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Original Article

Ultrasound as a diagnostic tool for vesicoureteral reflux grade in children: a comparative study with voiding cystourethrography

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ABSTRACT

Objective: Vesicoureteral reflux (VUR) is a prevalent congenital anomaly in children, with a higher incidence in those with febrile urinary tract infections. Early detection and management of VUR are crucial to prevent reflux nephropathy and its associated complications. This retrospective observational study aimed to evaluate the accuracy and advantages of ultrasonography (USG) in diagnosing VUR grade compared to voiding cystourethrography (VCUG), the gold standard.

Material and Methods: The study included 147 children aged 0-5 years who underwent VCUG for urinary tract infections, as well as antenatal and postnatal hydronephrosis. Patients were categorized into two age groups: 0-24 months (Group 1) and 25-60 months (Group 2). USG findings, including parenchymal thickness, renal pelvis anteroposterior diameter, renal parenchymal echogenicity, and distal ureteral dilatation, were compared between low-grade and high-grade VUR in both groups.

Results: Binary logistic regression analysis revealed that renal pelvis anteroposterior diameter and distal ureteral dilatation were independently associated with high-grade VUR in Group 1. The optimal cut-off value of renal pelvis anteroposterior diameter for predicting high-grade VUR was 5 mm, with 78.0% sensitivity and 76.0% specificity. However, no USG findings were independently associated with high-grade VUR in Group 2.

Conclusion: USG examinations performed by experienced radiologists can effectively decrease radiation exposure in children, especially those with high-grade VUR under two years of age, and may prevent unnecessary radiation exposure in some pediatric patients.

Keywords: Contrast Media, diagnostic imaging, ultrasonography, vesico-Ureteral Reflux, radiography

INTRODUCTION

Vesicoureteral reflux (VUR) is a common congenital anomaly in children. Its reported prevalence varies between 0.4% and 1.8% in healthy children, but it rises to about 30% to 40% in children with febrile urinary tract infections (1). Reflux nephropathy associated with VUR can lead to proteinuria, hypertension, and end-stage renal failure (2). Therefore, it is crucial to identify and manage VUR at an early stage. Urinary system ultrasonography (USG) is the main diagnostic method for initial assessment and subsequent monitoring in children with postnatal hydronephrosis and urinary system infections. Lower grades of VUR typically show normal USG results, and overall, USG is ineffective in detecting VUR. However, USG findings are more frequently associated with higher grades of reflux (3).

The gold standard for diagnosing VUR is voiding cystourethrography (VCUG). This diagnostic approach necessitates catheterization, rendering it an invasive technique that typically elicits substantial distress in pediatric patients and their caregivers. Additionally, the radiation exposure associated with VCUG has emerged as another concern (4). According to the most recent guidelines, VCUG is not advised for children under 2 years old when the USG results are normal and there are unusual or complicated circumstances during the initial urinary tract infection (5).

The objective of this research was to assess the accuracy and additional advantages of USG in diagnosing VUR across various

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reflux grades while comparing its performance to VCUG, the recognized gold standard.

METARIALS and METHODS

A retrospective observational analysis was performed from January 2020 to January 2024 at Ankara Bilkent City Hospital Department of Pediatric Nephrology. The research cohort consisted of children aged 0-60 months who were directed to the pediatric nephrology unit for urinary tract infections, as well as antenatal and postnatal hydronephrosis, and subsequently underwent VCUG procedures. The study was conducted by the principles outlined in the Declaration of Helsinki and approved by the Ethics Committee of Bilkent City Hospital (approval no 1236). We excluded patients who had previous genitourinary tract surgery, unilateral renal agenesis, multicystic dysplastic kidney, horseshoe kidney, duplex collecting system, posterior urethral valve, ureterovesical junction obstruction, chronic kidney disease, and neurogenic bladder. Patients whose records were incomplete were eliminated from the study. Patients above 60 months of age were excluded from the study. Each patient was included only once in the analysis. The records of 860 patients were assessed. The research involved 147 individuals and 294 kidney units. The study participants were categorized into two age-based groups. The first group, comprising 105 patients (71.4%), ranged from 0 to 24 months old. The second group, consisting of 42 patients (28.6%), included those between 25 and 60 months of age. Those with non-refluxing renal units were excluded from the study. Group 1 encompassed 175 renal units, while Group 2 had 64 renal units.

The VCUG results were classified from 1 to 5. Grade 1 was assigned when VUR affected only the ureter. Grade 2 indicated VUR extending to the renal pelvis without causing dilatation. Grade 3 dilation indicated mild ureter dilatation and mild to moderate pelvicalyceal dilatation. Grade 4 was characterized by dilatation of the renal pelvis and calyces with moderate ureteral tortuosity, blunting of fornicies. The most severe grade, 5, described VUR extending to the kidney with a tortuous ureter and dilatation ranging from moderate in the renal pelvis to extreme throughout the entire upper urinary tract (6). Reflux severity was categorized as follows: VUR grades 1, 2, and 3 were classified as low-grade, while VUR grades 4 and 5 were considered high-grade.

All images were done by experienced pediatric radiologists. Comprehensive data, including parenchymal thickness (mm), renal pelvis anteroposterior diameter [mm], renal parenchymal echogenicity (Grade 0, 1, and 2), and distal ureteral dilatation (positive or negative), were extracted from the USG images. These parameters were then used to compare Group 1 and Group 2.

Statistical analysis:

Descriptive parameters were expressed as mean and standard deviation for continuous variables and as numbers and percentages for categorical variables. Patients with low-grade and high-grade VUR were compared using independent sample t-tests and chi-squared tests. Variables with $p<0.050$ were included in the binary logistic regression analysis to identify the independent factors associated with high-grade VUR. Receiver operating characteristic (ROC) curve analysis was used to determine the cut-off value of renal pelvic diameter (mm) for predicting high-grade VUR. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) for Windows (version 21.0; IBM Corp., Armonk, NY, USA). Odds ratios (ORs) and 95.0% confidence intervals (CIs) were calculated, with statistical significance set at $p<0.050$.

RESULTS

In this study, 147 patients aged 0–60 months were retrospectively analyzed. The mean age of all patients was 18.4 ± 20.2 months. Seventy (47.6%) patients were female, and 77 (52.4%) were male. VUR was right-sided in 22 (15.0%) patients, left-sided in 33 (22.4%) patients, and bilateral in 92 (62.6%) patients. A total of 239 renal units were examined, of which 139 (58.2%) had undergone surgical intervention (Table I).

Group 1 comprised 175 renal units, while Group 2 consisted of 64 renal units. In Group 1, the number of renal units with low-grade and high-grade VUR were 74 (31.0%) and 101 (42.3%), respectively. In Group 2, the number of renal units with low-grade and high-grade VUR were 40 (16.7%) and 24 (10.0%), respectively.

USG findings [parenchymal thickness (mm), renal pelvis anteroposterior diameter [mm], renal parenchymal echogenicity (Grade 0, 1, and 2), and distal ureteral dilatation (positive or negative)] of renal units with low-grade and high-grade VUR in Groups 1 and 2 are presented in Table II. The mean renal parenchymal thickness and renal pelvis diameter, as well as renal parenchymal echogenicity and distal ureteral dilatation rates, were significantly different in patients with low-grade and high-grade VUR in both groups (all p values were <0.050) (Table II).

Table I: Clinical characteristics of patients, overall and according to age-related groups

Characteristics	0-24 months	25-60 months	All patients
Number of patients*	105 (71.4)	42 (28.6)	147
Age (months)†	6.3±4.9	48.5±9.4	18.4±20.2
Gender*			
Female	38 (25.8)	32 (21.8)	70 (47.6)
Male	67 (45.6)	10 (6.8)	77 (52.4)
VUR laterality*			
Right-side	16 (10.9)	6 (4.1)	22 (15.0)
Left-side	19 (12.9)	14 (9.5)	33 (22.4)
Bilateral	70 (47.6)	22 (15.0)	92 (62.6)

:** *n (%),* **†:** *mean±SD,* ***VUR: *vesicoureteral reflux*

Table II: Renal and urinary system USG findings in Group 1 and Group 2.

Characteristics	Group 1		p	Group 2		p
	Low-grade	High-grade		Low-grade	High-grade	
Number of Patients*	74 (42.3)	101 (57.7)	-	40 (62.5)	24 (37.5)	-
Renal parenchymal thickness (mm)†	7.9±1.4	6.7±1.9	< 0.010‡	10.0±2.1	8.2±2.7	< 0.010‡
Renal pelvis anteroposterior diameter (mm) †	3.3±3.8	8.5±5.6	< 0.010‡	2.7±2.9	7.5±6.4	< 0.010‡
Renal parenchymal echogenicity*						
Grade 0	61 (52.6)	55 (31.4)	< 0.010 §	34 (53.1)	13 (20.2)	0.010 §
Grade 1	12 (6.9)	34 (19.4)		6 (9.4)	9 (14.1)	
Grade 2	1 (0.6)	12 (6.9)		1 (1.6)	1 (1.6)	
Distal ureteral dilatation*						
Positive	66 (37.7)	62 (35.4)	< 0.010 §	2 (3.1)	7 (10.9)	0.010 §
Negative	8 (4.6)	39 (22.3)		38 (59.4)	17 (26.6)	

**: n (%), †: mean ±SD, ‡: Independent sample t-tests, §: Chi-squared tests . Groups 1 and 2 represent the renal units of patients aged between 0 – 24 months and 25 – 60 months, respectively were used to compare groups.*

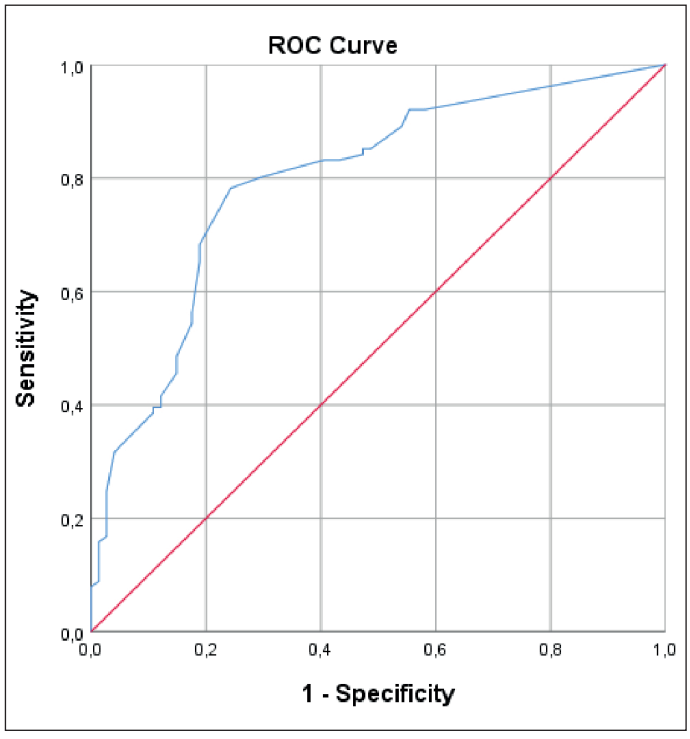

Figure 1: Receiver operating characteristic curve analysis of renal pelvis anteroposterior diameter for predicting patients with high-grade VUR.

Binary logistic regression analysis revealed that renal pelvis anteroposterior diameter (p<0.001; OR:1.2; 95.0% CI:1.12 – 1.35) and distal ureteral dilatation (p=0.010; OR: 4.6; 95.0% CI:1.79–11.67) were independently associated with high-grade VUR in Group 1. Furthermore, ROC curve analysis revealed that the optimal cut-off value of renal pelvis anteroposterior diameter for predicting high-grade VUR was 5 mm, with 78.0% sensitivity and 76.0% specificity (area under the curve: 0.79, standard error: 0.03, p<0.001) (Figure 1). However, binary logistic regression analysis revealed none of the USG findings was independently associated with high-grade VUR in Group 2.

DISCUSSION

Vesicoureteral reflux (VUR), which is primary in nature, is among the most prevalent urological disorders affecting infants and children. The methods for detecting VUR through renal imaging have evolved. There is ongoing debate regarding the optimal initial imaging technique for infants and children with hydronephrosis and urinary tract infections (7). Low-grade VUR generally has a favorable prognosis, with limited adverse effects and a propensity for self-resolution. Conversely, severe cases of reflux necessitate swift detection and intervention to prevent renal injury (8). Consequently, it is essential to correctly diagnose and manage patients with VUR using the most suitable approach at the appropriate time.

Studies on VUR identified after urinary tract infection show varying gender distributions. While some research indicates a female predominance, others report no significant gender difference (9). In our investigation, the gender split was nearly equal, with 47.6% of patients being female and 52.4% male. In a similar study, Chang et al.(10) reported rates of 9.6% for females and 10.7% for males. However, Naseri et al.(11) reported contrasting findings, with 18.37% (77 out of 419) of VUR cases being male, which differs from our results.

The study findings indicated that VUR manifested unilaterally in 37.4% of patients, with 15.0% (22 cases) affecting the right side and 22.4% (33 cases) affecting the left side. The majority of patients, 62.6% (92 cases), exhibited bilateral VUR. In comparison, Naseri et al.'s (11) research identified bilateral VUR in 45.85% of their 410 VUR patients (188 cases). Another investigation by Su et al. (12) reported an even distribution between unilateral and bilateral VUR, with each type occurring in 50.0% of their study participants.

Surgical intervention is often indicated for patients exhibiting grade 4-5 VUR, showing progression of scarring, experiencing febrile urinary tract infections despite prophylactic treatment, or in some cases, due to parental preferences (13). Our study

examined 239 kidney units, with mostly endoscopic surgical interventions performed on 139 (58.2%) of them. The majority of these cases exhibited severe VUR. According to published studies, endoscopic injections have shown effectiveness in initial treatments. Ripatti et al. (14) conducted a retrospective analysis of VUR patients over a decade. Their research revealed that out of 1484 children, 1212 underwent endoscopic surgical treatment during these ten years.

Our research revealed that high-grade reflux patients in Groups 1 and 2 displayed a decreased mean renal parenchymal thickness. In contrast, these individuals exhibited significantly higher renal parenchymal echogenicity and a larger anteroposterior renal pelvis diameter. The results of a binary logistic regression analysis showed that in Group 1, the anteroposterior diameter of the renal pelvis and dilation of the distal ureter were independently linked to high-grade VUR. In contrast, for Group 2, no correlation was found between USG findings and high-grade VUR. A study by Doğan et al.(15) examined the effectiveness of USG in performing VCUG procedures with clear indications. The investigation classified subjects into three age ranges: 0-2 years, 3-5 years, and 6-17 years. The USG reports included anteroposterior renal pelvic diameter measurements, kidney parenchyma, kidney dimensions, and ureter size. They found a correlation between VCUG and USG results in all age groups. Using a threshold of >10 mm for the pathologic anteroposterior renal pelvic diameter, the study found sensitivity, specificity, and negative predictive value to be 79.45%, 79.91%, and 71.17%, respectively. For children aged 0-2 years, the USG demonstrated its highest sensitivity and negative predictive value. Our research utilized ROC analysis to determine the optimal renal pelvis anteroposterior diameter threshold in predicting high-grade VUR. The results indicated that a cut-off value of 5 mm yielded the best performance, demonstrating a sensitivity of 78.0% and a specificity of 76.0% in Group 1. In a comparable investigation by Ilıkan, researchers categorized patients into two age groups: those younger than 6 years and those 6 years and older (16). Their findings demonstrated a link between USG and VCUG results for children under 6 years of age, while no such association was found in patients 6 years and above. In a similar study, You et al. (17) examined the effectiveness and predictive capabilities of USG with VUR in patients under 2 years of age. The researchers suggested that USG findings indicating thickened walls and expanded renal collecting systems should be considered indicative of severe VUR. Khater et al. (18) conducted a study that aligns with our findings, demonstrating that patients with high-grade VUR showed statistically significant increases in kidney dimensions, echogenicity, ureteral dilation and wall thickness, as well as renal pelvis diameter and pelvic wall thickness. Additionally, their ROC analysis revealed that USG demonstrated 100% specificity and 78.5% sensitivity in detecting VUR. Nevertheless, research also exists that highlights the potential for USG to cause delays in diagnosing high-grade VUR. The study by Nelson et al. (19) revealed that USG is inadequate as a screening method for identifying genitourinary abnormalities. Their findings suggest that USG and VCUG should be utilized in conjunction, as each technique offers unique and essential information. Some studies suggest that the distal ureter dilatation may play a more significant role in determining the clinical progression of primary VUR than dilation of the upper urinary tract. Consistent with our findings, Hodhod et al. (20), observed that refluxing hydroureter units had a median ureteric diameter of 10 mm, and a significant portion (74%) of refluxing renal units were classified as high-grade.

This study has various constraints, including its retrospective design. Additionally, the research is limited by a restricted number of patients in the sample. Furthermore, it is important to consider that the investigation was conducted at only one medical facility. Another limitation is that the degree of ureter dilation can vary with age, making it an unreliable indicator. Consequently, children who have not yet been toilet-trained may exhibit false ureter dilation. Additionally, bladder distention can alter the condition.

CONCLUSION

In conclusion, our results indicate that under two years of age, the anteroposterior diameter of the renal pelvis and dilation of the distal ureter were independently linked to high-grade VUR. A ROC analysis indicated that a cut-off value of 5 mm yielded the best performance, demonstrating a sensitivity of 78.0% and a specificity of 76.0% in this age group. For children, especially those under two years of age, the use of USG examinations performed by experienced radiologists can effectively decrease radiation exposure. This strategy may prevent some pediatric patients from being subjected to unnecessary radiation.

Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Bilkent City Hospital (approval no 1236).

Contribution of the authors

Taş N and Özlü SG: participated in study design, analysis, and manuscript preparation. ***Çiftci N, İnözü M, Aksoy ÖY, Yazıcıoğlu B, Çaycı FŞ, and Tiryaki HT:*** were involved in patient follow-up and analysed the manuscript. The ultrasonographic analysis was performed by ***Keçeli AM.***

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Conflict of interest

The authors declare that there is no conflict of interest.

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