Prevalence of Vesicoureteral Reflux in Children with Urinary Tract Infection

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ABSTRACT

Background: Vesicoureteric reflux is a frequent lower urinary tract abnormality observed in children with urinary tract infection. One to two percent of apparently healthy children have vesicoureteric reflux and it is observed in 30-40% of the children with urinary tract infection.
Objective: To determine the frequency of vesicoureteric reflux in patients with urinary tract infection and the association between demographic features, culture results, ultrasound findings, and severity of reflux. Also, to highlight the causes of vesicoureteric reflux in those patients.
Methods: A retrospective review study was conducted at the department of nephrology at Central Child Teaching Hospital in Baghdad. Patients enrolled in this study aged from one month to 14 years .They were attending the nephrology department during the period from the 1st of January 2012 to 31stof December 2013 whom they undergone ultrasonography and voiding cystourethrography after the diagnosis of urinary tract infection had been settled.
Results: One hundred fifty patients with documented urinary tract infection were investigated for vesicoureteric reflux. The number of patients, who proved to have vesicoureteric reflux, was 52 (34.6%). The majority of cases diagnosed were below 5 years who were 41 (78.8%) patients, vesicoureteric reflux had diagnosed in 30 (57.7%) males and in 22 (42.3%) females. Twenty-two (42.3%) patients were diagnosed with vesicoureteric reflux after their first urinary tract infection, whereas 30(57.7%) patients after recurrent urinary tract infection. Primary vesicoureteric reflux is more to be diagnosed during first attack of urinary tract infection (53.8%) and secondary vesicoureteric reflux more to be associated with recurrent attacks of urinary tract infection (92.3%). Vesicoureteric reflux grades are distributed as follows:
Grade I was 5 cases (9.6%), grade II; 5 cases (9.6%), grade III; 11case (21.2%), grade IV; 19 case (36.5%) and grade V; 12 case (23.1%). Abnormal urologic finding on abdominal ultrasound was abnormal in cases of vesicoureteric reflux 45 (86.5%). This ultrasound abnormality positively correlate with higher grades of vesicoureteric reflux.
Conclusion: vesicoureteric reflux is a frequent association in children with urinary tract infection even in first episode. Therefore, imaging studies like voiding cystourethrography is mandatory for detection of vesicoureteric reflux and its grading.
Keywords: Vesicoureteral Reflux, Urinary Tract Infection, Ultrasound, Voiding cystourethrography.

Iraqi Medicals Journal Vol. 64, No. 2, July 2018; p.134-143.

Urinary Tract Infection (UTI) in pediatrics is a microbial inflammation of the urinary system, which can be diagnosed by the isolation of a pure growth of bacteria in an uncontaminated sample of urine using semi quantitative culture methods. UTI can be grouped into three clinically distinct presentations: cystitis, acute pyelonephritis, and asymptomatic bacteriuria[1].

Untreated pyelonephritis is associated with serious sequelae in the form of renal scarring, proteinuria, hypertension, toxemia of pregnancy and end stage renal disease[2,3]. It is estimated that approximately 7% of children between 2

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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 for 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].

One to two percent of apparently healthy children have VUR and it is observed in 30-40% of the children with UTI[9]. The majority of children identified following a documented UTI are girls however when considering infants less than six months of age no gender difference is noted[10]. The condition occurs ten times more frequently in white children than black children, and is more prevalent in male newborns than in female newborns. Females older than 1 year are found to have vesicoureteral reflux (VUR) 5 to 6 times more frequently than are males of the same age[11]. The grading of VUR correlates with the degree of renal scarring as well as the potential for spontaneous resolution. Lower grades of VUR have greater potential for spontaneous resolution independent of the age of the patient at diagnosis[12]. In addition, the grade of VUR is a consideration when making the appropriate choice regarding the surgical management.

Grade I: Urine backs up into the ureters only, and the renal pelvis appears healthy.

Grade II: Urine backs up into the ureters, renal pelvis, and calyces. The renal pelvis appears healthy and has sharp calyces.

Grade III: Urine backs up into the ureters and collecting system. The ureter and pelvis appear mildly dilated and the calyces are mildly blunted.

Grade IV: Urine backs up into greatly dilated ureters.

Grade V: Massive reflux with significant dilatation, tortuosity and loss of papillary impression.

Serial radiological and nuclear medicine workup is critical for diagnosis of VUR and in determining appropriate therapy, follow up imaging, antibiotic prophylaxis and surgical correction. Most of the time diagnostic modalities utilized were renal and bladder ultrasonography (RUS) and voiding cystourethrogram (VCUG), followed by dimercaptosuccinic acid (DMSA) scan. Latest imaging modalities include magnetic resonance urography (MRU) and interactive voiding cystourethrography (IRVC) both offering exquisite anatomic detail in conjunction with dynamic, functional information without the need for radiation[16].

The rationales behind this study was to determine the frequency of VUR in children with UTI and to highlight the association between the age, gender, clinical feature, culture results, the causes (whether primary or secondary) and severity of VUR.

Methods

A retrospective review study was conducted at the department of nephrology; Central Teaching Hospital in Baghdad. A total number of 150 patients aged (1 month to 15 years), who had attended the nephrology department over a period of 24 months from 1st of January 2012 to 31st of December 2013 were enrolled in the study.

Approval of research committee and consent of participants has been obtained.

Inclusion criteria for performing VCUG were:

1. Male patients with first attack of UTI during their first year.
2. Female patients with recurrent attacks of UTI in different ages.
3. Structural abnormalities detected on ultrasound.
4. Cases of neurogenic bladder and duplicating collecting system.

Whereas; exclusion criteria were VCUG which has been conducted for purposes other than UTI work up (i.e. for studying anatomy of bladder, distal obstruction and posterior urethral valve).

The diagnosis of UTI was confirmed by either documented definite culture positive UTI or negative urine culture (on antibiotics), with urine dipstick positive for leukocyte esterase and/or nitrite.

Urinalysis by dipstick examination for nitrite and leukocyte esterase (LE) is a rapid and easy to perform. The nitrite test demonstrates the presence of gram-negative bacteria in urine that reduce dietary nitrate to nitrite. The nitrite test is 37% sensitive and 100% specific, with a positive predictive value and negative predictive value of 90% and 100%, respectively[17]. LE detects the presence of leukocytes in the urine and is best performed on a fresh specimen. In contrast to the nitrite test, the sensitivity and specificity is 73%, the positive predictive value is 34%, and the negative predictive value is 95%. (A positive predictive value is the proportion of patients who have positive test results and are correctly diagnosed with a clinical condition. The negative predictive value is the proportion of patients who have negative test results and are correctly diagnosed with a clinical condition[18]. Data were obtained from the patients' files include:

Age, gender, attacks of UTI, whether first or recurrent (Recurrent UTI defined as at least 2 episodes within 6 months or 3 episodes within one year time[19], signs and symptoms of UTI (fever, irritability, vomiting, diarrhea, frequency, dysuria, abdominal pain and neonatal sepsis), urine analysis results and urine culture.

The methods of collecting urine were also included in the data whether by urine bag (by application of sterile plastic bag to the perineum after carefully cleansing the peri-urethral area with plain water and transported to the lab within 30 minutes), mid-stream urine clean catch (which is used for toilet training children) and Foley catheter (for hospitalized children). The results of urine culture were analyzed according to the general criteria to diagnose UTI as shown in table 1.

Table 1: General criteria to diagnose a urinary tract infection by culture[2,4].

Urethral Catheterization	Greater than 10^3 colony forming units/ml for circumcised males and all females, $>10^5$ colony forming units/mL for uncircumcised males (if 10^4 to 10^5 colony forming units/mL, consider repeat sample)
Midstream Clean Catch	$>10^5$ colony forming units/ml. These values pertain to pure, one-pathogen colony growth and should be interpreted based on the child's symptom complex.

Data recording also include ultrasonography findings of the kidneys, ureters and bladder for the presence of urinary tract dilatation.

All cases included in the study with proven UTI undergone VCUG at the end of antimicrobial therapy for period of 10-14 days or after urine become sterile by urinalysis. The procedure was done by the radiologist by installation of Iohexol (Omnipaque) through a Foley's catheter; thereafter, anterior, full bladder and micturition radiological snaps were taken. Hence, the VCUG provided precise anatomic details about the presence or absence of VUR with its grades.

Statistical package for Social Sciences-version 20 (SSPS v.20) was for data input and analysis. Continuous variables presented as mean ± standard deviation,

while discrete variables presented as numbers and percentages. Mann-Whitney test for two independent variables used to test the significance of observed difference in means.

Chi-square test of independency was used to verify the significance of observed associations.

All P values were asymptotic and two sided. Findings with P value < 0.05 considered significant.

Results

The total number of patients with UTI was 150. The number of patients proved to have VUR was 52 (34.6%). The sample age range between one month and 14 years. The mean age was 4.1 year, (Table 2).

Age distribution of patients was as follow: those below one year 31(20.7%), those from 1-4 years was 58(38.7%) and those above 5 years 61(40.7%). The number of male patients was 72(48%) while the number of female patients was 78 (52%). The number of patients presented with first attack of UTI was 59 (39.3%) and with recurrent UTI, 91 (60.7%), (Table 3).

Regarding the clinical features of patients who presented to hospital, fever was the most common symptom affecting 111(74%) patients, followed by vomiting 83(55.3%) and abdominal pain 71(47.3%); whereas, the least frequent presentation was neonatal sepsis 19(12.7%), (Table 4).

In order to diagnose UTI, urinalysis was done to all patients, which was abnormal in all cases (100%), urine was collected by different methods either by midstream urine in 47(31.3%) patients, Foley's catheter was used for inpatients in 43(28.7%) patients or by urine bag 60(40%) patients.

Culture was positive in 108 cases (72%), abdominal ultrasound was abnormal in 99 cases (66%). VCUG was done to all patients; a diagnosis of VUR had settled in 52 patients, the grades of reflux were distributed as follow:

Grade I; 5 cases (9.6%), grade II; 5 cases (9.6%), grade III; 11 cases (21.2%), grade IV; 19 cases (36.5%) and grade V; 12 cases (23.1%), (Table 5).

Escherichia-coli (E-coli) was the most common organism isolated in patients with UTI encountered in 50 (46.2%) patients followed by Klebsiella in 24 (22.2%) patients, (Table 6).

Table 2: Demographic features of patients

Description		Value
•	**Total number**	150
•	**Lower age** (month)	1
•	**Upper age** (year)	14
•	**Mean ± SD*** (year)	4.1 ± 3.9

Table 3: Characteristics of studied sample.

	Variable	Number	Percent
Age group (year)	< 1	31	20.7
	1.0 – 5	58	38.7
	≥ 5	61	40.7
Gender	Male	72	48.0
	Female	78	52.0
Frequency of attack	First	59	39.3
	Recurrent	91	60.7

Table 4: Frequency of clinical features of the studied sample.

Clinical Feature		Number	Percent
	Fever	111	74.0
	Vomiting	83	55.3
	Abdominal pain	71	47.3
	Diarrhea	22	14.7
	Dysuria	58	38.7
	Frequency	27	18.0
	Neonatal Sepsis	19	12.7
	Irritability	41	27.3

Table 5: Distribution of patients according to methods of collecting urine and findings of investigations.

Procedure		No.	%
Methods of urine sample collection			
•	Mid-stream Urine	47	31.3
•	Foley's Catheter	43	28.7
•	Urine Bag	60	40.0
Positive finding in GUE		150	100.0
Culture Positive		108	72.0
Abnormal U/S finding		99	66.0
Diagnosed with VUR		52	34.6
Grade of VUR			
•	No VUR	98	65.4
•	I	5	9.6
•	II	5	9.6
•	III	11	21.2
•	IV	19	36.5
•	V	12	23.1

* General Urine Examination

Table 6: Frequency and distribution of the microorganisms encountered in patients with positive urine culture.

Micro-organism	No. of patients	Percentage
Escherichia coli	50	46.2
Klebsiella	24	22.2
Proteus	14	12.9
Pseudomonas	10	9.25
Staphylococcus aureus	7	6.48
Enterobacter	3	2.77

VUR is significantly associated with younger age (under 5 years). Among patients with VUR male to female ratio is 1.3:1 whereas, there was no significant association between gender or frequency of UTI (whether first or recurrent) with the diagnosis of VUR, (Table 7).

Neonatal sepsis is significantly associated with VUR. Children with VUR were significantly more likely to have abnormal U/S than other children with UTI with no VUR, (Table 7).

The prevalence of VUR in this studied sample of patients with UTI was 34.67%, (Table 5).

Patients with primary VUR were significantly younger than those with secondary VUR, that primary VUR is observed more in under years 5 children and secondary VUR found more frequently in older children, (Table 8).

Primary VUR was more to be diagnosed during first attack of UTI and secondary VUR more to be associated with recurrent attacks of UTI, (Table 8).

Grades of VUR were distributed as follow: grades I and II; 10 patients (19.2%), grade III; 11 patients (21.2%) grades IV and V; 31 patients (59.6%). In all age groups, severe grades (IV and V), were frequently associated with male gender (71%); whereas, female constituted (29%). The male to female ratio in these severe grades was 2.4:1, (Table 9).

The U/S findings were significantly associated with higher grade of VUR. Grades IV and V had a (96.8%) with abnormal U/S findings (Table 9).

Unilateral reflux was found in 24 cases (46.1%); whereas, bilateral reflux is found in 28 cases (53.8%), (Table 10).

Table 7: Distribution of the sampled patient according to the presence of VUR and different studied factors.

Characteristic		VUR		No.			
		N=52	%	N=98	%	X^2	P value
Age group (year)						13.205	**0.001**
•	< 1	16	30.8	15	15.3		
•	1.0 – 5	25	48.1	33	33.7		
•	≥ 5	11	21.2	50	51.0		
Gender						2.996	0.083
•	Male	30	57.7	42	42.9		
•	Female	22	42.3	56	57.1		
Attack of UTI						0.295	0.587
•	First	22	42.3	37	37.8		
•	Recurrent	30	57.7	61	62.2		
Clinical Feature							
•	Fever	43	82.7	68	69.4	3.126	0.077
•	Irritability	19	36.5	22	22.4	3.395	0.065
•	Vomiting	28	53.8	55	56.1	0.071	0.790
•	Diarrhea	10	19.2	12	12.2	1.325	0.250
•	Dysuria	23	44.2	35	35.7	1.039	0.308
•	Frequency	6	11.5	21	21.4	2.251	0.133
•	Neonatal Sepsis	11	21.2	8	8.2	5.183	0.023
•	Abdominal Pain	15	28.8	56	57.1	10.912	0.001
•	Abnormal ultrasound	45	86.5%	54	55.1%	14.962	< 0.001

Table 8: Distribution of patients with VUR according to the etiology.

Characteristic		Primary		Secondary		X^2	P value
		N=39	%	N=13	%		
Age Group (year)						12.091	**0.002**
•	< 1	15	38.5	1	7.7		
•	1.0 – 5	20	51.3	5	38.5		
•	≥ 5	4	10.3	7	53.8		
Gender						0.945	0.331
•	Male	24	61.5	6	46.2		
•	Female	15	38.5	7	53.8		
Attack of UTI						8.509	**0.004**
•	First	21	53.8	1	7.7		
•	Recurrent	18	46.2	12	92.3		

Table 9: Distribution of patients with VUR according to grade and different study factors.

Characteristic		Grade I & II		Grade III		Grade IV & V			
		N=10	%	N=11	%	N=31	%	X^2	P value
Age Group (year)								0.795	0.939
•	< 1	3	30.0%	4	36.4%	9	29.0%		
•	1.0 – 5	5	50.0%	4	36.4%	16	51.6%		
•	≥ 5	2	20.0%	3	27.3%	6	19.4%		
Gender								5.571	0.062
•	Male	4	40.0%	4	36.4%	22	71.0%		
•	Female	6	60.0%	7	63.6%	9	29.0%		
Attack of UTI								3.298	0.192
•	First	2	20.0%	4	36.4%	16	51.6%		
•	Recurrent	8	80.0%	7	63.6%	15	48.4%		
•	abnormal U/S	8	80.0%	7	63.6%	30	96.8%	8.108	**0.017**

Table 10: Distribution of children with VUR according to grade of VUR.

	Unilateral VUR		Bilateral VUR		All		
Grade of VUR	No.	%	No.	%	No.	%	P value
							0.964
• Grade I & II	5	20.8	5	17.9	10	19.2	
• Grade III	5	20.8	6	21.4	11	21.2	
• Grade IV & V	14	58.4	17	60.7	31	59.6	
Total	24	46.1%	28	53.8%	52	100.0	

Discussion

Urinary tract infections in children are a significant source of morbidity, particularly when associated with anatomic abnormalities. Vesicoureteral reflux is the most commonly associated abnormality[20].

In this study, the number of patient proved to have VUR were 52 (34.6%). This finding is comparable to a similar Iranian, Nepalese and Finland studies that had revealed that the prevalence of VUR was 30%, 35%, 36%, respectively, after UTI[21-23].

On the other hand, VUR was significantly commoner in the younger age group(less than 5 years) as compared to older one; this is in accordance with Nepalese study done by Shrestha et al[22] that had revealed that the most common age group was between two to twelve months. In another study from USA done by Chand et al[24], they found that age wise incidence of VUR was high below 6 years, Similar result was found by Zaki et al[25].

The number of male patients with UTI was 72(48%) and the number of female patients was 78(52%), of these 30 (57.7%) males and 22 (42.3%) females had diagnosed with VUR (1.3:1). These results are close to another two studies' results, one in Sri Lanka (male: female ratio 1.6:1)[26] and another in India (male: female ratio of 3:1)[20] who had reported male preponderance of VUR in children. This difference may be related to higher prevalence of UTI in males within the first year of life which could be due to uncircumcised male baby[2] .

In addition, the number of patients presented with first attack of UTI was (39.3%) and those with recurrent UTI was (60.7%). There was no significant difference when comparing the prevalence of VUR according to the attack of UTI, this is in accordance with a study conducted by Fridman et al[27] (performed at Children's Hospital of Michigan); whereas, in another study made by Ji LN et al[28] had revealed that the prevalence of VUR in recurrent UTI group was much higher than that in first UTI group. This probably in the Ji LN et al study had included a larger number of secondary cases whom are more prone to have recurrent UTI.

Regarding the clinical features of patients presented to hospital. Fever was the most common presenting feature 0f UTI, followed by vomiting and abdominal pain which is similar to the finding by a study done by Nadi HM et al[29] which had showed that fever was also the most common presenting feature.

In the current study, neonatal sepsis was significantly associated with VUR, which is similar to a study done by Chein-Wei Lin et al[30].

We also found that there is significant association between GIT symptoms like abdominal pain with UTI that is in accordance with an Egyptian study done by El-Ekiaby, A et al[31].

In this study culture was positive in 108(72%) and most common organism was E. coli 50 (46.2%), this is similar to another studies conducted by Islam MN et al[32], El-Ekiabi A et al[31] and Goonasekera CDA, Dillon MJ[33], that had shown E coli was the most common organism isolated in patients with UTI.

Patients with primary VUR were significantly younger than those with secondary VUR similar to study conducted by Muinuddin G et al[34]. Renal ultrasound was abnormal in 99 cases (66%) in our study. Children with VUR significantly more likely to have abnormal U/S than other children with UTI, which could be in the form of dilatation of the PCS, ureters, or both.

U/S abnormal findings were positively correlate with the higher grades of VUR that grades IV and V had abnormal U/S in (96.8%); whereas U/S was abnormal in (3.2%) in grade I and II(simple cystitis, mild dilatation of the PCS). Similar findings had been found by Sandrine Leroy et al[34]; who had demonstrated that U/S criterion had high sensitivity and specificity in detecting all and specially high grades of VUR.

Furthermore, male to female ratio of dilating reflux (IV and V) was 2.4:1 that is similar to a study done by Hirako M et al[36] who had reported higher grades of reflux in males.

The percentage distribution of VUR were as follow: mild reflux (grade I-II), moderate reflux (grade III) and severe reflux (grade IV-V) were 19.2% (10/52), 21.2% (11/52) and 59.6% (31/52), respectively. A nearly similar distribution of VUR grades was elicited by a study conducted by Afroza et al[37].

The higher incidence of reflux with advanced grades in our study may reflects parental ignorance and late referral of the patients who ultimately reach at our center with advanced stage of the disease, and also that our hospital is a tertiary center that deals with complicated cases.

Lastly, bilateral reflux was found in 28 cases (53.8%), unilateral in 24 cases (46.1%). Which was approximately similar to a study done by Soygur et al[38] who found 59.6% had bilateral reflux and 40.3% had unilateral reflux.

In conclusion; the current study shows that VUR was frequently associated with UTI (diagnosed by VCUG), which if not treated well can end with renal impairment. Many of these cases of VUR were diagnosed in the first attack of UTI. There was no significant difference related to the gender of patient with VUR and E. coli was the most common microorganism encountered in urine culture. The younger the patient associated with higher prevalence of VUR. Finally, U/S was valuable tool in detecting higher grade of VUR, as it was more abnormal in these grades.

Recommendations; we recommend that ultrasound and VCUG should be done even after first attack of UTI in young infants to establish an approach for early diagnosis, treatment and follow up to prevent serious complications and preserve renal functions. In addition, we emphasized family counseling and education for the high risk of VUR after the diagnosis of UTI had been settled down. These patients should be scheduled for VCUG. We recommend referral of patients that need surgery to urosurgical department.

References

1. Jurgen F, Richard J, Vesicoureteral efflux. In: Ranjiv Mathews and Tej K Mattoo (editors). Comprehensive Clinical Nephrology. 4th edition, Mosby, Philadelphia 2008. P.549-59.
2. Jack S. Vesicouretral reflux. In: Robert M Kligman, Richard E. Behrman (editors). Nelson Textbook of Pediatrics. 19th edition. Saunders, Philadilphia 2012. P. 1834-9.
3. Shaikh N, Morone NE, Bost JE. Prevalence of urinary tract infection in childhood. A meta-analysis. Pediatr Infect Dis J. 2008;27:302-8.
4. Leonard G, Feld K, Teg K .Urinary tract infection and vesicouretric reflux in infants and children. Pediatrics in Review 2010;31:451.
5. Lutter SA, Currie ML, Mitz LB. Antibiotic resistance patterns in children hospitalized for urinary tract infection. Arch Pediatr Adolescence Med 2005;159:924-8.
6. Hansson S, Svedhem A, Wenner storm A. Urinary tract infection caused by H-influenza and H-parainfluenza in children. Pediatr Nephrol 2007;22:1321-5.
7. Smellie JM, Barratt TM, Chantler C. Medical versus surgical treatment in children with severe bilateral vesicoureteral reflux and bilateral nephropathy: A randomized trial. Lancet 2001;357:1329-33.
8. Authors Update on vesicoureteral reflux: pathogenesis, nephropathy, and management. Rev Urol 2001; 3(4):172-8.
9. Larry A, Hrair-George O. Vesicoureteral reflux. Pediatr Clin N Am 2006;53:413-27.
10. Chen JJ. Infant vesicoureteral reflux: A comparison between patients presenting with a prenatal diagnosis and those presenting with a urinary tract infection. Urology 2003;61(2):442-7.
11. Patricio C, Gagollo, David A Diamond. Therapy insight article: what nephrologist need to know about grade I vesicoureteral reflux. Nature clinical practice nephrology 2007;3:551-63.
12. Brophy MM, Austin PF, Yan Y. Vesicoureteral reflux and clinical outcomes in infants with prenatally detected hydronephrosis. J Urol 2002;168:1716-19.
13. Bosio M, Manzoni GA, Detection of posterior urethral valves with voiding cystourethrography with echo contrast. J Urol 2002;168:1711-15.
14. Piaggio G, Degl' Innocenti ML, Toma P. Cystosonography and voiding cystourethrography in the diagnosis of vesicoureteral reflux. Pediatr Nephrol 2003;18:18-22.
15. Uhl M, kromeier J, Zimmerhackl LB. Simultaneous voiding cystourethrography and voiding urosonography. Acta Radiol 2003;44:265-68.
16. Mc Donald A. Voiding cystourethrography and urinary tract infection: how long to wait? Pediatrics 2000;105(4):50.
17. Sathapornwajana P, Dissaneewate P, Mc Neil E. Timing of voiding cystourethrography after urinary tract infection. Arch Dis Child. 2008; 93: 229-31.
18. Mahant S ToT, Friedman J. Timing of voiding cystourethrography in the investigation of urinary tract infection in children. J Pediatr 2001;139:568-71.
19. Unver T, Alpay H, Biyikli NK. Comparison of direct radionuclide cystography and voiding cystourethrography in detecting vesicoureteral reflux. Pediatr Int 2006;48:287-91.
20. Ross M, Baggo A. Management of urinary tract infections. Ind J Pediatr 2003;70:235-9.

21. Sharbaf TG, Fallahzadeh MH, Modarresi AR. Primary vesicoureteral reflux in Iranian children. Indian Pediatr 2007;44:128-30.
22. Shrestha S, Basukala S, Pokhrel N. Primary vesicoureteral reflux in Nepalese children. Kathmundu Univ Med J 2008;6:75-8.
23. Venhola M, Hannula A, Huttunen NP, Occurrence of vesicoureteral reflux in children. Acta Pediatr 2010;99:1875-8.
24. Chand DH, Rhoades T, Poe SA, Incidence and severity of vesicoureteral reflux in children related to age, gender, race and diagnosis. J Urol 2003;170(4 pt2):1548-50.
25. Zaki M, Mutari GA, Badawi M. Vesicoureteric reflux in Kuwaiti children with first febrile urinary tract infection. Pediatr Nephrol 2003; 18: 898-901.
26. Abeysekara CK, Yasaranta BMCD, Abeyagunawardena AS. Long-term clinical follow up of children with primary vesicoureteric reflux. Ind Pediatr 2006;43:150-4.
27. Friedman AA, Wolfe-Christensen C, Toffoli A. History of recurrent urinary tract infection is not predictive of abnormality on voiding cysto-urethrogram. Pediatr Surg Int 2013; 29(6): 639-43. doi: 10.1007/s00383-013-3301-0.
28. Ji LN, Cao L, Chen DK. Evaluation of the clinical and imaging examination in high-risk children with vesicoureteral reflux. Pediatrics 2011;49(4):282-6.
29. Nadi HM, Shalan YA, AL-Qatan HY. Urinary Tract Infection in boys less than five years of age: a general pediatric perspective. Kuwait Med J 2006;38(3):220-25.
30. Chein-Wei Lin, Yee-Hsuan Chiou, Ying-Yao Chen. Urinary tract infection in neonates. Clinical Neonatology 1999;6(2):1-4.
31. El-Ekiabi A, Gobran T, Rozeik A, Incidence of vesicoureteral reflux in children with urinary tract infection and methods of management. Z.U.M.J. 2013;19(1):8-13.
32. Islam MN, Khaleque MA, Siddika M. Urinary tract infection in children in a tertiary level hospital in Bangladesh. Mymensingh Med J 2010;19(4):482-6.
33. Goonasekera CDA, Dillon MJ. Reflux nephropathy and hypertension. Journal of Human Hypertension 1998;12:497-5.
34. Muinuddin G, Rahman H, Hossain MM. Urinary tract infection and vesicoureteric reflux in children 2008;17(2 Suppl):S28-31.
35. Sandrine Leroy, Sébastien V, Anis L. Vesicoureteral reflux in children with urinary tract infection: Comparison of diagnostic accuracy of renal US criteria. Radiology 2010;255(3):890-8.
36. Hirako M, Hori C, Tsukahara H. Vesicoureteral reflux in male and female neonates as detected by voiding ultrasonograpgy. Kidney Int 1999;55(4):1486-90.
37. Afroza Begum, Habibur Rahman, MM Hossain. Association of vesicoureteric reflux (VUR) in children with symptomatic urinary tract Infection (UTI) in a tertiary care hospital, Dhaka, Bangladesh. Bangladesh J Child Health 2013;37(2):79-84.
38. Soygür T, Arikan N, ÇetinYeşilli. Relationship among pediatric voiding dysfunction and vesicoureteral reflux and renal scars. Urology 1999;54:94.

IMJ 2018;64(2):134-143.