Original Paper

Urinary Tract Infection in Children after Voiding Cystourethrogram

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Abstract

Objective: Voiding cystourethrogram is a minimally invasive diagnostic procedure used to visualize the urinary tract and bladder and diagnose vesicoureteral reflux disease. We aim to determine the likelihood of developing a UTI after the VCUG.

Study design: A total sample of 125 children from the Jordan University Hospital who underwent 191 voiding cystourethrogram (VCUG) were retrospectively studied between 2002 and 2018, ages four days till 13 years old. Urine analysis and Culture were sent from selected patients, for post-VCUG-UTI.

Methodology: Electronic records were retrospectively reviewed in 125 pediatric patients at Jordan University Hospital.

Results: 60.7% of VCUG’s were abnormal (i.e., vesicoureteral reflux (VUR) or hydronephrosis). 5.24% had a negative urine analysis, 4.71% had a negative culture; 6.28% had a positive urine analysis, post-procedural urinary tract infection (ppUTI) was documented in 5.76% of the patients. The most common organism was Escherichia coli.

Conclusions: Voiding cystourethrogram is a significant risk factor for urinary tract infection in the pediatric age group; it is still debated whether ascending infection due to catheterization or the presence of a urinary tract abnormality is the cause of infection. Further studies on a larger scale must be considered to study other contributing factors.

Keywords
Urinary tract infection, Voiding cystourethrogram, Vesicoureteral reflux
1. Introduction
Urinary tract infection (UTI) is a severe public health problem, and it is a common problem in children and one of the most common childhood bacterial infections (J. American Academy of Family Physicians). High recurrence rates have been reported, and along with increasing antimicrobial resistance among the causative pathogens with time, all of that increase the economic burden of these infections (Flores-Mireles, Walker, Caparon, & Hultgren, 2015). One of the important UTI risk determinants is anatomic factors such as vesicoureteral reflux (VUR), one of the most common causes of urinary tract infection (UTI) in infants and young children. One of the crucial procedures necessary for diagnosing and treating VUR is voiding cystourethrography (VCUG) (Williams, Fletcher, Alexander, & Craig, 2008).

VCUG is a fluoroscopic study to visualize a patient's urethra and urinary bladder while the person urinates. It consists of catheterizing the person in order to fill the bladder with a contrast agent to watch it pass using the Xrays in order to determine the presence or absence of bladder and urethral abnormalities. Such procedures that require catheterization and using a contrast increase the risk of having a UTI (Hallett, Pead, & Maskell, 1976).

Some studies have shown that there is a relatively high risk of having a UTI after the VCUG, while others have shown a low risk. The percentages vary in the literature as it depends on many factors such as using antibiotics for prophylaxis, or criteria for choosing the population also differs between studies. Most children who undergo a VCUG have serious conditions in their urinary tract, and developing a UTI from the procedure would make their condition worse (Spencer et al., 2012). Hence, our study aims to find the incidence of UTI after performing VCUG, aiming to weigh the procedure's risk and benefits.

2. Methodology
A retrospective analytical study was carried out on children in Jordan University Hospital who underwent VCUG, regardless of the study’s primary indication, between 2002 and 2018 at the Department of Pediatric Surgery. We searched the electronic medical records (EMD) and included patients four days to 13 years old. The data about 191 VCUG’s done in 125 patients, 89 males and 36 females were reviewed. Full demographic characteristics are shown in Table1.

| Table1. Demographic Characteristics (n=125 Children, 191 Cystograms) |
|---|---|
| Age at study (years) (n=125 children)  | Mean: 6.5  |
|  | Median: 7 (0.0-13)  |
| Gender (n= 125 children)  |  |
| • Male  | 89 (71%)  |
| • Female  | 36 (29%)  |
The patients with documented UTI were considered the subjects of interest in our study, and further details of the diagnostic method of their UTI were gained. Informed consent was not taken from patients or their parents as data was obtained from their hospital records files.

Routine urine analysis has been done to all the patients before doing the procedure to ensure that the patient is UTI-free as part of the hospital guidelines. All patients were catheterized under standard aseptic techniques within our department by the involved doctors using an age-appropriate sized feeding tube. The contrast was injected, standard view x-ray films were taken of the bladder when full, during, and after micturition following the standard guidelines. A radiologist interpreted the images and reports about the presence or absence of any structural or functional abnormalities in the urinary tract. Post- VCUG patients’ data were analyzed for UTI symptoms reported by the physicians, and the results of Culture and sensitivity and urine analysis were obtained. Our exclusion criteria included the patients who underwent the procedure or received contrast through a suprapubic catheter, vesicostomy, or ureterostomy.

The data obtained from the patients’ record included the patient sex, age, whether a VCUG was performed or not, date and results of the VCUG, date, and findings of the urine analysis, and the urine culture results. Data were computed onto an excel sheet to be used for analysis. The data was analyzed using excel to obtain descriptive statistics about the number of research subjects who developed UTI after performing a VCUG. Due to the minimal number of UTI's identified, no further analysis was done.

3. Results

One hundred and twenty-five patients (71% males) of ages between 4 days and 13 years underwent one hundred and ninety-one VCUGs that met the eligibility criteria. A pediatric surgeon ordered most of the procedures. At the time of cystogram, each patient underwent a urine analysis before the procedure, and all were free, and so they underwent the procedure.

The VCUG result was abnormal in 60.7% of the patients (116/191). In 7.3% of studies, no reporting of images could be obtained, but they were included to measure the incidence of urinary tract infection after VCUG. Vesicoureteral reflux was detected in 47.1% of procedures. Other identified abnormalities included: hydronephrosis (5.8%), urinary bladder diverticulum (0.52%), posterior urethral valve (0.52%), vesicocolic fistula (0.52%) and bilateral pelvouretic junction stenosis (0.52%), see Table 2.

| VCUG findings     | n   | (%)  |
|-------------------|-----|------|
| Normal            | 75  | (39.3%) |
| VUR               | 90  | (47.1%) |
| Hydronephrosis    | 11  | (5.8%) |

Table 2. VCUG Findings (n=191 Cystograms, 125 Children)
Urinary bladder diverticulum 1 (0.52%)
Posterior urethral valve 1 (0.52%)
Vesicocolic fistula 1 (0.52%)
Bilateral pelviureteric junction stenosis 1 (0.52%)

Post-procedural UTI incidence and predictors:
In the seven days after cystogram patients were looked for if they were investigated by urine analysis and urine cultures. 88.48% of patients (169/191) were not investigated and had not put urine samples within two weeks of the procedure. So, they were presumed to be asymptomatic and that there was no clinical suspicion of urinary tract infection at that time. 5.24% of patients (10 out of 191) had a negative urine analysis, of which 9 patients had a negative culture.
Two patients (1.25%) had a mixed culture. 6.28% of patients (12/191) had a positive urine analysis, of which 11 patients had a positive urine culture since a single patient had a positive analysis but a negative culture.
Overall, strict diagnostic criteria for ppUTI (presence of symptoms, positive UA, and urine culture with >10,000 CFU/ml of a single organism) were documented in 5.76% (11/191) of VCUGs performed, and all children had both clinical symptoms and positive urine culture. See Table 3.

Table 3. Postprocedural UTI Incidence (n=191 Cystograms)

| Result                        | N (%)  |
|-------------------------------|--------|
| No urine analysis or Culture  | 169 (88.48%) |
| Negative urine analysis       | 10 (5.24%) |
| Negative urine culture        | 9      |
| Mixed Culture                 | 1      |
| Positive urine analysis       | 12 (6.28%) |
| Positive urine culture        | 11     |
| Mixed Culture                 | 1      |

The most common causative organisms were Escherichia coli (4/11). Other organisms included: Coagulase-negative staphylococci (CONS) (2/11), Diphtheroids (2/11) Enterococcus (1/11), Pseudomonas (1/11), Klebsiella (1/11) and Streptrophomonas maltophilia (1/11).
Ten children (10/11) who presented with a symptomatic ppUTI within 7 days of cystogram had an abnormal cystogram, including hydronephrosis (2/11), unilateral VUR (3/11), and bilateral VUR (4/11).
One patient had a normal cystogram, and another one his result could not be obtained. See Table 4.
Table 4. Diagnosis of Patients Who Developed UTI (n=11)

| Diagnosis     | N (%)   |
|---------------|---------|
| Hydronephrosis| 2 (18.2%)|
| Unilateral VUR| 3 (27.3%)|
| Bilateral VUR | 4 (36.4%)|
| Normal        | 1 (9.1%) |

*One patient’s result could not be obtained.

4. Discussion

Voiding cystourethrogram is still a substantial procedure to evaluate urinary tract abnormalities in children (Williams, Fletcher, Alexander, & Craig, 2008). Physicians use this imaging modality in the diagnosis of vesicoureteral reflux. The procedure is relatively easy and straightforward, but it carries high risks since it includes catheterization and radiation. The routine use of VCUG after a UTI has been controversial in the literature, as there have been questionable benefits in many cases with multiple complications such as the high risk of getting an infection, mechanical and psychological trauma, contrast reactions, and many others (Urinary Tract Infections following Micturating cystourethrography in Children). Unfortunately, there is no sufficient data to support this.

In this study, we aimed to study the risk of UTI after VCUG. Many studies have shown that the source of UTIs is the lower urinary tract; therefore, catheterization performed during VCUG can transfer pathogens retrograde to the upper UT (Schaeffer et al., 2017).

Urinary tract infections (UTIs) are a severe public health problem and are caused by a range of pathogens, but most commonly by Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Enterococcus faecalis and Staphylococcus saprophyticus. High recurrence rates and increasing antimicrobial resistance among uropathogens threaten to significantly increase the economic burden of these infections (Flores-Mireles, Walker, Caparon, & Hultgren, 2015).

Urinary tract infection is one of the most common childhood bacterial infections. It is estimated that at least 8% of girls and 2% of boys have UTI in childhood (J. American Academy of Family Physicians). According to a study published indicating the predominant UTI risk factors, it was reported that risk factors include female gender, sexual intercourse, and the use of spermicidal contraceptives. Other important UTI risk determinants in selected age groups include anatomic and physiologic factors, such as obstructing lesions and estrogen deficiency; genetic factors, such as blood group secretor status; antibiotic exposure; functional status; and possibly receptive anal intercourse and HIV infection (Harrington & Hooton, n.d.). However, VCUG was not considered a risk factor for UTI due to the scarcity of the data and the variability in the results obtained from multiple previous studies.
We aimed to identify the risk of UTI after VCUG in our institute and to compare it with other previously published research, by reviewing a 125 child’s medical records who underwent 191 voiding cystograms at Jordan University Hospital. We included patients between 4 days and 13 years old, older children were included aiming toward not missing a delayed diagnosis, differing from most of the other studies where patients under two years old were included in which they will most probably have antenatal hydronephrosis.

The frequency of UTI after VCUG was not investigated in too many studies. In this study, the incidence of UTI was 5.76%, which compares with other studies as it was a wide variation between the percentages. It is estimated to be between 1.0% and 17% (Johnson et al., 2017; Maskell, Pead, & Vinnicombe, 1978; Schaeffer et al., 2017). Unfortunately, we could not find any published studies in the Middle East.

Our investigation showed that cystograms were abnormal in 60.7% of studies, mostly being Vesicoureteral reflux, which was detected in 47.1% of procedures. 88.48 % of patients were not investigated for UTI and had not put urine samples within 2 weeks of the procedure, and there was no clinical suspicion of UTI at that time. This states that the risk of ppUTI after cystogram in children is very low, as stated by Johnson’s work (Johnson et al., 2017).

However, strict diagnostic criteria for ppUTI were found in 5.76% (11/191) of patients, and all children had both clinical symptoms and positive urine culture. This supports that catheterization performed during VCUG can transfer pathogens retrograde to the upper Urinary tract, as many other studies showed (Schaeffer et al., 2017; Maskell, Pead, & Vinnicombe, 1978).

Nine out of the eleven children had abnormal cystograms in the first place, which supports that the presence of a pre-existing urologic diagnosis such as VUR or hydronephrosis is strongly associated with ppUTI. Comparable to what Johnson and colleges have found, as only one child with a normal cystogram developed a ppUTI (Johnson et al., 2017).

In our study, there was also only one child with a normal cystogram who developed ppUTI.

In this study, 60.7% (116/191) of the cystograms were abnormal. VUR and hydronephrosis accounted for 52.9%. VUR was detected in 47.1%, which was consistent with most other studies where it is still the most common finding. In one of the studies, VUR accounted for 45.8% of the cases (Lee, Lorenzo, & Koyle, 2016). The other abnormalities were urinary bladder diverticulum, posterior urethral valve, vesicocolic fistula, and bilateral pelviureteric junction stenosis.

Numerous pathogens cause ppUTI; however, E.coli remains the most common pathogen among all others (Flores-Mireles, Walker, Caparon, & Hultgren, 2015; Hallett, Pead, & Maskell, 1976), and this was identified in our study since it was documented in 4 out of 11 patients.

The study encountered some critical limitations, considering it is a retrospectively written study, some information could not be attained. For example, most patients who did not do a urine test after the procedure might have been missed with a UTI. Additionally, some patients might have taken antibiotics prophylactically before the procedure and was not documented, due to the high prevalence of over the

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counter use of antibiotics in our country. Moreover, in some cystogram studies, no report could be obtained but was included to measure urinary tract infection incidence after voiding cystogram accurately.

5. Conclusion
Voiding cystourethrogram is a significant risk factor for urinary tract infection in the pediatric age group; it is still debated whether ascending infection due to catheterization or the presence of a urinary tract abnormality is the cause of infection. Further studies on a larger scale must be considered to study other contributing factors.

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