

A study of long-term follow-up of Vesicoureteral reflux in children

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Abstract

Background: Vesicoureteric reflux refers to retrograde flow of urine from the bladder to the ureter and renal pelvis. Although exact prevalence in the general population is unknown, 30-40% of children with urinary tract infections are found to have reflux.¹ VUR is a predisposing factor for UTI, which in turn may involve the kidney parenchyma to cause renal scarring leading to reflux nephropathy and end stage renal disease. **Objective:** To study the outcome of VUR in relation to Recurrence of UTI following diagnosis and to find out the incidence of renal cortical scarring as evidenced by DMSA scan on diagnosis and follow up. **Methodology:** A hospital based ambispective (Retrospective and Prospective) Study was carried out in Department of pediatrics, Kasturba Medical College, Manipal from August 2004 to August 2012. All children in the age group of 1 month to 18 years with Vesicoureteric Reflux, who presented to the Department of Pediatrics (Kasturba Hospital Manipal) between Aug 2004 to Aug 2010 were included in the study. **Results:** Majority (78.5%) presented before 5 years, youngest age at presentation was 1 month and oldest at 14 year 8 months. Among 93 children studied, 65 were males and 28 were females with male to female ratio of 2:3. Hydronephrosis was the commonest abnormality 35 followed by bladder wall trabeculations. Among 76 children who underwent a DMSA scan 41 children (54%) had detectable renal scars. Incidence of scarring was higher with increasing grades of VUR. **Conclusion:** After successful surgical reflux correction susceptibility to urinary tract infection continues for a number of years in many girls and women. Although modern management of VUR and urinary tract infections will improve the prognosis in the future, there is a need for long-term follow-up.

Key Word: Vesico Ureteric Reflex, UTI, Bladder, Children, Long term Follow up.

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INTRODUCTION

Vesicoureteric reflux refers to retrograde flow of urine from the bladder to the ureter and renal pelvis. Although exact prevalence in the general population is unknown, 30-40% of children with urinary tract infections are found to have reflux.¹ VUR is a predisposing factor for UTI, which in turn may involve the kidney parenchyma to cause renal scarring leading to reflux nephropathy and end stage renal disease. It can be either primary due to

congenital abnormality of vesicoureteric junction or secondary to high pressure in the bladder.² The severity of VUR is graded using the International study classification from grade I –V, based on the appearance of the urinary tract on contrast Micturating cystourethrogram (MCU). Children with high grade reflux (grade IV-V) who acquire a UTI are at significant risk of pyelonephritis and renal scarring. With bladder growth and maturation, there is tendency for reflux to resolve or improve. Lower grades of reflux (I-III) are much more likely to resolve than higher grades.³ Hypertension and uremia are two important serious complications of scarring due to pyelonephritis. Proteinuria is an important predictor of progression to end stage renal disease.²

OBJECTIVE

To study the outcome of VUR in relation to Recurrence of UTI following diagnosis and to find out the incidence of renal cortical scarring as evidenced by DMSA scan on diagnosis and follow up.

MATERIALS AND METHODS

A hospital based ambispective (Retrospective and Prospective) Study was carried out in Department of pediatrics, Kasturba Medical College, Manipal from August 2004 to August 2012. All children in the age group of 1 month to 18 years with Vesicoureteric Reflux, who presented to the Department of Pediatrics (Kasturba Hospital Manipal) between Aug 2004 to Aug 2010 were included in the study.

During follow up: Height, Weight, Blood Pressure, episodes of documented UTI, Serum Creatinine, follow up VUCG, DMSA scans whenever repeated was noted. BMI and Height standard deviations scores were calculated at the time of entry into the study and at last follow up. UTI was said to be present if either the urinary nitrite was positive or there was significant bacteriuria >10⁵ CFU/ml in a midstream clean catch urine.⁵⁸ The data was collected and entered in M S Excel and analyzed using SPSS v 21. The continues data was represented with mean and standard deviation. The data was presented in the form of Percentages and Proportions.

RESULTS

A total of 93 children were included in the study. Majority (78.5%) presented before 5 years, youngest age at presentation was 1 month and oldest at 14yr 8 months. Among 93 children studied, 65 were males and 28 were females with male to female ratio of 2.3. A total of 19 children were lost for follow up-6 with Grade I-II,8 with Grade III,5 with Grade IV-V. Outcome was evaluated in 74 cases. (Table 1). The Mean duration of follow up is 3.8 years, (Range 2 years to 16.5years)

Table 1: Age and Sex Incidence at Presentation of VUR (n=93)

Age group	Male(n=65)	Female(n=28)
<1YR(n=29)	23	6
1-5YRS(n=44)	31	13
5-10 YRS (n=14)	6	8
10-15 YRS(n=6)	5	1

The commonest presenting complaint was fever (58%), followed by recurrent UTI (40.8%), dysuria 32(34.4%) and reports of documented UTI was available in 23(24.7%) cases. H/o poor urinary stream was present in 43% of males (28/65). 4children had hypertension at presentation, 3 of them had associated posterior urethral valve. Following vesicostomy blood pressure normalized in 2. One child had scarred poorly functioning left kidney with persisting hypertension on maximal doses of Nifedipine and Envas. BP normalized following left nephroureterectomy and child is currently off antihypertensive. One child with grade 4 VUR had hypertension and BP normalized following ureteric reimplantation. Neurogenic bladder was present in 3

children, 2 had associated Anorectal malformation and one had meningomyelocele .1 child with chronic kidney disease stage 4 (GFR-17ml/min/1.73m² Serum Creatinine 1.7mg/dl) had clinical features of rickets.

Table 2 : Lab parameters at presentation

Investigations	Cases(n=93)
Positive urine culture at admission	35(37.6%)
Positive Nitrites	10(10.7%)
Elevated creatinine	14(15%)
Hyperphosphatemia	1(1%)

38.7% of children had documented UTI at 1st visit -35 C/S positive and 1 child had isolated positive nitrites. The commonest organism was E. coli (n=19) followed by Klebsiella (n=8), Proteus (n=3), Enterococcus(n=2), Citrobacter (n=2) and Pseudomonas(n=1) At 1st visit 14 children had elevated creatinine for age.5 of them had an associated PUV 8 of the children with elevated creatinine had Grade V reflux, in 3 of them, S. creatinine normalized and has remained so (mean follow up period 9.3 years range 4-12yrs).one child who was initially in stage 4 chronic kidney disease had maintained GFR on follow up at 3 years .one had associated meningomyelocele and was in stage 3 chronic kidney disease at diagnosis. (Table 2)

Table 3: USG findings at presentation (n=93)

Kidneys	Unilateral		Bilateral
	Right	Left	
Hydronephrosis (n=32)	7	13	12
Duplex system with hydronephrosis (n=3)	0	3	0
Contracted kidney(n=3)	2	1	
Unilateral Agnesis of kidney (n=2)	0	2	
Hypoplastic kidney (n=2)	1	1	
Ectopic kidney(n=2)	1	1	
Bladder			
1.Diverticulum	2		
2. Bladder wall trabeculations	13		

Ultrasound evaluation was done in all cases. Hydronephrosis was the commonest abnormality (35) followed by bladder wall trabeculations (13), contractedkidney (2), unilateral agnesis of kidney (2), hypoplastickidney (2) and ectopic kidney (2). Normal USG findings were observed in 34 children. (Table 3)

Table 4: MCU Finsding at presentation (n=93)

Grades of vur	Unilateral (n=43)		Bilateral (n=50)
	Right (n=21)	Left (n=22)	
Grade I and II(n=23)	8	5	10
Grade III(n=30)	6	5	19
Grade IV and V(n=40)	7	12	21

Fifty children had bilateral VUR and 43 had unilateral reflux (21 on the right side and 22 on the left). Majority (43%) had grade IV and V reflux, 32.3% had grade III reflux and 24.7% had grade I and II reflux. (Table 4) Cystoscopic evaluation was performed in 39 cases, Lateralized gaping ureteric orifice was seen in 30 cases, one had anterior urethral diverticulum and 8 had normal ureteric orifices.

Table 5: DMSA scan at presentation V/s Grades of VUR (n=76)

Grades of VUR	Scarring(n=41)	Normal(n=35)
Grade I and II(n=19)	4	15
Grade III(n=22)	6	16
Grade IV and V(n=35)	31	4

Among 76 children who underwent a DMSA scan 41 children (54%) had detectable renal scars. Incidence of scarring was higher with increasing grades of VUR (88.5% in Grade IV-V Vs 21% in Grade 1-2). (Table 5)

Table 6: Management V/S Initial Grade of VUR (n=74)

Grades of VUR	Medical (n=47)	Ureteric Re-implantation (n=27)
Grade I and II(n=17)	13	4
Grade III(n=22)	18	4
Grade IV and V(n=35)	16	19

4 children with Grade I-II needed surgical intervention-2 had associated bladder diverticulum and underwent diverticulectomy with ureteric reimplantation,² underwent ureteric reimplantation as the VUR had progressed to Grade III on follow up. 3 children with grade III reflux underwent ureteric reimplantation in view of associated scarring and age >6years. One child underwent reimplantation at 4yr 4 months in view of breakthrough UTIs. Among 19 children with grade IV and V reflux, 9 underwent ureteric reimplantation in view of associated scarring and age at presentation being >6yrs. 10 underwent early ureteric reimplantation (age < 5yrs),⁸ in view of breakthrough UTI,² had associated duplex system. (Table 6).

DISCUSSION

VUR has a unique distinction of having evolved from an anatomic curiosity around the first century AD into one of the most contentious and complex areas of urology today. Galen and da Vinci made the first references to VUR in western medicine when they alluded to the ureterovesical junction (UVJ) as a mediator of unidirectional flow of urine from the kidneys to the bladder. Sampson, in 1907, suggested that the oblique course of the ureter through the bladder wall created a locking mechanism at the UVJ and was also the first to imply that VUR might lead to renal infection.⁴ In one meta-analysis of studies of children undergoing cystography for various indications, the

prevalence of reflux was estimated to be approximately 30% for children with UTI and 17% without UTI.⁵ In contrast, reflux may be present in up to 70% of infants who present with UTI.⁶ The distribution of age and gender among study subjects in our study was comparable to the retrospective study conducted by Torre Rhoades *et al* (n=3771) 84.4% of cases presented before 7 years.⁷ In another study by Abeyssekara *et al*; Majority (76%) were below the age of 2 years with male to female ratio being 1.7:1(n=56).² The signs and symptoms of the subjects in our study was comparable with the nine year prospective by Greenfield *et al* (n=560), where majority of the children presented with recurrent UTI (54%), followed by voiding dysfunction (15%).⁸ The medical and surgical therapy for reflux has purported to offer similar benefit to patients. This has fueled the debate between fundamental choices of therapy for decades. The tension embedded in decision making for reflux management stems from the almost perfect results attainable by surgical correction of reflux, now commonly successful in more than 98% of cases. It is not clear how long to wait for reflux resolution in the individual patient. In newborn patients, it is reasonable to wait until approximately 5 years of age assuming no intercurrent breakthrough infections occur. Beyond this age, it is commonly believed that the kidneys become less prone to scarring after pyelonephritis.⁹ North American and European cooperative study that randomized children younger than 9 years old with high-grade reflux to watchful waiting with prophylaxis or corrective open surgery.^{10,11} Medical and surgical management was prospectively compared in a randomized cohort of 104 patients with high-grade reflux over a 5-year period.¹² Again, the incidence of new scars was the same using either treatment modality. Although more than half the patients continued to reflux at 5 years, all cases of new scarring occurred within the first 2 years, consistent with the "Big Bang" concept of post infectious renal injury mentioned previously.

Conclusion and Recommendation: The mean age at presentation of vesicoureteral reflux was 3.6 years with a range of 1 month-14 years 8 months. Majority (78.5%) of the children presented before 5 years. Incidence of scarring was higher with increasing grades of VUR. After successful surgical reflux correction susceptibility to urinary tract infection continues for a number of years in many girls and women. Although modern management of VUR and urinary tract infections will improve the prognosis in the future, there is a need for long-term follow-up. Patients with scars in both their kidneys should probably be followed and tested throughout their lifetime. In our study, hypertension of this subgroup was well diagnosed and treated.

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