Original Article

Renal Scarring and Vesico-Ureteral Reflux in Children with Urinary Tract Infection (UTI)

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ABSTRACT

Objective: To determine the extent of renal scarring in children with vesico-ureteral reflux (VUR) and upper urinary tract infection and to evaluate the relationship between different degrees of VUR and the renal scar.

Patients and Methods: Forty two patients (age ranging from one month to 14 years) with VUR were studied consecutively. VUR was diagnosed by voiding cystourethrography (VCUG) and dimercaptosuccinic acid (DMSA) scan was done at least 4-6 months after the last episode of pyelonephritis.

Results: Eighty-four kidney units were examined. VUR was positive in 64 units. Twenty two subjects had bilateral VUR and 20 patients had unilateral VUR. Forty units (62.5%) had scarring. Kidney units with VUR in boys had more scarring than girls (90% Vs 62.5%). 64% kidney units with children less than five years of age had renal scarring.

Conclusion: High grade reflux was associated with more severe reflux. Renal scarring is more common in younger children, boys and those with high grade reflux.

KEYWORDS: children, renal scar, urinary tract infection, vesico-ureteral reflux

INTRODUCTION

Urinary tract infection has a prevalence of 1-2% in girls and less than 1% in boys. Vesico-ureteric reflux (VUR) has been found in 35-40% of children with urinary infection. Renal scarring may be seen in 9.5-38% of those with reflux, in 12% of all infected children, and in a quarter of those with a history of recurrent urinary infection[1-4]. Renal scarring found in association with vesico-ureteric reflux (reflux nephropathy) is an important cause of hypertension and end stage renal disease in children and young adults and is to some extent preventable. Although damage associated with severe reflux can be developmental and may occur in utero[5], there is abundant clinical and experimental evidence that renal scarring can be acquired at any stage in childhood and that urinary infection as well as vesico-ureteric reflux is important in its pathogenesis[6-10]. It has been shown experimentally that when reflux and infection are present, the rapid introduction of antibacterial treatment can arrest or prevent the development of scarring[11-13].

Reflux nephropathy is irreversible[14] and hypertension, proteinuria and chronic renal failure are well-recognized sequelae of renal scars[15]. Renal scarring is present in approximately 25% of patients with chronic renal failure[16]. Therefore, it is important that after the diagnosis of urinary tract infection is established, a radiological investigation of the urinary tract should be done to evaluate reflux and assess the kidneys. It is equally important to review the risk factors associated with a urinary tract infection. Medical records of forty two children with vesico-ureteral reflux and urinary tract infection attending the Amirkola Children Hospital were retrospectively reviewed to determine the extent of renal scarring and to ascertain if the renal damage might have been limited or prevented.

PATENTS AND METHODS

This cross-sectional study was performed using medical records of 13 boys and 29 girls (aged one month to 14 years) attending the Pediatric Nephrology department of Amirkola Children Hospital (Babol, Caspian Sea, North Iran) for urinary tract infection from 1995-2001. All children had a history of urinary infection. Details of presentation, treatment, and patient's and family history were obtained from clinical records. Further specific information was obtained by a structured interview with the parents. Each patient with a febrile urinary tract infection underwent renal ultrasound and voiding cystourethrography (VCUG) 4-6 weeks later as part of the initial investigation. DMSAscans were obtained at least 4-6 months after last episodes of pyelonephritis in all patients with VUR. The grade of VUR was based on International Reflux Committee classification

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Table 1
The frequency of reflux and scar in boys and girls in the study population

	Boys	Girls	Total
Reflux	21	43	64
Grade I	1	7	8
Grade II	5	19	24
Grade III	8	15	23
Grade IV	2	0	2
Grade V	5	2	7
Scar	19	21	40
Stage I	5	10	15
Stage II	5	5	10
Stage III	9	6	15

(International Reflux Study Committee. Medical versus surgical treatment of primary vesico-ureteral reflux, Pediatrics 1981; 67:392). The grading system for scarring was based on Goldraich and co-workers grading system (Goldarich NP, Rames OL, Goldarich IH.Urography versus DMSA scan in children with vesico-ureteral reflux. Pediatr Nephrol 1989; 3:1). All patients were treated with appropriate antibiotic therapy and then remained on prophylaxis as indicated

RESULTS

The mean age was 45 ± 40 months in the patient population. Vesico-ureteral reflux was detected after urinary tract infection in all patients. Out of 42 patients, 22 had bilateral and 20 had unilateral reflux. Out of 84 studied kidney units, 64 units had reflux (28 in right and 36 in left side) while 20 were normal. Of these 64 kidney units with reflux, 40 units (62.5%) had scar, whereas in 20 normal kidneys, 3 kidneys (15%) showed scar in DMSA. Reflux grade II, scar stage I and III were the most prevalent sequelae seen in the kidneys and kidney units in boys had more sequelae than girls (90% vs. 62.5%, Table 1).

Twenty-five percent of kidneys with reflux grade I, 54% of those with reflux grade II, 74% of those with reflux grade III, 100% of those with reflux grade IV and 85% of those with reflux grade V had scars ($p < 0.001$). Forty-two percent of scars were seen in the upper lobe, 22.2% in the middle lobe and 30.9% in the lower lobe of kidneys ($p < 0.05$). In this study, 18 children were aged less than two years, 13 between three and five years and 11 more than six years. Grade II reflux in children aged less than two years, grade III reflux in children aged three to five years and grade I and III in children aged six years and more were prevalent (Table 2). Forty four percent of VUR was on the right side while 56 percent was on the left side but 48% of right side and 52% of left side kidneys with VUR had scars.

Among seven kidneys units with grade V reflux, five units (71.4%) had scar and 90% of boys with VUR had a scar (Table 3). Three children (7.1%) had hypertension.

Table 2
The age-wise distribution of kidney units with reflux and scar

	1 month-2 years	3-5 years	6 years and more
Reflux	33	17	14
Grade I	1	2	5
Grade II	15	5	4
Grade III	8	10	5
Grade IV	2	0	0
Grade V	7	0	0
Scar	18	14	8
Stage I	6	8	1
Stage II	4	3	3
Stage III	8	3	4

DISCUSSION

In the past, intravenous pyelography (IVP) was a standard method for evaluation of renal scarring, but it has now been replaced by renal scintigraphy with dimercaptosuccinic acid (DMSA) scan. Goldrich *et al* and Merick et al showed that sensitivity and specificity of DMSA is more than IVP (92% and 98% Vs 80% and 92% respectively)[17,18]. Others have reported a greater sensitivity of DMSAscan for detection of scar[19-20].

Transient DMSA abnormalities may be seen after acute phase of pyelonephrits. It is a valid diagnostic tool for confirming the presence of acute pyelonephrits and for documenting the presence of renal scarring, but routine use of this imaging method during the acute illness does not alter treatment in a majority of patients and is not considered necessary[21-24].

Our policy is to screen every child with acute pyelonephrits with DMSA scan over 4-6 month to detect vesico-ureteral reflux.

Our study showed that 62.5% of kidney units (90% boys and 51% girls) with VUR have renal scarring. Szlyk *et al* and Polito *et al* reported that 38% and 37% of kidney units had scars respectively[3-4]. Lama *et al* reported that 66% girls and 44% boys in the first year of life with VUR and UTI had renal scarring[25].

Risks of hypertension and chronic renal failure are higher with diffuse scarring[26]. Our study shows that hypertension occurred in 7.1% patients with renal scarring and 23.5% of kidney units with VUR had diffuse scar.

Merguerian *et al* showed 32.2% of children younger than one year, 33.2% between one to five years and 62.5% older than six years with grade IV, V of VUR had diffuse scarring[27]. In our study 24.2%, 18% and 28.5% kidney units in children younger than two years, between 3-5 years and older than six years had diffuse renal scarring

Table 3
The sex-wise distribution of kidney units with reflux and scar according to the grading of reflux and staging of scar

Scar	Stage I			Stage II			Stage III			Total		
Reflux	F	M	T	F	M	T	F	M	T	F	M	T
Grade I	1	1	2	-	-	-	1	-	1	2	1	3
Grade II	6	2	8	3	1	4	1	1	2	10	4	14
Grade III	4	1	5	2	3	5	3	4	7	9	8	17
Grade IV	-	-	-	-	1	1	-	1	1	-	2	2
Grade V	-	-	-	1	-	1	1	3	4	2	3	5
Total	11	4	15	6	5	11	6	9	15	23	18	41

F=female, M=male, T=total

respectively. We did not grade IV and V VUR in children older than six years.

Our study shows that about 70% of kidney units with grade V, one of two with grade IV and 30.4% of those with grade III VUR have diffuse scar. Therefore, higher grades of reflux were associated with higher incidence of diffuse scar. It is very important to detect VUR and renal scarring, especially in the first five years after birth, because the kidneys are more vulnerable to reflux nephropathy. In children less than two years, 27.6% of kidney units had grade IV and V VUR and in this age group, 54% patients with VUR had diffuse renal scarring.

CONCLUSION

Our study suggests that incidence of diffuse renal scarring is higher in children with high grade VUR, especially in the younger age group. Also, boys with VUR have higher risk for renal scar than girls.

We recommend performing DMSA scan in all children with reflux, especially in boys, younger age and in those with higher grade VUR.

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