

Renal Impairment in 79 Pediatric Patients (158 Renal Units) with Repeated Urinary Tract Infection in Relation to Vesicoureteric Reflux



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خلاصة

تتضمن هذه الدراسة 79 طفلاً يعانون من الإلتهابات المتكررة بمجرى البول تم فحصهم باستخدام النظائر المشعة (الطريقة المباشرة وغير المباشرة) مع محاولة توضيح دور الارتجاع البولي في حدوث التليف الكلوي باستعمال مادة (دم س ا).

وقد أوضحت الدراسة وجود ارتجاع بولي في 38 مريضاً (59 كلية) مع وجود التهابات متكررة بمجرى البول في 50% من الحالات. تم تقسيم 158 كلية إلى مجموعتين: المجموعة السليمة (71 كلية) وجد بها ارتجاع بولي ذو الدرجة العالية (الدرجة الثالثة والرابعة) بنسبة 20.6% بينما المجموعة الثانية المتليفة (85 كلية) وجد بها ارتجاع بولي بنسبة 43.5% مع وجود فرق إحصائي بين المجموعتين.

ومما سبق نرى أن دراسة الارتجاع البولي وآثاره على الكلى له أهميته للتشخيص المبكر في حالات التهابات الكلى المتكرر حتى يمكن التدخل قبل حدوث تليفات الكلى.

Abstract

Seventy nine patients with repeated urinary tract infection were evaluated for detection of vesico-ureteric reflux (VUR) by direct (DRC) and indirect (IRC) radionuclide cystography as well as assessment of renal scarring using ^{99m}Tc -DMSA.

Positive VUR was evident in 38 patients (59 renal units), 50%, patients had history of recurrent urinary tract infection.

Patients kidneys were divided into 2 groups : group A with normal if kidneys (74 renal units), but still they have high grade VUR in 20 renal

units (20.6%. Group B with scarred kidneys (84 renal Units) with high grade VUR in 36 renal units (42.9%) with significant difference between both groups ($P < 0.05$).

To conclude: Combined renal scanning with ^{99m}Tc -DMSA with VUR assessment are essential in pediatric patients with urinary tract infection for detection of high grade VUR which may contribute to renal scarring and damage.

Introduction:

Epidemiologic surveys have shown that 21-57% of children who have had bacteruria are subsequently found to have VUR (1). Besides, there is a close relationship between UTI, VUR and renal scarring which is referred recently as reflux nephropathy which may lead to delayed hypertension and progressive renal dysfunction without apparent further urinary infection (2).

The use of radionuclide techniques in assessment of reflux was first described by Winter, (3) and Dodge, (4). Both direct and indirect radionuclide cystourethrography are widely used with good results, but with less radiation exposure to bladder and gonads compared to contrast cystourethrography (5).

The aim of this work to assess the value of radionuclide cystourethrography in detection and grading of VUR as compared to standard VCUG and to assess the impact of reflux on renal function and cortical integrity.

Materials and Methods:

The 79 patients included in this study have age ranged 3 months - 13 years. All were referred to nuclear medicine department with recurrent or persistent urinary tract infection for radionuclide renal evaluation. Children with acute UTI were excluded. All patients were subjected to clinical assessment, laboratory investigation (urine analysis, creatinine and urine culture) and standard micturition cystourethrogram to be compared with radionuclide results.

Radionuclide studies:

A) Direct cystourethroscintigraphy:

The patient is supine with large field of view gamma camera under couch. Bladder catheterization with I.V. line to a bottle containing 1 mCi

of ^{99m}Tc in 500 cc. saline suspended at a level of 100 cm to permit bladder filling. Framing every 5 - 10 sec. during filling phase and every 3 - 5 sec during voiding phase.

B) Indirect cystourethroscintigraphy:

Following dynamic renal study, the patient is positioned on the commode chair with full bladder with his back facing the gamma camera. Serial rapid images every 3 - 5 sec. during voiding. Any rise of activity in the ureters and kidneys indicate the presence of reflux. Region of interest on bladder and ureters with generation of time activity curves for quantitative evaluation were done.

Grading of reflux:

Grade I : into the ureter only.

Grade II : into renal pelvis without dilatation.

Grade III : into ureter, renal pelvis with mild degree of dilatation.

Grade IV : into ureter, renal pelvis with moderate dilatation.

Grade V : into dilated corkscrew ureter and severely dilated pelvis.

C) ^{99m}Tc -DMSA static renal imaging:

Three hours following injection of 50-100 $\mu\text{Ci}/\text{Kgm}$ of ^{99m}Tc -DMSA, anterior and posterior images each for 500,000 counts were acquired. Oblique projections were taken when needed.

System for grading of scarring:

Grade 0 : No scars.

Grade I : Single focal defect.

Grade II : Two focal defects.

Grade III : Multiple scars.

Grade IV : Complete loss of cortical tissue.

Statistical analysis using Chi square test or Fischer's exact test for comparison between groups with P-value ≤ 0.05 considered significant. Sensitivity, specificity, positive and negative predictive values were calculated.

Results:

Vesicoureteric reflux was diagnosed in 19 patients (24 refluxing renal units) using voiding cystourethrography (VCUG) (16.7%). The majority of refluxing units were in high grade III, IV in 95.8% versus a single reflux unit in grade II (4.2%).

Using direct radionuclide cystography, 35 positive refluxing units were detected (15 unilateral and 20 bilateral) with high detection of early grade I, II in 20% versus 80% in grade III, IV. Also, indirect radionuclide cystography showed 45 positive refluxing units (11 unilateral and 34 bilateral) with high grade reflux III and IV in 93.4% versus grade I, II in 6.6% (Table 1).

Table (1) : Frequency of vesicoureteric reflux in 158 renal units of 79 patients with urinary tract infection using radiologic and radionuclide methods

	VCUG*		DRC**		IRC***	
	No.	%	No.	%	No.	%
Negative VUR	120	83.3	121	77.6	85	65.4
Positive VUR	24	16.7	35	22.4	45	34.6
Unilateral	14	58.3	15	42.9	11	24.4
Bilateral	10	41.7	20	57.1	34	75.6
Grade I	0	0	3	8.6	2	4.4
Grade II	1	4.2	4	11.4	1	2.2
Grade III	11	45.8	13	37.1	28	62.3
Grade IV	12	50	15	42.9	14	31.1

* Ascending cystourethrography (VCUG) was not done in 7 patients (14 renal units).

** Direct radionuclide cystography (DRC) was not done in one patient (2 renal units).

*** Indirect radionuclide cystography (IRC) was inconclusive in 14 patients (28 renal units).

Table (2) : Correlation of VUR with Tc-99m DMSA tubular functional assessment in 158 kidneys of 79 patients with UTI.

Group I: Normal kidneys				
	G ₀	G ₁₋₂	G ₃₋₄	Total
	53	5	15	73
%	72.6*	6.8	20.6**	
Group II: Scarred kidneys				
	G ₀	G ₁₋₂	G ₃₋₄	Total
G ₁	11	0	8	85
G ₂	4	0	12	
G ₃	18	2	12	
G ₄	13	0	5	
Total	46	2	37	
%	54.1*	2.4	43.5**	

* P-value = 1×10^{-3} (highly significant)

** P-value = 1.08×10^{-3} (highly significant).

Comparison of sensitivity, specificity and accuracy for diagnosis of VUR using DRC compared to the standard VCUG were 81.8%, 87.5% and 86.6% respectively. Whereas using IRC compared to VCUG sensitivity, specificity and accuracy were 66.7%, 81.7% and 79.2% respectively. Table 2 showed tubular function using ^{99m}Tc -DMSA and its correlation with VUR. Seventy three renal units have normal cortical function, 53 renal units have no evidence of scars with G0 reflux in 72.6%, low grade G₁ & G₂ VUR in 6.8% and high grade G₃ & G₄ in 20.6%. Whereas 85 renal units have evidence of scarring of different grades with 54.1% had G0 VUR, low grade G₁ & G₂ VUR was evident in 2.4% and high grade G₃ & G₄ in 43.5% an involved kidneys. Comparison between high grade reflux in normal and scarred kidney groups showed significant statistical difference ($P < 0.05$).

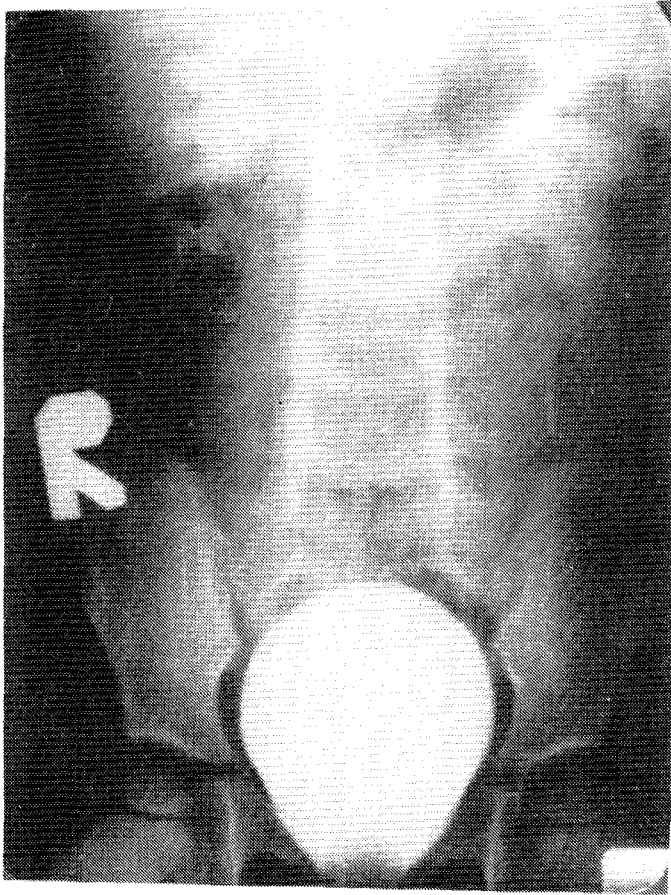
Discussion:

Vesicoureteric reflux may be followed by late consequences such as impaired renal function, but more importantly the development of reflux nephropathy a significant cause of end stage renal disease and hypertension in children (6). Although, mild degree of reflux may resolve spontaneously. Therefore, repeated follow up reflux studies in children with recurrent UTI over a number of years may be necessary to avoid such complications (7).

Nasrillah et al., (8) reported that DRC correlate well with results of VCUG, with superior sensitivity in 17.4% detecting clinically significant reflux. Also, Kogan et al., (9) reported 10 patients with UTI and negative VUR using VCUG, whereas DRC demonstrated VUR in all cases. In this study 14 of 59 refluxing units (23.7%) were detected DRC, while VCUG were negative. The superior sensitivity of DRC can be explained by continuous dynamic monitoring during DRC as compared to intermittent views during VCUG. However, we should emphasize that VCUG provides more anatomical details as urethral anomalies. In this study, two male patients were diagnosed to have posterior urethral valve by VCUG only.

In our study, although IRC revealed 45 refluxing units (RUs), yet 7 RUs were seen by VCUG, while IRC was inconclusive in 17.7% due to renal functional impairment. Similar missing rate ranging 21-51% were reported (10,11). Also, we should emphasize on the value of the quantification of VUR using ROIs with time activity curve generation as applied in this study which lead to better diagnosis of VUR as compared to visual

(a)



(b)

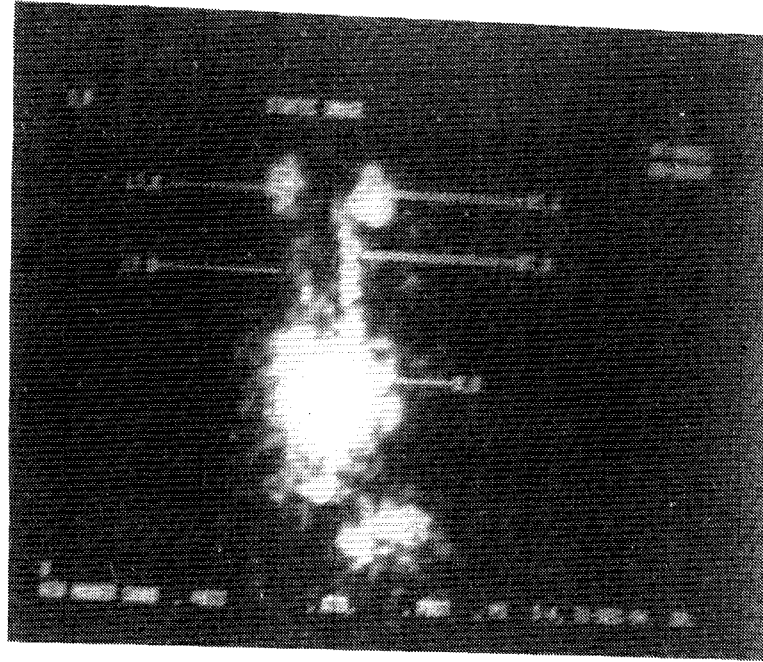


Figure (1) : (a) Bilateral grade III VUR seen on straining in micturition cystourethrography. (b) Bilateral grade III VUR diagnosed by direct radionuclide cystography.

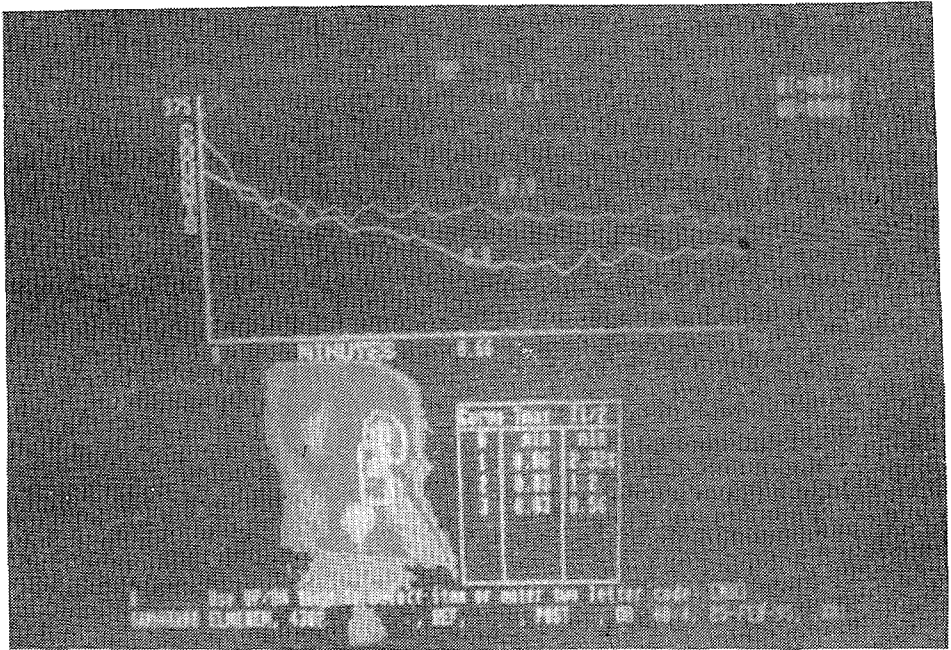
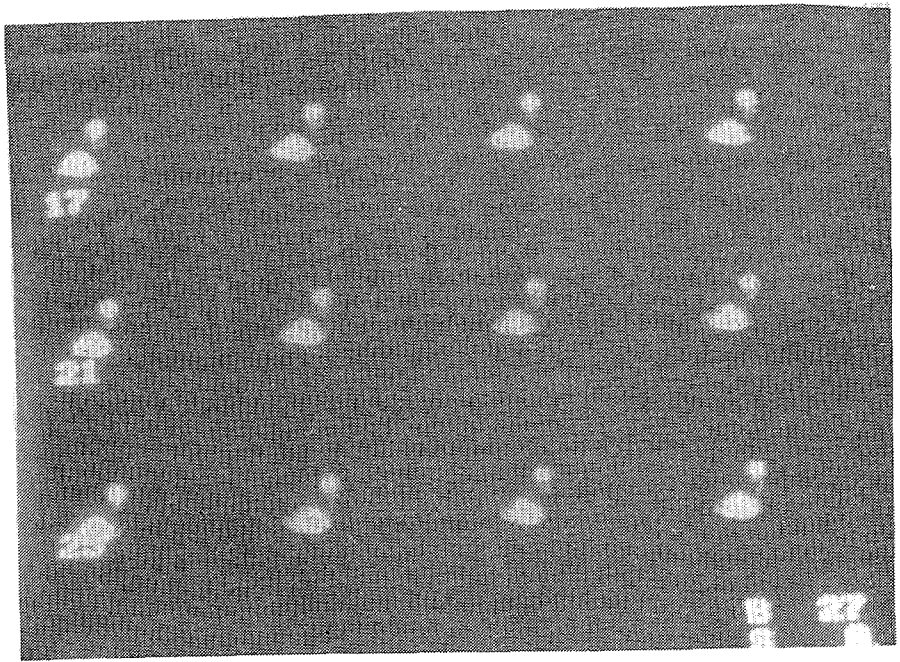


Figure (2) : (a) Right grade III, VUR during filling phase using direct radionuclide cystography. (b) Bilateral grade III VUR diagnosed from time activity curve and visually on right side using indirect radionuclide cystography.

inspection only as used in DeBoe et al. (12), with low detection of VUR by IRC in 46% compared to 91% using VCUG and DRG.

In this study, higher sensitivity (82%) in DRC as compared to (67%) in IRC, although both methods have nearly the same degree of accuracy. Still DRC is the method of choice as VUR can be detected during both filling and voiding phases. In this study 13/59 RUs (22%) were detected during filling phase of DRC. Similarly, Conway and Kruglick (13) reported 21% (29 of 137) of RUs were seen only during filling phase of their study.

Rushton et al., (14) stated that pyelonephritis is essential pre-requisite for renal scarring but VUR contributes to the development of pyelonephritis and scarring. In this work, the scarred kidneys showed high grade VUR in 43.3% versus 20.5% in non scarred kidneys with significant difference between both groups ($P < 0.05$). This suggests the significant role of VUR in the development of scarring and its progression.

Finally, we should emphasize that although the role of VUR in the development of scarring is incompletely understood, yet its detection remains a standard part of evaluation in patients with UTI.

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