Prediction of Vesicoureteral Reflux by Ultrasonography and Renal Scan in Children

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Abstract

Background. In recent studies, renal ultrasonography and dimercapto-succinic acid (DMSA) scan have a role in predicting vesicoureteral reflux in children with febrile urinary tract infection (UTI). Materials and Methods. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), and negative likelihood ratio (NLR) were defined for ultrasonography and DMSA scan to predict vesicoureteral reflux in 70 children with febrile UTI. Results. Renal ultrasonography sensitivity, specificity, PPV, NPV, PLR, and NLR for vesicoureteral reflux prediction was 0.57, 0, 1, 0, 0.57, and 0.47 and sensitivity, specificity, PPV, NPV, PLR, and NLR of DMSA scan for predicting vesicoureteral reflux was 0.75, 0.9, 0.33, 0.98, 7.5, and 0.27, respectively. Conclusions. Ultrasonography cannot predict the presence of VUR, but DMSA scan has a good sensitivity in this context. Therefore, by observation of DMSA scan results, it can be decided whether to perform VCUG or not.

Keywords

urinary tract infection, diagnostic imaging, vesicoureteral reflux, ultrasonography, 99m Tc DMSA

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Introduction

Urinary tract infection (UTI) is one of the most common bacterial infections in children, accounts for 4% to 8% of childhood febrile illnesses. By the age of 7, 8.4% of girls and 1.7% of boys have symptomatic UTI once or more. Late diagnosis and inadequate treatment of UTI may lead to renal scarring, chronic renal failure and hypertension. The prevalence of renal scarring following acute pyelonephritis is between 15% and 38.2%. The most common risk factor for pyelonephritis in children is vesicoureteral reflux (VUR). Nearly half of the children with renal scars have VUR, also renal scar progression is more prevalent in VUR grade III-V. Voiding cystourethrogram (VCUG) is performed for VUR diagnosis, but it accompanied radiation exposure. VCUG is an invasive procedure and less than half of the children with UTIs have VUR, so researchers are looking for other ways to avoid unnecessary VCUG. One of these strategies is to use ultrasound and dimercapto-succinic acid (DMSA) renal scan for predicting of renal scars. This study was performed to determine the value of renal ultrasound and DMSA renal scan in predicting VUR in children with the first Febrile UTI.

Methods

In this cross-sectional study, we studied infants and children with febrile UTI hospitalized in Qazvin Children’s Hospital affiliated to Qazvin University of Medical Sciences (Qazvin-Iran) in 2018 to 2019. Sample size was calculated 70 febrile UTI children based on two-sided confidence level (1-alfa) equal to 0.95 and at 80% power. Sampling was performed sequentially until the required sample size was completed.

Infants and children aged over 1 month and less than 12 years with the following conditions were included in the study. Clinical and laboratory diagnosis of febrile UTI based on fever with axillary temperature greater than 38°C, symptoms of urinary irritation, abdominal and flank pain. In addition, with urine analysis including:

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white blood cell (WBC) more than 10/µl, positive nitrite and leukocyte esterase, positive urine culture (more than 100,000 colony forming unit (CFU)/ml of a single pathogen in a midstream urine sample or urine bag or 50,000 CFU/ml of a single pathogen via catheter). Exclusion criteria included congenital urinary anomalies in ultrasonography, history of previous UTI and existence of underlying comorbidities.

Ultrasoundography was performed for all patients by an ultrasound transducer (probe), Curve frequency 2.5 MHz, 730PRO, LBN Medical. Renal ultrasonography was reported abnormal when showing hydronephrosis, decreased cortical thickness, and decreased corticomedullary differentiation. Renal scans were performed using a dual-head gamma camera by 140 keV and 99m technetium. Values from anterior, posterior, left, and right views were obtained. All these children had one or more indications to perform VCUG in first febrile UTI (positive urine culture after 48 hours or fever lasted more than 72 hours despite proper antibiotic therapy, abnormal findings in kidney ultrasonography, microbial growth other than Escherichia Coli in urine culture).12

After recording patients’ information including demographic features, symptoms at admission, bacterial growth in urine culture, and antibiotic sensitivity in antibiogram, the results of specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), and negative likelihood ratio (NLR) were recorded in questionnaire prepared.

**Statistical Methods**

Data were analyzed using the SPSS software version 18.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed by means and standard deviations while categorical variables were presented in frequencies and percentages. Findings were compared using the Mann-Whitney U test and Pearson’s correlation coefficient. Statistical test was two-tailed and was considered significant when \( P \) less than .05. Chi-squared analysis was used to determine differences of statistical significance between renal ultrasonography and renal scan with the results of VCUG. Logistic regression analysis showed statistically significant associations between renal scar and DMSA scan.

**Ethical Consideration**

This project was approved by the ethics committee of Qazvin University of Medical Sciences (IR.QUMS.REC.1398.114). All parents were provided information regarding the research method in simple language.

| Table 1. Demographic Features in 70 Children with Febrile UTI. |
| Data | Patients |
|---|---|
| Age (months) | 34.69 ± 3.23 |
| Sex | |
| Female | 65 (92%) |
| Male | 5 (8%) |
| Symptoms at admission | |
| Fever | 70 (100%) |
| Dysuria | 18 (25.7%) |
| Vomiting | 16 (22.9%) |
| Restlessness | 15 (21.5%) |
| Poor feeding | 14 (20%) |
| Abdominal pain | 12 (17.1%) |
| Frequency | 10 (14.3%) |
| Flank pain | 4 (5.7%) |
| Seizure | 4 (5.7%) |
| Incontinence | 1 (1.4%) |
| Bacterial growth in urine culture | |
| Escherichia coli | 60 (85.7%) |
| Klebsiella | 4 (5.7%) |
| Enterococcus | 3 (4.3%) |
| Proteus | 2 (2.9%) |
| Gram positive bacillus | 1 (1.4%) |
| Antibiotic sensitivity in antibiogram | |
| Imipenem | 61 (87.1%) |
| Amikacin | 58 (82.9%) |
| Ceftriaxone | 25 (35.7%) |
| Cefotaxime | 25 (35.7%) |
| Ceftazidime | 23 (32.9%) |
| Gentamicin | 15 (21.4%) |
| Ampicillin | 13 (18.6%) |

Children were included in the study after their parents agreed and signed the informed consent form.

**Results**

Of the 70 children with febrile UTI, 65 (92%) were female with the mean age of 34.69 ± 37.35 months. The range of patient’s age were 1 month to 12 years. Dysuria (18%) was the most common complaint. Escherichia coli 60 (85.7%) was the most common causing bacteria. The highest sensitivity in antibiogram was for imipenem (87.1%) (Table 1). Kidney ultrasound was normal in 40 children (58%) and abnormal in 30 children (42%). DMSA renal scan was normal in 9 children (13%) and shows dysplasia or scar in 61 (87%) patients. The frequency of normal VCUG in children with the first febrile UTI was 56 (80%). No significant relationship was observed between renal ultrasound and VCUG results (\( P > .05 \)) (Table 2). A significant correlation was
observed between DMSA scan and VCUG results ($P < .05$) (Table 2). There was no significant relationship between renal ultrasound and DMSA renal scan ($P > .05$) (Table 3). Kidney sonography sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), negative likelihood ratio (NLR), and positive likelihood ratio (PLR) for VUR prediction was 0.57, 0, 1, 0, 0.57, and 0.47, respectively, and of DMSA renal scan for VUR prediction was 0.75, 0.9, 0.33, 0.98, 7.5, and 0.27, respectively.

Discussion

This study showed that ultrasonography of the kidneys is not able to predict the presence of VUR. In contrast, DMSA renal scan has a good sensitivity to predict the presence of VUR. Therefore, by observing the results of DMSA renal scan, it can be decided whether to perform VCUG or not. Studies in this field are contradictory.13-17 A study by You et al on 38 children under 2 years of age with febrile urinary tract infections reported that normal renal ultrasonography indicates the absence of high-grade VUR and abnormal findings on renal ultrasonography such as: dilatation of the renal collecting system, wall thickening of the renal collecting system, and DMSA scans that was observed significantly the presence of high-grade VUR ($P = .38, .27, \text{and } .1$, respectively).

According to a report of Bayram et al, the normality of ultrasound of the kidney indicates the absence of high-grade VUR. The researchers suggested that VCUG should not be performed unless there is another risk factor. A study performed by Bayram et al14 on 228 patients with urinary tract infections showed that the sensitivity, specificity, positive predictive value, negative predictive value, and odds ratio of renal ultrasonography for predicting VUR were 68%, 80%, 38%, 93%, and 8.2% respectively. In Mohkam et al18 study on 2550 pyelonephritic children, the sensitivity (95% CI), specificity (95% CI), positive predictive value (PPV), and negative predictive value (NPV) of ultrasonography for prediction of renal cortical defect in compare with DMSA scan as gold standard test were 69.2 (62.1-72.6), 89.3 (80.2-94.9, 65.6-70.9), and 81.5 (75.9-84.7) respectively.

Sorkhi et al found that DMSA renal scan alone could not predict VUR by renal ultrasound. In the study of Sorkhi et al,16 the rates of NPV and PPV of DMSA scan or renal ultrasonography for predicting VUR were 44% and 56%, respectively. A study by Balestracci et al on 122 patients aged 3 to 18 years with a urinary tract infection showed that the sensitivity, specificity, negative predictive value, and positive predictive value of DMSA renal scan for the diagnosis of all VUR grades were 93.1%, 75%, 92.3%, and 77.1% and high-grade VUR had sensitivity and NPV 100%. In the study, the researchers found that kidney ultrasonography was abnormal in 53 (43.4%) and 58 patients (47.5%) had VUR. In this study, DMSA renal scan was abnormal in 70 patients (57.4%) and had a significant relationship with each grade of VUR ($P = .0001$) and high-grade VUR ($P = .0001$).17 Thus, the results of our study were similar to findings of Balestracci et al. A study by Sheu et al10 on 473 children with UTI showed that sensitivity and negative predictive value of ($99m$) Tc DMSA scan for predicting dilating VUR is 95.8% and 97.9%, respectively. The researchers referred to the predictive value ($99m$) of Tc DMSA for VUR diagnosis. The results of Lee et al’s study showed that the sensitivity, specificity, positive predictive value, and negative predictive value of DMSA Renal scan for predicting VUR were 88%, 37%, 63%, and 37% respectively. Findings of the study of Lee et al19 is consistent with the present study. The predictive value of DMSA Renal scan for the diagnosis of VUR in children with the first urinary tract infection has been confirmed in the Fouzas study and the findings of these researchers are the same as the present study.11 Jafarzadeh and Jafari20 have shown that the sensitivity and specificity of DMSA Renal scan in predicting VUR are 67% and 44%. A study by Zhang et al on 523 children equal to or less than 2 years of age with a urinary tract infection showed that DMSA scan was a good predictor of VUR and that normalization was likely to rule out VUR. The sensitivity and predictive properties of high-grade VUR in this study were reported to be 97% and 9%.21 In contrast, Mantadakis et al22 reported that it was not possible to decide whether or not to perform

| Table 2. Relationship Between Renal Ultrasonography and DMSA with VCUG Results. |
|-----------------------------------------------|
| VCUG Results | Normal N (%) | Abnormal N (%) | P-value |
|-----------------|---------------|-----------------|--------|
| Renal sonography | Normal        | 48 (42.1)       | 14 (53.8) | .7 |
|                  | Abnormal      | 66 (57.9)       | 12 (46.2) |    |
| DMSA             | Normal        | 18 (15.8)       | 96 (84.2) | .03 |
|                  | Abnormal      | 0               | 26 (100)  |    |
VCUG to diagnose VUR based on the results of renal scanning DMSA.

Conclusions
This study showed that ultrasonography of the kidneys is not able to predict the presence of VUR. In contrast, DMSA renal scan has a good sensitivity to predict the presence of VUR. Therefore, by observing the results of DMSA renal scan, it can be decided whether to perform VCUG or not.

Author Contributions
Conceptualization and Supervision: Banafsheh Arad and Abolfazl Mahyar; data Collection: Mahmoud Vandaie; data Analysis: Sonia Oveisi; Writing Original Draft, review and editing: All authors.

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Table 3. Relationship Between Kidney Ultrasound Results and DMSA Results.

| Renal sonography | Normal N (%) | Abnormal N (%) | P-value |
|------------------|-------------|---------------|---------|
| DMSA             | 14 (53.8)   | 4 (46.2)      | 0.058   |
|                  | 66 (57.9)   | 56 (43.1)     |         |

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