



**Clinical manifestation and radiologic findings of high grade VUR in children
and frequency of renal scarring at presentation: A 17-year evaluation**

**Mitra Naseri, MD , pediatric nephrologist, associate professor , Mashhad
University of Medical Sciences, Mashhad, Iran**

**Shokufeh Sadat Ebrahimi, MD , Mashhad University of Medical Sciences,
Mashhad, Iran**

Objective :

The aim of this study was to determine the clinical manifestations, and kidney and bladder ultrasound findings in patients with high grade(grades Iv & V) vesicoureteral reflux (VUR).

Materials & Methods :



In a 17-year period (March 2003 to March 2019), patients under 18 years of age with diagnosis of high grade VUR enrolled the study. Demographic information, clinical manifestations at initial visit, and findings on kidney and bladder ultrasound were assessed.

Results


- A total of 197 individuals entered including 107(54.3%) girls and 90 boys (45.7%).
- They aged 40.03 ± 36.68 months.
- The distribution of patients in age groups ≤ 2 months, 2-24 months, 3-5 years and > 5 years were 21 (10.7%) ,71(36.2%) ,48 (24.5%) and 56 (28.6%) cases, respectively .
- The age of one patient at presentation was not defined.

Table 1 • Clinical manifestations of the patients

Variable	N (%)
Urinary tract infection	159 (80.7)
Prenatal hydronephrosis	28(14.2)
History of VUR in sibling	27(13.7)
Nocturnal enuresis	22(11.2)
Abdominal pain	16(8.1)
Abnormal kidney US findings	9 (4/5)
Daytime incontinence	9 (4/5)
Dysuria and negative U/C	8(4)
Intermittency	5(2.5)
Frequency with negative U/C	5(2.5)
Straining	4(2)
Dribbling	4(2)
Nausea and vomiting	2 (1)
Abdominal mass	1(0.5)
Infantile colic	1(0.5)
Total cases	197(100)

- As the Table 1 presents 57 cases (**28.9%**) presented by abnormal lower urinary tract symptoms suggestive of voiding dysfunction.

Table 2: kidney and bladder ultrasound findings in the patients

Ultrasound findings	N (%)
Normal kidney US	46(23.4)
Mild to moderate hydronephrosis	121(61.4)
Severe hydronephrosis	29(14.7)
Hydro ureter	76(38.6)
Decreased kidney size	27(13.7)
Renal scar	27(13.7)
Nephrolithiasis	11(5.6)
Ectopic kidney	2(1)
Horseshoe kidney	1(0.5)
Normal bladder US	143(72.6)
Increased bladder wall thickness (≥ 3 mm)	43(21.8)
trabeculated bladder	12(6.1)
Total patients	197(100)

- Totally VUR was unilateral in 146 (74.1%) and bilateral in 51(25.9%) cases.
- Serum creatinine levels at presentation (n=127) were **0.3-6 (0.72 ± 0.62)** mg/dl.
- Tc99m - DMSA scan was done in 154 cases (78.2%) after diagnosis of VUR and 4-6 months after febrile UTI.
- **It revealed renal scarring in 120 (77.9%) cases.**
- Urodynamic studies showed abnormal findings consistent with voiding dysfunction in **16 of 70 cases (22.85%)**.
- Urologic abnormalities associated with secondary VUR such as neurogenic bladder and posterior urethral valve each were reported in 5 (2.5%) of patients.

Discussion:

- Al Qahtani et al¹ (2020) evaluated 67 children < 15 years with bilateral high grades VUR with **F/M ratio of 0.55**.
- Mean age of patients at presentation was **7 months** and **61% were asymptomatic** and evaluated because of prenatal hydronephrosis.
- **Urinary tract infection**, chronic kidney diseases and neonatal sepsis were the first presentation in **21%**, 10% and 3% of the cases, respectively.
- Renal scarring was reported **in 61%** of cases at the time of diagnosis of VUR.
- They reported **mild and severe hydronephrosis in 53% and 38%** of cases, respectively.

1) Al Qahtani W , Sarhan O , Al Otay A , El Helaly A , Al Kawai F . Primary Bilateral High-Grade Vesicoureteral Reflux in Children: Management Perspective. Cureus.2020;2(12):e12266.

Discussion:

- In contrast to this study, in our series the **F/M ratio was 1.18**.
- Patients were older at presentation (mean age **40.3 months**).
- Majority of cases were symptomatic at the time of diagnosis (**UTI, 80.7% compare to 21%** in study by Al Qahtani et al).
- Renal scar was reported **in 77.9%** at first evaluation (vs . **61%** in study by Al Qahtani et al) .
- We found **mild to moderate hydronephrosis in 61.4%** and **severe hydronephrosis in 14.7%**, respectively.

Conclusion:

- We defined that UTI was the most common presentation in our series ; it means that unfortunately we diagnose VUR when it is symptomatic.
- However abnormal findings in kidney ultrasound was common, normal kidney US was not uncommon (**23.4%**). As a result , it seems that normal kidney US cannot rule out presence of high grade VUR.
- Hydronephrosis was the most common kidney ultrasound findings.
- Renal cortical damage (renal scar) was common (about 2/3 of cases) at the time of diagnosis of VUR.



**Clinical course of high grades VUR and frequency of new renal scar formation
in one to three year follow – up**


**Mitra Naseri, MD , pediatric nephrologist, associate professor , Mashhad
University of Medical Sciences, Mashhad, Iran**

**Nooshin Tafazoli, MD , Mashhad University of Medical Sciences, Mashhad,
Iran**

Objective :

To define the clinical course of high-grade VUR in one to three- year follow- up and also determine frequency of new renal scar development during follow up.

Methods & Materials

A cross study was performed in a  9-year period (March 2003 to March 2022), patients < 18 years with diagnosis of high grade VUR enrolled the study if they underwent radionuclide cystography for ≥ 12 months after diagnosis of VUR.

Those who performed Tc 99m-DMSA scan as baseline and during follow up evaluated for new renal scar formation.

Results:

- A total of 83 individuals entered including 42(50.6%) girls and 41 boys (49.4%). They aged 47.93 ±41.8 months.
- Most of patients were diagnosed following pyelonephritis (%54.2) .
- In 24 patients (28.9%) both kidneys were affected by high grade VUR.



- Baseline DMSA scan was performed in 81 patients (97.6%) & in 43 patients (51.8%) control scan was performed in follow- up.
- Renal scar in the first scan was reported in 39(48.1%) & 44 (54.3%) right & left KUUs, respectively.
- Patients followed-up for median 34 months (IQR, 17.6-59 months).

Table 1: Changing in the grade of VUR in 11 patients; 16 KUUs with high grades VUR (one year after diagnosis)

Change in grade of VUR KUUs¹ with high grade VUR	No change N (%)²	Change to moderate VUR N (%)	Change to Mild VUR N (%)	Resolution of VUR N (%)
Right KUUs	2 (12.5)	0	1(6.25)	0
Left KUUs	1(6.25)	2(12.5)	0	0
Both kidneys	6 (37.5)	2(12.5)	0	2(12.5)
Total KUUs; N (%)	9 (56.25)	4(25)	1(6.25)	2(12.5)

1) Kidney ureter unit

2) Number and % of total KUUS affected by high grade VUR

Table 2: Changing in the grade of VUR in 41 patients; 49 KUUs with high grades VUR (13-24 months after diagnosis)

Change in grade of VUR KUUs¹ with high grade VUR	No change N (%)²	Change to moderate VUR N (%)	Change to Mild VUR N (%)	Resolution of VUR N (%)
Right KUUs	10(20.4)	3(6.1)	0	1(2.05)
Left KUUs	11(22.45)	5(10.2)	2(4.1)	1(2.05)
Both kidneys	10(20.4)	5(10.2)	0	1(2.05)
Total KUUs ; N(%)	31(63.25)	13(26.5)	2(4.1)	3(6.15)

1) Kidney ureter unit

2) Number and % of total KUUS affected by high grade VUR

Table 3: Changing in the grade of VUR in 24 patients; 34 KUUs with high grades VUR (25-36 months after diagnosis)

Change in grade of VUR KUUs¹ with high grade VUR	No change N (%) ²	Change to moderate VUR N (%)	Change to Mild VUR N (%)	Resolution of VUR N (%)
Right KUUs	2(5.9)	1(2.9)	0	1(2.9)
Left KUUs	4(11.8)	0	0	6 (17.65)
Both kidneys	8(23.5)	6 (17.65)	2(5.9)	4(11.8)
Total KUUs ; N(%)	14(41.2)	7(20.55)	2(5.9)	11(32.35)

1) Kidney ureter unit 2) Number and % of total KUUS affected by high grade VUR .

In 3-year follow-up:

- **Resolution of high grade VUR was reported in 16 of 99 KUUs (16.2%).**
- **Three cases had the resolution of VUR after anti-reflux surgery , thus in 13 (15.7%) spontaneous resolution was occurred .**
- **54 KUUs (54.5%) had no change in grade of VUR.**
- **in 29 KUUs (29.3%) the grade of VUR decreased.**
- **Totally 15 cases (18.1%) performed their first DRC or repeated DRC after 3 years.**

- **Tc 99 m-DMSA scan was repeated in median 5 months (IQR, 1-12.25 months).**

indications for repeated scan were:

1) Pyelonephritis during follow-up .



2) Evidence suggestive of new scar .

3) Evidence of new cortical damage on kidney US.


Table 4: changes in renal scarring during the follow-up (43 patients, 84 KUUs) ¹

Change in stage of renal scar Kidney unit	No change N (%)	Increase in stage of scar; N (%)	Decrease in stage of scar; N (%)	New scar N (%)	Resolution of uptake defect	Total kidney units
Right kidney	20(23/8)	12(14.3)	5(5.9)	2 (2.4)	3(3.6)	42(50)
Left kidney	19(22.6)	8(9.5)	11(13.1)	3 (3.6)	1(1.2)	42(50)
Total units	39(46.4)	20(23.8)	16 (19)	5(6)	4 (4.8)	84(100)²

1) Kidney ureter units ;2) One patient had left renal agenesis and the result of scan in one kidney unit was not clear

Scar progressed or new scars formed in 23 kidney units (34.8%) during the follow-up.

Table 5: Complication of high grade VUR at follow-up

Complication	N (%)
Febrile urinary tract infection	28 (33.7)
Cystitis	22 (26.5)
Chronic kidney disease on supportive treatments	 4(4.8)
Hypertension	3 (3.6)
End stage renal disease	1(1.2)
Total cases	83 (100)

- **As Table 5 shows in 8 cases (9.6%) complications of reflux nephropathy occurred.**

- **Totally in 3-year follow-up, 23 cases (27.7%) underwent surgery including anti-relax surgery (N=15, 65.2%) or endoscopic repair of VUR (n=8, 34.8%).**

- **Anti-relax surgery resulted to VUR resolution in 3(20%) and decrease in grade of VUR in 2 patients (13.3%).**

- **Endoscopic repair of VUR resulted to decrease in grade of VUR in 2 patients (25%).**

Discussion:

- **Filho et al study ¹(2007) showed that spontaneous resolution is directly related to VUR severity and is less likely to occur in grades IV and V.**
- **They reported spontaneous resolution of high grade VUR in 16.5 % of cases during follow-up. We found spontaneous resolution of VUR in 15.6% of KUUs during 3-year follow-up.**
- **Alsaywid et al.² (2010) reported new scar development in 10 -15% of boys with high grade VUR presented by prenatal hydronephrosis and UTI, respectively. In our series new scar was found in 2 girls (4.8%) and 2 boys (4.9%), increased in stage of renal scar was reported in 10 girls (23.8%) and 9 boys (22%).**

1) Filho MZ, Calado AA, Barroso jr U, Amaro JL. Spontaneous resolution rates of vesicoureteral reflux in Brazilian children: a 30-year experience. *Int Braz J Urol.*2007; 3 (2):204-12.

2) Alsaywid BS , Saleh H, Deshpande A , Howman-Giles R , H Smith GH . High grade primary vesicoureteral reflux in boys: long-term results of a prospective cohort study. *J Urol.* 2010; 184(4 Suppl):1598-603.

Conclusion:

- We found that spontaneous resolution of high grade VUR in 3- year follow-up is low (about 16% of KUUs).
- Also decrease in grade of VUR is not so common (30% of KUUs).
- Additionally about 1/3 of KUUs had progression of renal scars or developed new scarring.
- It seem that surgical intervention should be considered earlier to decrease the new scar development.

**Prevalence of vesicoureteral reflux and high grade VUR in
children with postnatal detected hydronephrosis**

**Mitra Naseri, MD , pediatric nephrologist, associate
professor , Mashhad University of Medical Sciences,
Mashhad, Iran**

**Banafsheh Farzadfar, MD, Mashhad University of Medical
Sciences, Mashhad, Iran**

Objective:

- The aim of this study was to determine the prevalence of vesicoureteral reflux (VUR), and high grades VUR in children with postnatal detected hydronephrosis, and to define factors associated with VUR and high grades VUR.


Materials & Methods :

- A cross-sectional retrospective study in children <18 years with hydronephrosis detected after birth was designed from March 2009 to March 2019.
- Children referred to the nephrology clinic of Dr. Sheikh children hospital or nephrology office enrolled if they had no nephrolithiasis, hydronephrosis persisted after bladder emptying and also patients had underwent VCUG .

Results:

- Of 482 eligible patients 303 cases (62.9%) had the inclusion criteria and enrolled.
- They included 55.1% girls, the patients aged 51.68 ± 43.68 months.
- Mild, moderate and severe hydronephrosis were found in 68.3%, 17% and 14.7% of patients, respectively.
- Hydronephrosis was bilateral in 28% of cases and hydro ureter was reported in 19.8% of patients.
- Totally 135 case (44.5%) had VUR, including 43 patients (14.2% of total cases) with high grades VUR.

Table 1: Reasons for doing kidney ultrasound in the patients

Clinical manifestation	N (%)
urinary tract infection	111(36.6)
Abdominal pain	58(19.2)
Dysuria	28(9.2)
Vomiting	26(8.6)
Daytime incontinence	21(6.9)
Enuresis	21(6.9)
Asymptomatic cases 	19(6.3)
Frequency	19(6.3)
irritability	15(5)
Gross hematuria	11(3.6)
History of VUR in siblings	10(3.3)
Straining	8(2.6)
Dribbling	6(2)
Abnormal findings in abdominal examination	4(1.3)
\Microscopic hematuria	(1.3)
Intermittency	3(1)
Total cases	303(100)

Patients with vs . cases without VUR

- Mean age at presentation was lower in cases with vs. those without VUR (43.9 ± 40.16 months compared to 52.45 ± 41.68 months respectively; $P= 0.049$).
- There was no significant difference considering gender (57.8% of girls and 42.4% of boys had VUR, $P= 0.404$).
- Abnormal urinalysis, positive urine culture at presentation and presentation with UTI were significantly more frequent in cases with vs. those without VUR ($P < 0.05$ for all).
- Totally 37.9% and 23.9% of cases with and without VUR, respectively had UTI at initial assessment ($P=0.011$).
- Presentation with abdominal pain or frequency were significantly more common in those without VUR ($P= 0.001$ and 0.009 , respectively).

- Considering the severity of hydronephrosis, there was no significant difference between cases with compared to those without VUR ($P > 0.05$ for all) .Mild, moderate and severe hydronephrosis were reported in 71.1%, 20% and 13.3% of VUR population compared to 67.3% ,18.5% and 17.3% of cases without VUR ; respectively .

Comparing characteristics of cases with high grade Vs mild to moderate VUR


- No significant difference considering age, gender, abnormal urinalysis , positive urine culture, clinical presentation , and transient  compared to persistent hydronephrosis was not present between 2 groups ($P > 0.05$ for all).
- **Mild hydronephrosis was significantly more prevalent in those with mild to moderate VUR, moderate hydronephrosis and hydro ureter were significantly more common in cases with high grades VUR ($P < 0.05$ for all).**

Table 2 : Comparing the degree of hydronephrosis in patient with high grade vs. cases with VUR grades I-III

Degree of hydronephrosis		High grade VUR ¹ (grades Iv & V) ;N (%)	Mild to moderate VUR (Grades I-III);N (%)	P value
Mild (APRPD ² =5-10mm)	Yes	25 (58.1)	71(77.2)	0.023
	No	18 (41.9)	21 (22.8)	
Moderate(APRPD=11-15 mm)	Yes	13 (29.2)	14 (15.2)	0.042
	No	30(69.8)	78 (84.8)	
Severe (APRPD> 15 mm)	Yes	9 (20.9)	9 (9.8)	0.076
	No	34 (79.1)	83(90.2)	
		43 (100)	92(100)	

1) Vesicoureteral reflux 2) Anteroposterior renal pelvis diameter

Association of hydronephrosis with hydro ureter (Ureteral diameter ≥ 4 mm)

- Hydro ureter was found in 60 patients (19.8%) and 78 of 606 kidney ureter units (12.9%).
- Hydro ureter was found 24.4% of patients with and 16.07% of cases without VUR (p= 0.069).
- It was significantly more prevalent in cases with high grade vs. mild to moderate VUR (46.5% compared to 14.1%, respectively; **P < 0.001**).

Discussion:

- Vesicoureteral reflux is responsible for 20-30% of Post-natal hydronephrosis (neonatal hydronephrosis)¹.
- The majority of studies about the etiologies of hydronephrosis focus on prenatal hydronephrosis.
- Vesicoureteral reflux accounts for 15- 19 % of prenatal hydronephrosis.^{2, 3}



- 1) Marra G, Barbieri G, Moioli C, Assael B, Grumieri G, Caccamo M. Mild fetal hydronephrosis indicating vesicoureteric reflux. *Archives of Disease in Childhood-Fetal and Neonatal Edition*. 1994; 70(2):F147-F50.
- 2) Zee RS, Herbst KW, Kim C, McKenna PH, Bentley T, Cooper CS, et al. Urinary tract infections in children with prenatal hydronephrosis: A risk assessment from the Society for Fetal Urology Hydronephrosis Registry. *Journal of pediatric urology*. 2016; 12(4):261. E1- e7.
- 3) Gloor J, Ramsey P, Ogburn P, Danilenko-Dixon D, DiMarco C, Ramin K. The association of isolated mild fetal hydronephrosis with postnatal vesicoureteral reflux. *The Journal of Maternal-Fetal & Neonatal Medicine*. 2002; 12(3):196-200.

Conclusion:

- Vesicoureteral reflux is a common findings in children with hydronephrosis.
- Factors significantly associated with VUR including abnormal urinalysis, positive urine culture at presentation and presentation with UTI.
- Presentation with abdominal pain or frequency significantly associated with absence of VUR.
- Also moderate hydronephrosis significantly associate with high grade vs. mild to moderate VUR.
- In addition hydro ureter is significantly more frequent in cases with high vs mild to moderate grades VUR.

