IJKD KIDNEY DISEASES

Diagnostic Values of Kidney Ultrasonography for Vesicoureteral Reflux (VUR) and High Grade VUR

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Introduction. Vesicoureteral reflux (VUR) is a well-known risk factor for urinary tract infection (UTI). We aim to define diagnostic values of kidney ultrasonography (US) as a predictor of VUR and high grades VUR in children presented by UTI.
Methods. This retrospective study was conducted during October 2003 to 2016. Children aged ≤ 18 years with history of UTI who had underwent kidney US and direct cystography [voiding cystourethrography (VCUG) or radionuclide cystography (RNC)] enrolled in the study. Diagnostic values of hydronephrosis, hydro ureter, renal scaring, hydroureteronephrosis, decreased kidney size and abnormal kidney US for diagnosis of VUR and high grades VUR (grades IV-V) were evaluated.
Results. Hydro-ureter, renal scaring, and hydroureteronephrosis were significantly more prevalent in VUR^+ versus VUR^- cases, also in higher grades compared with lower grades (grades I-III) VUR ($P < .05$ for all). Additionally, hydronephrosis was more common in VUR^+ compared with VUR^- patients ($P < .0001$). As a predictor of VUR and higher grades of VUR, abnormal kidney US had the highest sensitivity (24.87% and 40.84%, respectively), abnormal kidney US and hydro ureter reached the highest NPV (70.42% and 81.27%, respectively), hydroureteronephrosis and hydro ureter showed the highest accuracy (68.51% and 82.21%, respectively) .
Conclusion. Kidney US is a valuable screening test, abnormal renal US significantly increases the probability of VUR and high grades VUR , but if used as the only screening test , about 2/3 and 1/3 and 20% of VUR , high grades VUR and grade V VURs will be missed.

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INTRODUCTION

Urinary tract infection (UTI) is common in pediatric age with prevalence rate of 8 and 2% in girls and boys, respectively.[1] Vesicoureteral reflux (VUR), a well-known risk factor for childhood UTI, accounts for up to 25% of all causes of end-stage renal disease (ESRD) in children.[2] American Academy of Pediatrics (AAP) guideline for UTI in infants between 2 to 24 months recommends voiding cyst urethrogram (VCUG) or radionuclide cystography (RNC) following the first febrile UTI if the kidney US is abnormal.[3] Low compliance for performing VCUG because of its invasive nature which requires urethral catheterization is an important challenge.[4] In contrast, no radiation exposure and noninvasive nature make Ultrasonography (US) the preferred method for assessment of urinary tract anatomy.[5] However diagnostic value of kidney

US as a predictor of VUR remains controversial. Whereas some studies reported a low diagnostic value [6,7], other investigations claimed that it can predict VUR accurately.[8,9]

This study was carried out to define the diagnostic values of abnormal kidney US findings (hydronephrosis, hydro ureter, decreased kidney size, renal scarring, hydroureteronephrosis) as a predictor of VUR and high grades VUR. Direct cystography (VCUG or RNC) was used as the gold standard imaging for diagnosis of VUR. Diagnostic accuracy measures including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) were evaluated.

MATERIALS AND METHODS

A cross-sectional, retrospective study was designed on a database of patients aged 0 to 18 years with history of UTI who underwent both kidney-bladder US and direct cystography (VCUG or RNC). Those with missing details of abnormal kidney US findings (such as side of renal scar in unilateral scarring) were excluded. Cases were referred to nephrology clinic of a tertiary pediatric academic center. This study took place between October 2003 to 2016. Growth of a single organism with a colony forming unit (CFU) of $\geq 10^5$ was considered as a positive culture and diagnosed as UTI. Regarding the toilet-trained patients with symptomatic UTI (e.g., fever and lower urinary tract symptoms), a growth of $\geq 10^4$ CFU of a single urinary pathogen was regarded as a positive culture. In the samples obtained via urinary bags, the presence of leukocyturia, in addition to positive urine culture, was necessary for the diagnosis of UTI. Leukocyturia was defined as a white blood cell count of (WBC) ≥ 5 (or approximately 25 WBCs per liter) in the high-power field (HPF) of urinary sediment in a centrifuged urine sample.

Three types of infections were determined based on the presence or absence of fever (≥ 38.5 °C) or symptoms of UTI, febrile UTI, cystitis, and asymptomatic bacteriuria (ABU). The latter ones were defined as the presence of an organism with a CFU of $\geq 10^5$ in two consecutive urine specimens without any clinical signs or symptoms of UTI.[10] We recommended VCUG in any case of pyelonephritis irrespective of the age or kidney US findings. Indication of VCUG in those with cystitis were: girls aged < 5 years with first and > 5 years with recurrent cystitis, all boys regarding to their ages, in case of abnormal kidney US or those with prenatal hydronephrosis.

After 2015, all cases with recurrent pyelonephritis considered for VCUG (regarding to their ages and kidney US findings). In cases with first episodes of pyelonephritis, top-down approach was used. Patient with normal kidney US, recommended to do Technetium- 99m dimercaptosuccinic acid (TC99m-DMSA) scan. If the renal scan showed uptake defects, VCUG was performed. Also, patients with cystitis recommended to do VCUG in case of abnormal kidney US, recurrent cystitis or single episode of cystitis in patients with history of prenatal hydronephrosis even if the kidney US was normal.

Our series consisted of a heterogeneous group of patients, 486 (55.5%) and 389 patients (44.5%) had a single or recurrent episodes of UTI, respectively. Majority of our cases had not underwent screening prenatal renal US. Prenatal abnormal renal US (prenatal hydronephrosis) was reported in 12 (1.4%) cases. A total of 875/1243 (70.4%) children included in this study. The study was approved by local ethics committee (ID code: IR.MUMS.MEDICAL .REC.1397. 169). Kidney US was done within first month after diagnosis of UTI (in outpatient series) and within first day after hospitalization (mean time of seven days for both groups). The time for performing VCUG or RNC was different from few days after cessation of fever in febrile inpatient subjects to days or months after diagnosis of UTI in outpatient cases (mean time of one month). Routinely VCUG was recommended for diagnosis of VUR, but in a few cases (n = 27, 3.08%), RNC was performed before referring to the nephrology clinic.

Using VCUG or RNC findings of reflux as the gold standard, diagnostic accuracy measures including sensitivity, specificity, positive predictive value, and negative predictive value were calculated for hydronephrosis, hydro ureter, decreased kidney size ,renal scarring , hydroureteronephrosis , and abnormal kidney US (any of above-mentioned findings).

Hydronephrosis and Hydro ureter defined as anteroposterior diameter of renal pelvic ≥ 5 mm, and abnormal dilation (> 4 mm) of the ureter, respectively. Renal scarring assessed using the following criteria: 1) proximity of sinus echoes to cortical surface, 2) loss of pyramids, 3) irregular outline, and 4) loss of definition of capsular echo.[11]

The international system of radiographic grading of VUR[12] was used (based on VCUG), and the term high grades VUR used for description of VUR grades IV–V.[13] Mild, moderate, and high grades VUR defined as VUR grades I-II, grade III and grades IV-V; respectively. Based on RNC, VUR was defined as mild, moderate and severe (high grade). Regarding presence or absence of VUR, patients were divided into VUR^+ and VUR^- cases, respectively. The kidney ultrasonography apparatuses used were Adra model, Siemens, Berlin, Germany, Esoate Class C (Italy) or Samsung H60 (Korea). Kidney ultrasonography was performed using 5, 7.5, and 10 MHz probes.

As the study was performed in a longtime period, doing kidney-bladder US examination by one radiologist was not possible. Majority of kidney ultrasounds (about 95%) were done by 4 pediatric expert radiologists. We did not check inter-rater reliability and agreement. To improve the reliability of US, we tried to repeat it, so that every patient had at least two kidney US examinations which were performed by two different radiologists. In majority of cases, results were similar or the differences in kidney US reports were insignificant.

Nevertheless US examination is operator dependent, and results depend on the experience of the operator , a new study showed a very high rate of inter-rater agreement in US examination performed by trained general practitioners compared with radiologists.[14]

Sample Size

A sample size of 875 patients calculated according to sensitivity of US in diagnosis of VUR = 48% which was reported in Preda study,[9] prevalence of VUR in children with UTI = 50%[13] and $\alpha = 0.05$.

Statistical Analysis

Statistical analysis was performed using SPSS version 16 (SPSS Institute, Inc., Chicago, IL, USA). All experimental values were presented as means ± standard deviation (SD). Comparison between groups was done by chi square or independent t test, and P value < .05 was considered statistically significant. Diagnostic values of sensitivity, specificity, PPV, NPV, and accuracy were calculated according to following formulas:

Sensitivity = True Positive (TP) / (TP + False Negative (FN))

Specificity = True Negative (TN) / (TN + False Positive (FP))

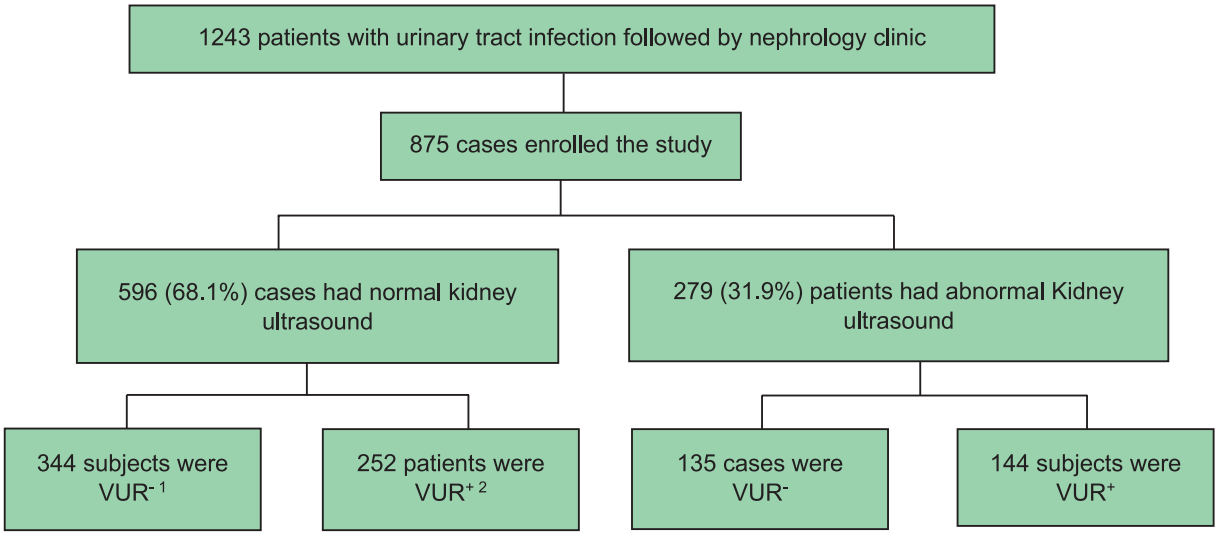
PPV (Positive Predictive Value) = TP / (TP+FP)

NPV (Negative Predictive Value) = TN / (TN+FN)

Accuracy = (TP + TN) / (TP + TN + FP + FN)

RESULTS

Totally 875 of 1243 patients enrolled in the study, 757(86.5%) and 118 (13.5%) cases were girls and boys, respectively. They aged 3 days to 214 (33.19 ± 33.15) months. Figure presents a review of main imaging findings in enrolled cases. Imaging



Imaging Findings in Enrolled Patients
[1]Patients who had not vesicoureteral reflux.
[2]Patients who had vesicoureteral reflux.

investigations (VCUG or RNC) revealed VUR in 396/875 (45.25%) patients, and 579/1750 (33.08%) kidney ureter units (KUUs). Age at first episodes of UTI in VUR^- and VUR^+ cases were 39.66 ± 36.07 and 25.53 ± 27.87 months, respectively ($P < .001$) which indicates that VUR^+ versus VUR^- cases were significantly younger at the time of their first UTI episode.

Overall, 325/757 (42.9%) girls and 71/118 (60.1%) boys had VUR. It means that frequency of VUR was significantly higher among boys compared with girls ($P = .0001$). Additionally, 62/325 (19.07%) girls and 29/71 (40.84%) boys in VUR^+ population had high grade VUR. High grade VUR was significantly more prevalent in boys compared with girls ($P < .0001$). The age at VUR presentation was not significantly different between genders (25.49 ± 25.78 in girls and 24.92 ± 35.24 in boys, $P < .05$).

Of 1750 KUUs (n = 875 patients), 1171 (66.9%) and 579 (33.1%) units were non-refluxing and refluxing, respectively. Non refluxing units included 958 (n = 479 patients) plus 213 KUUs in VUR^- cases, and those with unilateral VUR (n = 213 cases), respectively. Also, high grades VUR (grades IV & V) were found in 91/875 patients (10.4%), and 142/1750 (8.11%) KUUs. Totally 23% of VUR^+ population (91/396 subjects) and 24.5% (142/ 579) of refluxing KUUs had high grades VUR.

Unilateral VUR was reported in 213/396 (53.8%) VUR^+ patients, and 40/91 (44%) cases with high grades VUR. Bilateral VUR found in 46.2% (n = 183) VUR^+ subjects and 56% (n = 51) cases with high grades VUR. In VUR^+ patients, 310 (53.55%) and 269 (46.45%) KUUs in left and right sides involved, respectively. High grades VUR were found in 75/142 (52.8%) and 67/142 (47.2%) KUUs in left and right sides, respectively.

Kidney Ultrasound Findings

Kidney US was normal in 68.1% (n = 596) and abnormal findings were reported in 31.9% (n = 279) of total. The most frequent abnormalities were hydronephrosis [240/875 (27.4%) patients and 307/1750 (17.5%) KUUs], followed by hydro ureter [59/875 cases (6.75%) and 73/1750 (4.17%) KUUs], and hydroureteronephrosis [53 patients (6.05%) and 64/1750 (3.65%) KUUs] (Table 1).

Hydronephrosis, hydro ureter, and hydroureteronephrosis were significantly more prevalent in refluxing compared with non-refluxing KUUs ($P < .0001$ for all) (Table 1). Meanwhile they were the most prevalent abnormal findings in high grades VUR which reported in 30.3, 29.6, and 19% of KUUs; respectively. Hydro-ureter, hydroureteronephrosis and renal scaring were significantly more prevalent in high grade versus low grade VUR ($P < .0001$, .001, and .001; respectively) (Table 2). Abnormal kidney US was more prevalent in VUR^+ versus VUR^- patients (36.4% compared with 28.2%, respectively; $P = .011$), and also in cases with high versus low grade VUR (63.7% compared with 28.2%, respectively; $P < .0001$) (Table 3).

Diagnostic Value of Kidney US Compared with Direct Cystography

Diagnostic values of each abnormal kidney US finding for VUR and high grade VUR were calculated separately (Tables 4 and 5). The highest sensitivity, specificity, PPV, NPV, and accuracy for diagnosis of VUR belonged to abnormal kidney US (24.87%),

Table 1. Comparing Kidney Sonography in Refluxing with Non–refluxing Kidney Ureter Units

Abnormal Kidney Ultrasound Finding	Refluxing KUUs† n (%)	Non-refluxing KUUs n (%)	Total KUUs n (%)	*P*‡
Hydronephrosis	140 (24.18)	167 (14.26)	307 (17.55)	< .0001
No Hydronephrosis	439 (75.82)	1004 (85.74)	1443 (82.45)	
Hydro-ureter	45 (7.78)	28 (2.4)	73 (4.17)	< .0001
No Hydro-ureter	534 (92.22)	1143 (97.6)	1677 (95.83)	
Decreased Kidney Size	10 (1.7)	22 (1.9)	32 (1.82)	> .05
Normal Kidney Size	569 (98.3)	1149 (98.1)	1718 (98.18)	
Renal Scaring	17 (2.94)	11 (0.94)	28 (1.6)	> .001
No Renal Scar	562 (97.06)	1160 (99.06)	1722 (98.4)	
Hydroureteronephrosis	46 (7.95)	18 (1.55)	64 (3.65)	< .0001
No Hydroureteronephrosis	533 (92.05)	1153 (98.45)	1686 (96.35)	
Total KUUs	579 (100)	1171 (100)	1750 (100)	—

†Kidney Ureter Units
‡Chi square test was used for analysis.

Table 2. Kidney ultrasound findings in kidney ureter units with high versus low grade VUR

Ultrasound Finding	High Grade VUR† KUUs§ (%)	Low Grade VUR‡ KUUs (%)	*P*#
Hydronephrosis			
Yes	43 (30.3)	97 (22.2)	> .05
No	99 (69.7)	340 (77.8)	
Hydro-ureter			
Yes	42 (29.6)	3 (0.7)	< .0001
No	100 (70.4)	434 (99.3)	
Decreased Kidney Size			
Yes	3 (2.1)	7 (1.6)	> .05
No	139 (97.9)	430 (98.4)	
Renal Scarring			
Yes	10 (7.05)	7 (1.6)	= .001
No	132 (92.95)	430 (98.4)	
Hydroureteronephrosis			
Yes	27 (19)	19 (4.35)	= .001
No	115 (81)	418 (95.65)	
Total KUUs	142 (100)	437 (100)	

†Grades IV & V of Vesicoureteral Reflux
‡Grades I-III of Vesicoureteral Reflux
#Chi square test was used for analysis.
§Kidney Ureter Units

renal scaring (99.06%), hydroureteronephrosis (71.87%), abnormal kidney US (70.42%), and hydroureteronephrosis (68.51%); respectively (Table 4). For high grade VUR, abnormal kidney US showed the highest sensitivity (40.84%). The highest specificity, PPV, NPV, and also accuracy belonged to hydro ureter (99.31%, 93.33%, 81.27%, and 82.21%; respectively) (Table 5).

DISCUSSION

Direct cystography is an invasive method which needs bladder catheterization. Furthermore, radiation exposure is another concern especially when VCUG is selected for diagnosis of VUR. Different investigations had been conducted to define whether kidney US is a reliable method for selecting patients who would benefit from VCUG.

In current study, 875 children with history of UTI evaluated. We aimed to define the diagnostic values of kidney US findings versus direct cystography (VCUG and RNC) in diagnosis of VUR and also high grade VUR. Based on our results, the probability of finding abnormal kidney US in patients with VUR and high grade VUR was about 36% and 63 %, respectively. It means that we could miss VUR and high grade VUR in 2/3 and 1/3 of patients if kidney US was used as the only screening test.

Diagnostic value of kidney US as a predictor of VUR in children with febrile UTI have been evaluated by different studies [15-18]. These studies focused on patients aged < 2 years[12,15] or < 5

Table 3. Abnormal Kidney Ultrasound and Its Diagnostic Value for Predicting VUR and High Grade VUR

Variable	VUR- Cases (n = 479)	VUR+ Cases (n = 396)	*P*	High Grades‡ VUR (n = 91)	Low Grades VUR# (n = 305)	*P*
Abnormal Kidney US†	135 (28.2)	144 (36.4)	< .05	58 (63.7)	86 (28.2)	< .0001
Normal Kidney US, n (%)	344 (71.8)	252 (63.6)		33 (36.3)	218 (71.8)	
	Diagnostic Value of Abnormal Kidney US for Predicting VUR			Diagnostic Value of Abnormal Kidney US for Predicting High Grade VUR		
Sensitivity	24.87			40.84		
Specificity	88.47			80.09		
PPV	51.61			40		
NPV	70.42			80.64		
Accuracy	67.42			70.46		

†Presence of One or More Abnormal Kidney Ultrasound Findings
‡VUR Grades IV & V
#VUR Grades I-III

Table 4. Diagnostic Value of Kidney Ultrasonography Compared to Direct Cystography† for Diagnosis of VUR‡

Kidney Ultrasonography Findings	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Hydronephrosis	24.17	85.73	45.60	69.57	65.37
Hydro-ureter	7.77	97.60	61.64	68.15	67.88
Renal Scarring	2.93	99.06	60.71	67.36	67.25
Decreased Kidney Size	1.72	98.12	31.25	66.88	66.22
Hydroureteronephrosis	7.94	98.46	71.87	68.38	68.51

†It includes voiding cystourethrography and direct radionuclide cystography.
‡Vesicoureteral Reflux

Table 5. Diagnostic Values of Kidney Ultrasonography Versus Direct Cystography† for Diagnosis of High Grade VUR‡

Ultrasonography Results	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy
Hydronephrosis	30.28	77.80	30.71	77.44	66.14
Hydro ureter	29.57	99.31	93.33	81.27	82.21
Renal scarring	7.04	98.39	58.82	76.51	75.99
Decreased kidney size	2.11	98.39	30	75.57	74.95
Hydroureteronephrosis	19.01	95.65	58.69	78.42	76.85

†It includes voiding cystourethrography and direct radionuclide cystography.
‡Vesicoureteral Reflux

years.[13,14] The main advantage of the current study was that our enrolled cases consisted of all pediatric ages (≤ 18 years) with either pyelonephritis (n = 595, 68%) or cystitis (n = 268, 30.6%). In 12 cases (1.4%) parents were not sure about history of febrile UTI. Presentation as febrile UTI was reported in 297/392 (75.75%) VUR^+ and 298/471 (63.25%) VUR^- cases ($P < .0001$).

We found VUR in 95/268 (34.4%) and 297/595 (49.9%) patients with history of cystitis and pyelonephritis, respectively ($P < .0001$). Despite significantly higher prevalence of VUR among cases with pyelonephritis, high grade VUR was as frequent in cases with pyelonephritis as those with cystitis [68/297 (22.9%) and 21/95 (22.1%), respectively; $P > .05$]. In 561/595 (94.3%) patients with history of febrile UTI, the first episode of infection presented with pyelonephritis and in the remaining , with recurrent infections associated with fever. Abnormal kidney US was as common in patients with pyelonephritis as those with cystitis [177/561 (31.55%) and 84/275 (30.54%) patients, respectively ($P > .05$).

Study in children younger than 2 years presented with febrile UTI[15] demonstrated that hydronephrosis and wall thickening of the renal collecting system significantly predicted VUR ($P < .05$, and $< .05$; respectively). However, their sensitivity and NPV were 85.7%, 64.2%, 93.3%, and 89.7%; respectively. In our series the sensitivity and NPV of hydronephrosis for diagnosis of VUR and high grade VUR found to be 24.17% and 69.57%, 30.28%, 77.44%; respectively.

An extended study in 2259 patients with history of UTI showed normal renal bladder US in 75% of cases.[16] They found VUR and high grade VUR in 41.7% and 2.8% of total patients, respectively.[16] However, many kidney US findings significantly were associated with VUR, using different multivariate modeling could not find a predictive model. Finally, they concluded that abnormal finding on kidney US is poor screening test for predicting VUR. In our series 699/875 (79.9%) cases aged < 5 years, including 217 (31.04%) patients with abnormal kidney US. Abnormal kidney US was significantly more frequent in VUR^+ versus VUR^- cases [124/349 (35.5%) and 93/350 (26.6%) patients, respectively; $P = .01$]. 45 out of 73 cases (61.65%) with high versus 79/275 (28.7%) subjects with low grades VUR had abnormal kidney US ($P < .0001$).

One study used database of patients aged < 5 years (n = 134) with a history of UTI. They reported abnormal kidney US and VUR in 25% and 41.7% of cases, respectively.[17] Also, they noted sensitivity, specificity, PPV, NPV, and accuracy of 37%, 81%, 82%, 35%, and 50%; respectively for hydronephrosis as a predictor of VUR. Our series consisted of children aged 3 days to 214 (33.19 ± 33.15) months. We found VUR in 45.25% patients and 33.08% of KUUs. Abnormal kidney US findings were reported in 279/875 (31.9%) subjects. Using hydronephrosis as a predictor of VUR, the calculated sensitivity, specificity, PPV, NPV, and accuracy showed 24.1%, 85.7%, 45.6%, 69.5%, and 65.36%; respectively. Our investigation and study by Kovanlikaya *et al.*[17] both indicate a low sensitivity of hydronephrosis for predicting VUR. Kovanlikaya *et al*,[17] reported a valuable PPV for hydronephrosis (83%) as a predictor of VUR, while in our series it was very low (45.6%). Their calculated sensitivity for hydronephrosis as a predictor of VUR grade IV and V was 76% and 91%, respectively. In current study the sensitivity of hydronephrosis for predicting high grades (both grades IV & V) VUR was 30.28%. Like their series, in our cases hydronephrosis was significantly more prevalent in VUR^+ versus VUR^- cases ($P > .001$ and $< .0001$, respectively).

They found a sensitivity, specificity, PPV, NPV, and accuracy for visualized ureter (hydro ureter) as a predictor of VUR of 13, 97, 92, 32, and 38%;

respectively. Sensitivity, specificity, PPV, and NPV for hydro ureter in current study showed to be 7.7, 97.6, 61.6, and 68.1%; respectively. Both studies (current study and investigation by Kovanlikaya *et al.*) indicate a high specificity for hydro ureter as a predictor of VUR (97 and 97.6%, respectively). We found a low sensitivity for hydroureteronephrosis as a predictor of VUR and high grades VUR (7.94 and 19.01%, respectively).

Kovanlikaya *et al.*[17] reported that normal kidney US is rare in high grade VUR, whereas in current study about 1/3 of patients with high grade VUR had normal kidney US. Hung and colleagues[18] evaluated children aged ≤ 2 years (n = 310) following first febrile UTI to define the diagnostic value of abnormal kidney US in predicting VUR. They considered kidney US abnormal if there was one of the following findings: hydronephrosis with anteroposterior diameter of the renal pelvis ≥ 7 mm, dilatation of the calyces or ureters, thickening of pelvic or ureteral wall, absence of corticomedullary differentiation, renal outline irregularity, and renal hypoplasia. We defined hydronephrosis as anteroposterior diameter of the renal pelvis ≥ 5 mm. Except than hydronephrosis, dilatation of ureter and renal hypoplasia (decreased kidney size), other US parameters were not evaluated in our study. Our enrolled population included cases with first and recurrent UTI, patients with either history of pyelonephritis or cystitis, and enrolled cases were ≤ 18 years. Despite different methodology, the frequency of abnormal renal US in our series was similar with the study performed by Hung *et al.*[18] (31.9 versus 33.9%, respectively), but the prevalence of VUR was higher (45.25 compared with 34.5%). They found hydronephrosis in 17.4% and renal hypoplasia in 5.1% of cases, whereas in our investigation hydronephrosis and decreased kidney size were found in 35.08 and 3.65% of cases, respectively. Of course, as before mentioned our definition for hydronephrosis was different from that used by their study.

Hung *et al.*[18] reported that abnormal kidney US is significantly more prevalent in cases with VUR rather than those without VUR (24.1% in VUR^- and 52.3% in VUR^+ cases ; $P < .001$). Our investigation revealed similar results, 28.2 % of VUR^- and 36.4 % of VUR^+ cases had abnormal kidney US findings ($P < .05$). In their series the sensitivity and NPV of abnormal kidney US as a predictor of VUR and VUR grades III-V (moderate to high grades) were 52.3 and 75.1%, 68.4 and 87.8%; respectively. We found sensitivity of 24.87% and NPV of 70.42% for abnormal kidney US as a predictor of VUR, and 40.84 and 80.64 % for VUR grades IV-V; respectively. Higher sensitivity of abnormal kidney US in mentioned study compared with our investigation might be due to different methodology. They reported abnormal kidney US in all cases with VUR grade V. We found VUR grade V in 34/875 (3.9%) cases, which was bilateral in 50% of subjects, and associated with abnormal kidney US in 79.4% of patients (n = 27). It means that if kidney US was the only screening test, we would miss nearly 20% of grade V VURs.

Urinary biomarkers have been used for prediction of VUR in pediatric cases.[19,20] Based to these investigations, ratio of urinary neutrophil gelatinase-associated lipocalin (NGAL) to urinary creatinine[19] showed sensitivity of 61% and specificity of 53% for prediction of VUR, whereas urinary ratio of liver-type fatty acid binding protein (L-FABP) to creatinine was not a useful test, but can predict renal scarring, the most concerning complication of VUR .[20]

CONCLUSION

Although abnormal kidney US significantly increases the probability of VUR and especially high grades VUR, using US as the only screening test could end up in missing of VUR , high grades VUR and grade V VUR in about 2/3 and 1/3 and 20% of cases, respectively. Among different abnormal kidney US findings, the highest sensitivity and NPV for predicting VUR belong to abnormal kidney US (24.87 and 70.42%, respectively), and hydroureteronephrosis had the highest accuracy (68.51%). Additionally abnormal kidney US had the highest sensitivity for predicting high grade VUR (40.84%), and the highest NPV and accuracy belong to hydro ureter (81.27 and 82.21%, respectively). It seems that while kidney bladder US and VCUG provide important, but diverse information, they should be considered as complementary techniques.

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