

ORIGINAL PAPER

# A new insight into the management of high-grade vesicoureteral reflux

Mohamed Adel Atta<sup>1</sup>, Asmaa Ismail<sup>2</sup>, Ahmed Fouad Kotb<sup>2</sup>

<sup>1</sup>Alexandria University, Alexandria, Egypt

<sup>2</sup>Northern Ontario School of Medicine, TBRHSC, Thunder Bay, Canada

## ABSTRACT

**Introduction:** High-grade vesicoureteral reflux (VUR) is a major dilemma to urologists, with no clear time for intervention in children without evidence of urinary tract infection. The aim of our study was to show our experience in managing high-grade VUR in children with high postvoiding residual.

**Material and methods:** Our study included 24 children with high-grade reflux persistent while being on surveillance and continuous antibiotic prophylaxis. Besides radiological investigations, 24-hour urine output and postvoiding residual were our main clinical parameters to study.

**Results:** All the children with high-grade reflux in our study were found to have polyuria and high postvoiding residual. Surgical correction was done through open surgical ureteral reimplantation combined with the use of vasopressin. Reduction cystoplasty was done for 2 children. One-year follow-up showed satisfactory outcomes in reducing bladder capacity and treating reflux.

**Conclusions:** Children with high-grade VUR should be assessed for polyuria. The presence of polyuria should be an indication for early surgical management.

## KEY WORDS:

vesicoureteral reflux, ureteral reimplantation, polyuria, diabetes insipidus.

## INTRODUCTION

High-grade vesicoureteral reflux (VUR) is a major dilemma to urologists. Surveillance with or without continuous antibiotic prophylaxis (CAP) has been proven to be successful in some groups of these patients. A Swedish trial could find no outcome difference for children with high-grade reflux managed by CAP versus those treated with early endoscopic intervention. However, they showed that high postvoiding residual (PVR) was a significant factor correlating with recurrent urinary tract infection (UTI) [1]. European Association of Urology guidelines recommend conservative management initially, with consideration of surgical management if there is

no improvement [2]. Most surgically managed children with high-grade reflux have open or laparoscopic ureteric reimplantation [3].

Guney *et al.* studied 122 surgically managed children by ureteral reimplantation for VUR and identified a rate of redo reimplantation of 8% among patients but failed to find any factor correlating with the initial reimplantation failure [4]. An interesting study did find that the absence of high PVR in these children significantly correlated with a higher resolution rate of VUR [5]. Another study found that PVR was the single factor correlating with the prognosis of management of VUR [6].

The aim of our study was to show our experience in managing high-grade VUR in children with high PVR.

## ADDRESS FOR CORRESPONDENCE:

Ahmed Fouad Kotb, MD, FRCS, FRCS Urol, FEBU, Northern Ontario School of Medicine, Thunder Bay, Canada, e-mail: [drahmedfali@gmail.com](mailto:drahmedfali@gmail.com)



**FIGURE 1.** Preoperative voiding cystourethrogram showing large bladder capacity and high-grade vesicoureteral reflux



**FIGURE 2.** Postoperative voiding cystourethrogram for the same child showing reduced bladder capacity and no reflux

## MATERIAL AND METHODS

Our study included 24 children. All children were initially managed with surveillance and CAP, with no improvement in the grade of reflux. The study was approved by the Ethics Committee of our institution.

Inclusion criteria included having had grade 3/4 VUR, absence of neurogenic or other secondary cause for reflux, and at least one year on surveillance and CAP.

Our initial approach was 24-hour measurement of urine output for these children and measurement of PVR. Polyuria was defined as  $> 4$  ml/kg/hour urine output. The urine output was measured by weighing the diapers. In toilet-trained children, urine collection was done and measured. High PVR was defined as a residual of more than 10% of bladder capacity. Vasopressin 1–2 micrograms intranasally was given before the surgery and continued for one year after the surgery. Open surgery was used for all children. Embedded nipple technique was our preferred way of reimplantation to all children [7]. Success of surgery was defined as complete resolution of VUR at one year after surgery. Descriptive statistics was done using median and interquartile range. The Wilcoxon rank test was used to compare the PVR outcomes before and after surgery.

## RESULTS

Our study included 24 children. The median age was 2 years (range 1–7 years). The study included 10 girls and 14 boys. Bilateral VUR was present in 8 children while being unilateral in 16 children. All children were consistently found to always have high PVR and polyuria. All patients had embedded nipple ureteral reimplantation,

**TABLE 1.** Pre- and post-operative outcomes

Parameters		Outcome
Median, IQR of age (years)		2, 1
Sex	Males	14
	Females	10
Laterality	Unilateral	16
	Bilateral	8
Median, IQR of preop urine output [ml]		1200, 275
Median and IQR of preop PVR [ml]		100, 50
Median and IQR of postop urine output [ml]		650, 50
Median and IQR of postop PVR [ml]		20, 0
Reduction cystoplasty	Yes	2
	No	22
VUR at 1 year post-operatively	Yes	0
	No	24

*IQR – interquartile range, PVR – postvoiding residual, VUR – vesicoureteral reflux*

and 2 of them had reduction cystoplasty as well, for markedly distended bladder. Figure 1 shows a case with large bladder and high-grade VUR before surgery, and Figure 2 shows the same child one year after surgery. Table 1 illustrate the children's pre- and post-operative findings. Voiding cystourethrogram (VCUG) at one year postoperatively confirmed resolution of VUR to all children. Twelve children had a further ultrasound scan 6 months later confirming no hydronephrosis and empty bladder. There was a significant improvement of postoperative PVR measurements compared to preoperative findings ( $Z = 4.28, p < 0.00001$ ).

## DISCUSSION

Polyuria has a deleterious effect on voiding and bladder physiology, especially in children. This has been appreciated as a complicating factor in patients with posterior urethral valve, resulting in a secondary bladder dysfunction referred to as valve bladder [8, 9].

In our study, there was polyuria, increased bladder capacity, and PVR in all children. Interestingly, these children had good urine flow rate but high PVR. The cause of polyuria in these cases is not known, but it can be assumed that the hammering effect of urine reflux on the developing kidneys in these children leads to tubular dysfunction with consequent loss of concentration function of the distal convoluted tubules. This is known to happen in patients with obstructed kidneys, resulting in temporary loss of kidney function manifested initially by the loss of the concentration power of the kidney [10, 11]. This has been known as nephrogenic diabetes insipidus (NDI).

Aquaporins are known proteins responsible for water movement in our body. Aquaporin 2 (AQP2) is the chief regulator of collecting duct permeability and is under the control of vasopressin, which helps translocation of AQP2 from the intracellular vesicles to the apical membrane of the collecting ducts cells. This vasopressin control is downregulated in several forms of acquired NDI characterized by severe polyuria [12, 13].

Traditionally it is stated that vasopressin is not effective in NDI because the latter lacks ADH receptors in the distal nephron. Naghizadeh *et al.*, however, showed that the use of vasopressin was successful in decreasing the polyuria in children with posterior urethral valves [14].

The present study conveys an important clinical message. We mostly do ultrasounds, VCUG, and dimercaptosuccinic acid scans to our children with VUR, but we miss simple important clinical tools, i.e. measurement of 24-hour urine output and PVR. We believe that polyuria in these children is an added absolute indication to stop surveillance and proceed with surgical management. Missing polyuria and continuous surveillance based on no febrile UTI or no diagnosed renal scarring may result in long-term deterioration of kidney function. Surgery is a mandatory step, once polyuria is detected, to maintain kidney function. Polyuria in these children was reversible with vasopressin and surgical correction.

Our study represents our own experience and is not strongly supported in the literature. Although we trust our data and use its outcomes for our children, multi-institutional studies on greater numbers of children need to be performed to improve our quality of care for future generations.

## CONCLUSIONS

Children with high-grade VUR should be assessed for polyuria. The presence of polyuria should be an indication for early surgical management.

## DISCLOSURE

The authors declare no conflicts of interest.

## REFERENCES

- Nordenström J, Sjöström S, Sillén U, Sixt R, Brandström P. The Swedish infant high-grade reflux trial: UTI and renal damage. *J Pediatr Urol* 2017; 13: 146-154.
- Tekgül S, Riedmiller H, Hoebeke P, et al. EAU guidelines on vesicoureteral reflux in children. *Eur Urol* 2012; 62: 534-542.
- Esposito C, Escolino M, Lopez M, et al. Surgical management of pediatric vesicoureteral reflux: a comparative study between endoscopic, laparoscopic, and open surgery. *J Laparoendosc Adv Surg Tech A* 2016; 26: 574-580.
- Guney D, Tiryaki TH. The prevalence of redo-ureteroneocystostomy and associated risk factors in pediatric vesicoureteral reflux patients treated with ureteroneocystostomy. *Urol J* 2019; 16: 72-77.
- Cakmak O, Tarhan H, Akarken I, et al. Can we predict vesicoureteral reflux resolution in patients with non-neurogenic lower urinary tract dysfunction?. *Int J Urol* 2019; 26: 638-642.
- Beksac AT, Koni A, Bozacı AC, Dogan HS, Tekgul S. Postvoidal residual urine is the most significant non-invasive diagnostic test to predict the treatment outcome in children with non-neurogenic lower urinary tract dysfunction. *J Pediatr Urol* 2016; 12: 215.e1-8.
- Abou Youssif TM, Fahmy A, Rashad H, Atta MA. The embedded nipple: an optimal technique for re-implantation of primary obstructed megaureter in children. *Arab J Urol* 2016; 14: 171-177.
- Koff SA, Gigax MR, Jayanthi VR. Nocturnal bladder emptying: a simple technique for reversing urinary tract deterioration in children with neurogenic bladder. *J Urol* 2005; 174: 1629-1632.
- Hale JM, Wood DN, Hoh IM, et al. Stabilization of renal deterioration caused by bladder volume dependent obstruction. *J Urol* 2009; 182: 1973-1977.
- Leslie SW, Sajjad H, Sharma S. Postobstructive Diuresis. In: *StatPearls*. Treasure Island (FL): StatPearls July 1, 2020.
- Roth JD, Lesier JD, Casey JT, et al. Incidence of pathologic postobstructive diuresis after resolution of ureteropelvic junction obstruction with a normal contralateral kidney. *J Pediatr Urol* 2018; 14: 557.e1-557.e6.
- Su W, Cao R, Zhang XY, Guan Y. Aquaporins in the kidney: physiology and pathophysiology. *Am J Physiol Renal Physiol* 2020; 318: F193-F203.
- Kortenoeven ML, Fenton RA. Renal aquaporins and water balance disorders. *Biochim Biophys Acta* 2014; 1840: 1533-1549.
- Naghizadeh S, Kefi A, Dogan HS, Burgu B, Akdogan B, Tekgul S. Effectiveness of oral desmopressin therapy in posterior urethral valve patients with polyuria and detection of factors affecting the therapy. *Eur Urol* 2005; 48: 819-825.