

Primary Vesicoureteral Reflux in Iranian Children

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Background: Experience with vesicoureteral reflux (VUR) differs in different centers and there are plenty of controversies. **Objective:** The aim of this study was to evaluate the outcome of primary VUR complications and the rate of recurrence of UTI. **Methods:** The medical charts of all infants and children with primary VUR who were followed up by two nephrologist were reviewed. During 19 years (1985-2004), 330 patients (271 females, 59 males) with 496 refluxing ureters were followed up as primary VUR. **Results:** The patients' age at diagnosis was 54 days to 16 years (Mean: 4.1 years) and the mean duration of follow-up was 4.5 years. Urinary tract infection (UTI) was the presenting symptom in 95% and fever was recorded in 35% of cases. Frequencies of different grades of VUR at initial investigation were 10%, 35%, 30%, 13% and 12% for grades I to V, respectively. Recurrence of UTI in VUR of grades I to V, were 22.2%, 18.1%, 20%, 23.4% and 17.9% respectively. Follow-up voiding cystourethrogram revealed resolution of VUR in 55%, improvement in 27.5%, no change in 12%, and deterioration in 5.5%. Complications such as chronic renal failure and hypertension were observed in 13 and 13 patients, respectively. Renal scarring was present in 52% of boys and 29% of girls. **Conclusion:** The present study indicates that symptomatic primary VUR is more common and has better prognosis in girls. Recurrence of UTI is not related to the grade of VUR.

Keywords: Urinary tract infection, Vesicoureteral reflux.

Vesicoureteral reflux (VUR) is defined as the backup of urine from the bladder to the ureters and is a risk factor for pyelonephritis. Primary VUR is congenital and is not associated with any underlying neuromuscular or obstructive phenomenon(1). Primary VUR is usually detected during radiological evaluation of children with urinary tract infection (UTI). It can also be identified in the uninfected siblings or offspring of the index patients and with prenatal diagnosis of hydronephrosis(2).

Complications such as renal scarring, chronic renal failure and hypertension are well known in patients with VUR and UTI. Antireflux surgery offers no short-term advantages other than abolishing the reflux. It also does not result in improved renal function or renal growth, and does not affect the rate of new scar formation or the incidence of hypertension. To evaluate the outcome of primary VUR, complications and the rate of recurrence of UTI, we reviewed the charts of 330 patients with VUR who were treated and followed at a university center in Mashhad and Shiraz, Iran.

Subjects and Methods

The medical charts of all the patients with primary VUR during the last 19 years (1985-2004) in Mashhad and Shiraz, Iran were reviewed. Patients with VUR secondary to lower urinary tract obstruction, neurogenic bladder, bladder diverticulum or nonneurogenic neurogenic bladder were excluded. Of the 330 children with primary VUR, 319 who had conventional voiding cystourethrogram (VCUG) were included in this study. UTI were considered in presence of defined positive urinary culture and urinalysis (Pyuria and positive nitrite) in symptomatic patients. Urine culture was considered positive when two consecutive cultures showed a growth of more than 100,000 colony-forming units/mL of one microorganism in clean-catch midstream specimens in children with urinary control, and urine collected by sterile bags in those without it. Follow-up urine cultures were done within an interval of 1-3 months or at any time when a fever of unknown origin or urinary symptoms appeared. Positive urine culture in symptom free cases (asymptomatic bacteriuria) was not

considered as UTI. Ultrasonography was performed in all, dimercaptosuccinic acid (DMSA) renal scan in 157 and follow-up VCUG (with a mean interval of 2 years) in 147 cases. DMSA scan performed at least 6 months later than acute UTI. Renal scarring was defined as an area of photon deficiency or small sized hypofunctioning kidney on DMSA or renal parenchymal thinning on ultrasonogram. Antireflux surgery was done in 46 (14.7%) of the patients (17 with grade V, 12 with grade IV, 10 with grade III and 7 with grade II). Most (93%) of the patients received prophylactic antibiotics (*Table I*). Statistical analysis was done using χ^2 and the Student's t-tests.

Results

There were 479 refluxing ureters of 319 patients; 50% cases were bilateral. The age at diagnosis ranged from 54 days to 16 years (mean: 4.1 years) and the male-to-female ratio was 0.21 (girls = 262, boys = 57) ($p = 0.002$). In 95% patients VUR was found during the investigation for UTI. In 4.5% of the patients positive family history was the main clue for the investigation. In 90.5% of the patients the isolated microorganism in the first episode of UTI was *E. coli*. The initial grading of VUR, prophylactic antibiotic administration and the rate of recurrence of UTI in different grades of reflux is shown in *Table I*. The risk of recurrent of UTI was not significant in different grades of VUR with or without surgery.

DMSA showed cortical scars in 76 (48.4%) patients. Follow-up VCUG done in 150 (47.9%) of the patients (mean interval: 2.2 years), showed no VUR in 55%, lower grades of VUR in 27.5%, higher grades in 5.5% and no change in 12% of these patients. Anti-reflux operation was performed in 7, 10, 13 and 16 patients with VUR of grades II to V, respectively. Long term complication such as

chronic renal failure and hypertension were occurred in 13 patients each (*Table II*). Renal scarring was found by ultrasonography in 21 and by DMSA scan in 76 patients. Of 76 patients with renal scan 55 were girls and 21 were boys. The frequencies of grades (I to V) of VUR were 4, 12, 17, 20 and 22, respectively. Fifteen patients, showed bilateral scars in VUR of grades IV and V renal scars were seen in 60% boys and 37.5% in girls ($p = 0.006$). Taking all grades together, renal scarring was present in 52% of boys and 29% of girls ($p = 0.001$).

Discussion

Primary VUR is the most common hereditary disorder of the genitourinary tract and is transmitted in an autosomal dominant fashion(3). Its grading VUR is important because the natural history and the risk of renal damage differ in different grades(4). Patients with high grade VUR (IV and V) are 4 to 6 times more likely to develop scarring than those with low or moderate (I to III) grade VUR and 8 to 10 times more likely to do so as compared to those without VUR(5). In this study, 21% of the kidneys with scarring had lower grades of VUR. It is probable that these lesions are of pyelonephritis as reported by other works(6). In patients with higher grades of reflux the lesions may be due to both VUR and pyelonephritis or at least in some, associated with congenital defects of the kidney. In one study, severe VUR diagnosed at birth was associated with congenital renal damage and males were affected more often and more severely than females(7). Our results are similar to this report in many aspects, including the frequency of bilateral lesions. In contrast to several previous reports the male to female ratio in our study is surprisingly different(7-10). It is notable that girls outnumbered boys in this study; nevertheless kidney scar formation was for more common in the latter group.

TABLE 1—Number of Patients Using Prophylactic Antibiotics and Recurrence of UTI in Different Grades of VUR

VUR grading	No. of patients (%)	Patients on prophylactic antibiotics	Patients with recurrent UTI
I	22 (7.8)	20 (86.8)	38 (22.2)
II	164 (50.5)	156 (91.6)	31 (18.1)
III	78 (26.2)	72 (93.5)	34 (20)
IV	35 (10.9)	28 (80)	40 (23.4)
V	20 (6.2)	14 (70)	31 (17.9)
Total	319	290	174

What this Study Adds

- VUR is more common and less severe in girls and the rate of recurrence of UTI is not directly related to the grade of VUR.
- Complication such as hypertension and renal failure are common complication of VUR, therefore arterial blood pressure and renal function need to be continuously monitored in these patients.

TABLE II—Complications of VUR in Relation to Treatment Groups

Patient group	Surgical (N = 46)	Medical (n = 273)
Renal damage (scar)	25 (46.5%)	51 (19%)
Hypertension	4 (13.5%)	9 (2.8%)
Chronic renal failure	6 (16.5%)	7 (1.5%)
Recurrence of UTI	21 (45.0%)	125 (54.5%)

* Reflux was bilateral in 36 (73.5%) and 125 (47.5%) patients treated surgically and medically respectively.

While the rate of renal damage in the present study was lower than that in some previous reports(11-13), it was higher than the rate reported in Chinese children (28% boys and 11% girls)(14). We found that the risk of renal scarring in boys was 52%. We performed DMSA scan in the high risk cases, so some patients with minor defect might have been missed. Despite this fact, the high proportion of renal damage in the boys was a matter of concern which might be explained by higher grades of VUR. As anticipated, we observed higher rate of renal damage in the surgically treated group. This could be due to the fact that surgical intervention was implemented predominantly in higher grades of VUR. In 16 patients the renal scar was documented before the antireflux operation was performed and in 9 patients it was found after the surgery. Although VCUG was not repeated in some of the low risk patients in whom resolution of the VUR was more predictable, the total number of cure, improvement or spontaneous recovery was more than 80%. This is significant as compared to the results of other reports(9,12).

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