

Comparison of the Voiding Pattern in Toilet-trained Filipino Children with Urinary Tract Infection With and Without Vesicoureteral Reflux: A Prospective Study

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Objectives: Vesicoureteral reflux (VUR) is a common abnormality of the urinary tract in children and remains a dilemma that is commonly seen by physicians. Unrecognized VUR associated with UTI may lead to long term effects on renal function and overall patient health. To date, there is no current study on voiding patterns of children presenting as recurrent UTI with and without VUR. In this study, the authors aim to determine if there is a difference in the voiding pattern of toilet trained Filipino children with UTI between those with and without VUR and to see if there is association between these parameters with the degree of VUR.

Materials and Methods: The study employed a prospective research design. Population consisted of pediatric patients seen in the clinic diagnosed as a case of UTI documented with positive urine culture. Voiding cystourethrogram was done to determine presence or absence of VUR. The procedure was done by a single Urologist at a single institution. The patients were then subdivided into 2 groups, the first group consisted of patients with UTI with VUR and another group had those with UTI but without VUR. A subanalysis was done to determine association depending on the degree of reflux. Logistic regression analysis, chi-square test and ANOVA were used to determine if there was any statistically significant difference between the two groups.

Results: A total of 223 pediatric patients with ages ranging from 2 years to 17 years with mean age of 9.5 years with documented urinary tract infection were noted. Among these, only 140 patients underwent VCUG hence included in the study. It consists of 57 male patients (40%) and 83 female patients (59%). Among these patients, 65 patients (46%) had vesicoureteral reflux and 75 patients (53%) had no vesicoureteral reflux. Each patient's voiding parameters such as bladder wall thickness, bladder capacity, postvoid residual, Qmax and voiding pattern were noted and compared between groups. A subanalysis was also done to determine any association of these parameters to the degree of reflux.

Conclusion: In the present series, bladder capacity was the only parameter found to be statistically different between those with and those without VUR. Furthermore, this difference was only seen among those with grades 3, 4 and 5 refluxes. Future study must be carried out to determine its clinical significance. Physicians must be vigilant and must have a high index of suspicion in dealing with patients with episodes of febrile UTI. To date, voiding cystourethrogram is still the gold standard to diagnose this disease entity.

Keywords: voiding pattern, urinary tract infection, vesicoureteral reflux

Introduction

Vesicoureteral reflux (VUR) is characterized by the retrograde flow of urine from the urinary bladder to the kidneys and can be associated with urinary tract infection, hydronephrosis and abnormal kidney development.¹ Voiding cystourethrogram remains the gold standard to assess vesico-ureteral reflux. However, this procedure is invasive, associated with ionizing radiation, and can be poorly tolerated by infants which can be a cause of concern for the parents. Unrecognized VUR with concomitant UTI may lead to long term effects on renal function and overall patient health.⁴ The probability of VUR in children assessed to have UTI may reached as high as 50%.³

The significant effects of VUR on the kidney establish the need for accurate diagnosis and correction of reflux. Currently, the American Academy of Pediatrics guidelines recommend VCUG if patient has febrile UTI, hydronephrosis and renal scarring.² According to Darge, up to 20% cases of hypertension and 25% cases of patients with end stage renal disease.³ Early diagnosis and vigilant monitoring of VUR are the cornerstones of management.

Up to 50% of children with VUR is associated with voiding dysfunction. It is thus regarded as an important determinant of the severity and resolution of VUR.⁷

To date, there is no current study on voiding patterns of children presenting as recurrent UTI with and without VUR. Knowing these voiding patterns will help clinicians better understand the etiology and presentation of voiding dysfunction in patients and minimize the use of VCUG.

In this study, the authors aim to compare the voiding pattern in toilet-trained Filipino Children with UTI with and without VUR.

Patients and Methods

Design and Conduct

The study employed a prospective design. All patients seen in the pediatric clinic from September 2014 to June 2017 and diagnosed as a

case of UTI documented by urinalysis and urine culture were included in this study. These patients underwent voiding cystourethrogram to determine presence and absence of VUR. This procedure was done by a single Urologist. All data were transcribed by a personnel assigned by the author. The statistical analysis was done by independent statisticians hired by the authors. The authors have assumed responsibility for the completeness and integrity of the data.

Patients and Treatments

From September 2014 to June 2017, a total of 223 pediatric patients with ages ranging from 2 to 17 years (mean age of 9.5 years) with documented urinary tract infection were noted. Among these, only 140 patients underwent VCUG hence included in the study. These were 57 male patients (40%) and 83 female patients (59%). Among these patients, 65 patients (46%) had VUR and 75 patients (53%) had no VUR. Among patients with VUR, 29 patients (45%) had grade 1 and 2 VUR and 36 patients (55%) had grade 3,4,5 VUR.

The parents were asked to complete a 3-day bladder chart. The patients were then subdivided into 2 groups: One group consisting of patients with UTI with VUR and another group of patients with UTI without VUR.

Toilet-trained patients and those neurologically normal children without any urogenital anatomical problem except VUR were included in the study. Those with no consent, not toilet-trained and with other urogenital anatomical conditions such as posterior urethral valves, ureterocele, meatal stenosis, labial synechiae were excluded from the study.

The initial evaluation of all patients included a detailed history of voiding patterns and physical examination. Complete urologic and neurologic investigations, urinalysis and urine culture, VCUG and renal ultrasound were performed in all patients. Urodynamic studies were performed using the Delphis apparatus.

All patients underwent Uroflow twice and Uroflow with EMG with the use of Urodynamic machine. Estimated bladder capacity was computed using the formula (age + 1) x 30.

Values for bladder capacity, post-void residual and Qmax were recorded and their mean was obtained and used in the computation. Uroflow pattern based on Uroflowmetry was also utilized in this study. Bladder wall thickness was measured using ultrasound.

A sub-analysis was done comparing patients without VUR to those patients with grade 1, 2 hydronephrosis and grade 3,4,5 hydronephrosis as documented by VCUG.

Endpoints:

Determining the voiding pattern of toilet-trained patients with UTI with and without VUR, the significant difference between the two groups using the following parameters: bladder wall thickness (cm), bladder capacity, post-void residual (mL), Qmax (mL), voiding pattern: Bellshape, tower, staccato, interrupted and plateau and the association of these voiding patterns with the degree of VUR.

Statistical Analysis:

The analysis was done by an independent statistician employed by the authors. SPSS Statistics 17.0 was used for the analysis of the data. Logistic regression analysis and Chi square test were used to determine statistical difference between the two groups. ANOVA was used to determine association of these parameters depending on the degree of reflux.

Results

A total of 223 pediatric patients with ages ranging from 2 years to 17 years (mean age of 9.5 years) with documented urinary tract infection were noted. Among these, only 140 patients underwent VCUG and thus, included in the study. It consists of 57 male patients (40%) and 83 female patients (59%). Among these patients, 65 patients (46%) had VUR and 75 patients (53%) had no VUR. Among patients with VUR, 29 patients (45%) had grade 1 and 2 VUR and 36 patients (55%) had grade 3,4,5 VUR.

Table 1. Voiding characteristics of patients with UTI with or without vesicoureteral reflux.

Parameters	Patients without Vesicoureteral reflux	Patient with Vesicoureteral reflux	P-value	Interpretation
Bladder Capacity (mL)	122	145	0.0110	With significant difference
Bladder wall Thickness (cm)	3.44	3.71	0.8787	No significant difference
Post-void Residual (mL)	13.24	14.25	0.5593	No significant difference
Qmax (mL/sec)	15.5	16.1	0.0520	No significant difference
Voiding Pattern: Bellshape, tower, staccato, interrupted plateau	Bellshape: 82/128= 64% Tower: 16/128=12.5% Staccato: 13/128= 10.15% Interrupted: 10/128= 7.8% Plateau: 7/128= 5.4%	Bellshape: 71/95= 75% Tower: 6/95= 6.31% Staccato: 9/95= 9.4% Interrupted: 4/95= 4.2% Plateau: 5/95= 5.2%	0.472	No significant association

Statistically significant: pvalue <0.05 at 95% confidence interval

Table 1 shows the voiding characteristics of patients with UTI with and without VUR. Among the 5 parameters, only bladder capacity showed significant difference between the two groups.

Subanalysis was done to determine the degree of reflux that has significant correlation with bladder capacity.

Table 2 shows the subanalysis done in which only patients with no reflux vs Grade 3,4,5 has statistical difference in terms of bladder capacity.

Table 2. Post-hoc analysis on bladder capacity.

Comparison	p-value	Interpretation
No reflux vs Grade 1 & 2	0.058	No significant difference
No reflux vs Grade 3,4,5	0.039	With significant difference
Grade 1, 2 vs Grade 3,4,5	>0.999	No significant difference

Discussion

The flow of urine from the ureter to the bladder is normally one directional across the vesicoureteral junction.⁵ Normally, VUR does not occur because there is compression of the tunneled, submucosal ureter as the bladder fills with urine.⁷ VUR is a developmental anomaly created by an inadequate length of the intravesical submucosal tunnel of the ureter in relation to the pressures experienced by the patient's bladder.¹² VUR is classified as either primary or secondary VUR. VUR is primary if it is thought to be an isolated, fundamental deficiency in the above described anatomic ureteral tunnel.⁹ Secondary VUR refers to one that is due to abnormal bladder dynamics and/or elevated voiding pressures.⁹ These abnormalities are seen with lower urinary tract dysfunction stemming from bladder outlet obstruction such as posterior urethral valves, ureterocele, neurogenic bladder and dysfunctional voiding.¹¹

In young children, urinary tract infection is relatively common. One of the risk factors is VUR, which is seen in 30-50% of children and 40-50% of them present with febrile urinary tract infection.⁶

Once the diagnosis of VUR is established by VCUG, VUR is categorized or graded in severity by the degree of ureteral dilation on VCUG. The grading system for VUR that is globally accepted is based on the radiologic grading system established by the International Reflux Study Committee in 1981.¹⁰ Grade I shows reflux into a non-dilated ureter; Grade II, into pelvis and calyces without dilatation; Grade III, mild to moderate dilatation of ureter, renal pelvis and calyces with minimal blunting of fornices; Grade IV, moderate ureteral tortuosity and dilatation of pelvis and calyces; and Grade V, gross dilatation of ureter, pelvis and calyces, loss of papillary impressions and ureteral tortuosity.¹⁰

According to Buscarini, et al. (2011), there is a 15 to 30% association between voiding dysfunction and reflux. Bilateral, rather than unilateral, VUR in association with voiding dysfunction is often found not only in children with neuropathic bladder abnormalities but also in neurologically intact children.⁸ It has also been shown that improvement in voiding dysfunction decreases the incidence of urinary tract infection and hastens the resolution of reflux.⁸

The effects of bladder dysfunction in children with urinary tract abnormalities are well-recognized. Patients with poor bladder compliance often have poor drainage from the upper urinary tract and experience progressive hydronephrosis.⁶ Pediatric urologists have recognized the importance of bladder dysfunction in VUR management. In 1979, Koff, et al.¹⁰ studied 53 neurologically normal children with UTI and detrusor-sphincter discoordination, finding that 52% had VUR.⁹

In the present series, the authors compared the voiding parameters of patients with UTI with and without VUR. Bladder capacity was the only parameter found to be statistically different between those with and those without VUR. Furthermore, this difference was only seen among those with grades 3, 4 and 5 refluxes. Future research and investigation must

be carried out to determine its clinical significance.

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