, Vijay K. Urinary tract infection. Indian Pediatr 1996;33:211-7.
29. Hobermann A, Charron M, Hickey RW, Baskin M, Kearne DH, Wald ER. Imaging studies after a first febrile urinary tract infection in young children. N Eng J Med 2003;348:195-202.
30. Pennressi M, L'erario I, Travan L, Venture A. Managing children under 36 month of age with febrile urinary tract infection: A new approach. Pediatr Nephrol 2012;27:611-5.
31. Ismaili K, Wissing KM, Lolin K, Le PQ, Christophe C, Lepage P, *et al.* Characteristics of first urinary tract infection with fever in children: A prospective clinical and imaging study. Pediatr Infect Dis J 2011;30:371-4.
32. Tekgül S, Riedmiller H, Hoebeke P, Kočvara R, Nijman RJ, Radmayr C, *et al.* EAU guidelines on vesicoureteral reflux in children. Eur Urol 2012;62:534-42.
33. Indian Society of Pediatric Nephrology, Vijayakumar M, Kanitkar M, Nammalwar BR, Bagga A. Revised statement on management of urinary tract infections. Indian Pediatr 2011;48:709-17.
34. National Institute for Health and Clinical Excellence (NICE). UTI in children. Diagnosis, Treatment and Long Term Management. London: NICE; 2007.
35. Uthup S, BinithaR, Geetha S, Hema R, Kailas L. A follow-up study of children with posterior urethral valve. Indian J Nephrol 2010;20:72-5.
36. Parkhouse HF, Barratt TM, Dillon MJ, Duffy PG, Fay J, Ransley PG, *et al.* Long-term outcome of boys with posterior urethral valves. Br J Urol 1988;62:59-62.
37. Gupta P, Mandal J, Krishnamurthy S, Barathi D, Pandit N. Profile of urinary tract infections in paediatric patients. Indian J Med Res 2015;141:473-7.
38. Shaikh N, Ewing AL, Bhatnagar S, Hoberman A. Risk of renal scarring in children with a first urinary tract infection: A systematic review. Pediatrics 2010;126:1084-91.
39. Michael M, Hodson EM, Craig JC, Martin S, Moyer VA. Short compared with standard duration of antibiotic treatment for urinary tract infection: A systematic review of randomised controlled trials. Arch Dis Child 2002;87:118-23.
40. Schroeder AR, Shen MW, Biondi EA, Bendel-Stenzel M, Chen CN, French J, *et al.* Bacteraemic urinary tract infection: Management and outcomes in young infants. Arch Dis Child 2016;101:125-30.
41. Hoberman A, Wald ER, Hickey RW, Baskin M, Charron M, Majd M, *et al.* Oral versus initial intravenous therapy for urinary tract infections in young febrile children. Pediatrics 1999;104:79-86.
42. Neuhaus TJ, Berger C, Buechner K, Parvex P, Bischoff G, Goetschel P, *et al.* Randomised trial of oral versus sequential intravenous/oral cephalosporins in children with pyelonephritis. Eur J Pediatr 2008;167:1037-47.
43. Bocquet N, Sergent Alaoui A, Jais JP, Gajdos V, Guigonis V, Lacour B, *et al.* Randomized trial of oral versus sequential IV/oral antibiotic for acute pyelonephritis in children. Pediatrics 2012;129:e269-75.
44. Warren J, Pike JG, Leonard MP. Posterior urethral valves in eastern Ontario - A 30 year perspective. Can J Urol 2004;11:2210-5.
45. Shaikh N, Morone NE, Bost JE, Farrell MH. Prevalence of urinary tract infection in childhood: A meta-analysis. Pediatr Infect Dis J 2008;27:302-8.
46. Mårild S, Jodal U. Incidence rate of first-time symptomatic urinary tract infection in children under 6 years of age. Acta Paediatr 1998;87:549-52.
47. Pewitt EB, Schaeffer AJ. Urinary tract infection in urology, including acute and chronic prostatitis. Infect Dis Clin North Am 1997;11:623-46.
48. Keren R, Shaikh N, Pohl H, Gravens-Mueller L, Ivanova A, Zaoutis L, *et al.* Risk factors for recurrent urinary tract infection and renal scarring. Pediatrics 2015;136:e13-21.
49. Hanson LA, Korotkova M, Håversen L, Mattsby-Baltzer I, Hahn-Zoric M, Silfverdal SA, *et al.* Breast-feeding, a complex support system for the offspring. Pediatr Int 2002;44:347-52.
50. Park YS. Renal scar formation after urinary tract infection in children. Korean J Pediatr 2012;55:367-70.
51. Blumenthal I. Vesicoureteric reflux and urinary tract infection in children. Postgrad Med J 2006;82:31-5.
52. Mingin GC, Hinds A, Nguyen HT, Baskin LS. Children with a febrile urinary tract infection and a negative radiological workup: Factors predictive of recurrence. Urology 2004;63:562-5.
53. Najib KH, Fallahzadeh E, Fallahzadeh MK, Fallahzadeh MH, Erjaee A. Renal scar formation in children with recurrent urinary tract infections. Iran Red Crescent Med J 2009;11:93-5.
54. Piepsz A, Tamminen-Mobius T, Reiners C. Five-year study of medical and surgical treatment in children with severe vesico-ureteric reflux dimercaptosuccinic acid findings. Eur J Pediatr 1998;157:753-8.
55. Benador D, Benador N, Slozman D. Are younger patients at higher risk of renal sequelae after pyelonephritis? Lancet 1997;349:17-9.
56. Ronald A. The etiology of urinary tract infection: Traditional and emerging pathogens. Dis Mon 2003;49:71-82.
57. Zmysłowska A, Kozłowski J, Zielińska E, Bodalski J. Urinary tract infections in children under three years of age. Pol Merkur Lekarski 2003;14:319-21.
58. Orellana P, Baquedano P, Rangarajan V, Zhao JH, Eng ND, Fettich J,

et al. Relationship between acute pyelonephritis, renal scarring, and vesicoureteral reflux. Results of a coordinated research project. Pediatr Nephrol 2004;19:1122-6.
59. Salo J, Ikäheimo R, Tapiainen T, Uhari M. Childhood urinary tract infections as a cause of chronic kidney disease. Pediatrics 2011;128:840-7.
60. Jacobson SH, Eklöf O, Eriksson CG, Lins LE, Tidgren B, Winberg J, *et al.* Development of hypertension and uraemia after pyelonephritis in childhood: 27 year follow up. BMJ 1989;299:703-6.
61. Hannula A, Perhomaa M, Venhola M, Pokka T, Renko M, Uhari M, *et al.* Long-term follow-up of patients after childhood urinary tract infection. Arch Pediatr Adolesc Med 2012;166:1117-22.

How to cite this article: Vinodkumar MS, Mohan MV. Outcome of Children with First Episode of Urinary Tract Infection. Int J Sci Stud 2018;6(1):163-173.

Source of Support: Nil, **Conflict of Interest:** None declared.