

ORIGINAL PAPER

The prevalence of vesicoureteral reflux and other genitourinary tract abnormalities in children with a history of urinary tract infection undergoing voiding cystourethrography: single-centre study

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ABSTRACT

Introduction: In this study we aimed to establish the prevalence of vesicoureteral reflux (VUR) and other genitourinary tract abnormalities in children with a history of urinary tract infection (UTI), who underwent voiding cystourethrography (VCUG), in light of the current recommendations of the Polish Society of Paediatric Nephrology (PTNFD).

Material and methods: Retrospective chart analysis included 366 children aged 0.25-16.17 years, median 1.96 years, interquartile range 3.84 years, with a history of UTI, who underwent VCUG according to PTNFD guidelines in the period from 2019 to 2022 in the Division of Paediatric Nephrology, Department of Paediatrics, Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Katowice, Poland. We analysed the outcomes of VCUG among participants reflecting PTNFD indications for VCUG: (1) recurrent UTI, (2) a history of febrile UTI with a septic course, and (3) UTI with ultrasound renal and bladder abnormalities.

Results: VUR was detected in 118 patients (32.2%). Among the remaining participants, 243 children (66.4%) presented with normal VCUG. In 5 children (1.4%) VCUG revealed urinary bladder diverticulum or posterior urethral valve. In group 1, VUR was found in 90/270 participants (33.3%), in group 2, in 23/70 participants (32.9%), and in group 3, in 5/26 participants (19.2%). There were no significant differences in the occurrence of VUR between study groups.

Conclusions: The prevalence of VUR in children with a history of UTI who underwent VCUG in light of the current recommendations of PTNFD, which comprise children with recurrent UTI, after septic UTI and after UTI with ultrasound renal and bladder abnormalities, in our study achieved 32.2%. The fact that no aberrations in VCUG were found in nearly two-thirds of children undergoing this procedure may add some relevant arguments for further discussion on the optimisation of the indications for VCUG in children.

KEY WORDS:

urinary tract infection, vesicoureteral reflux, voiding cystourethrography.

INTRODUCTION

Vesicoureteral reflux (VUR) is a backward flow of urine from the bladder into one or both ureters and often into the kidneys. It mainly affects infants and young chil-

dren. In more advanced conditions, dilatation of the ureter, the renal pelvis, and the calyces may be seen. VUR is associated with increased risk of urinary tract infection (UTI), renal scarring, and reflux nephropathy [1]. Recent studies suggest that as much as 25–40% of children

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may be affected with VUR [1]. The probability of VUR is greater in children with UTI who have urinary tract anomalies on ultrasound, children with fever who have a culture of a pathogen other than *Escherichia coli*, and those with hypertension. The likelihood of VUR is also higher in children with recurrent febrile UTI (≥ 2 episodes), regardless of age [2].

Voiding cystourethrography (VCUG) is an essential fluoroscopic technique in paediatric urology for the evaluation of the lower genitourinary tract. VCUG provides information on VUR grading and anatomical abnormalities such as bladder diverticula, bladder trabeculation, ureterocele, posterior urethral valve, and urethral stenosis [3].

According to the current recommendations of the Polish Society of Paediatric Nephrology (PTNFD) on the management of a child with UTI, published in 2016 and updated online on a web side of PTNFD in 2021, VCUG should be performed in children after a history of UTI with urinary tract abnormalities based on ultrasound, in children with recurrent UTI, and in children after septic UTI [4]. VCUG should be a method of choice for diagnosing and staging VUR [4].

Because VUR used to be considered as a major risk factor of renal scarring, its early detection seemed to be pivotal. But recent analyses have shown that renal scars may appear independently of VUR [5]. Moreover, studies have shown that surgical treatment of VUR does not exceed conservative treatment in the prevention of recurrences of UTI as well as renal scarring [6]. VCUG is rather expensive, is often stressful for the child, requires bladder catheterisation, and exposes the patient to radiation doses of 0.03–0.3 mSv, depending on the technique and equipment used [7]. Although the advantages generally exceed the risks, it is reasonable to optimise the quality and consistency of the results obtained from each VCUG and to compromise indications for VCUG because this is an invasive procedure [7].

The goal of our study was to establish the prevalence of VUR and other genitourinary tract abnormalities in children with a history of UTI who underwent VCUG and were considered as meeting the criteria of the current recommendations of PTNFD. We aimed to obtain data helpful for further discussion on the optimisation of the indications for VCUG in children with UTI.

MATERIAL AND METHODS

The retrospective chart review conveyed 366 patients: 245 females (66%) and 121 males (34%) aged 0.25–16.17 years, median age 1.96 years, interquartile range (IQR) 3.84 years, with a past history of UTI, who were admitted to the Division of Paediatric Nephrology, Department of Paediatrics, Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Katowice, Poland between January 2019 and December 2022 and underwent VCUG. Median age for girls was 2.83 years, range (0.25–16.17), IQR

4.33 years, and the median age for boys was 1.08 years, range (0.29–12.75), IQR 1.81 years. Inclusion criteria were as follows: age 0–18 years, history of UTI, first VCUG, indications that could be considered as reflecting PTNFD recommendation for VCUG established in 2021 (recommendation 30, strength of recommendation BI): 1) a history of recurrent UTI, 2) a history of septic UTI, 3) a history of UTI with urinary tract abnormalities based on ultrasound, and complete medical records [4]. Children, who underwent VCUG in the years 2019–2021 according to recommendations of PTNFD from 2016 (recommendation 10, strength of recommendation 1C) who did not meet the updated 2021 criteria: a history of atypical UTI, abnormal urinary tract picture on ultrasound, a history of UTI with a positive family history of VUR, as well as children who underwent VCUG due to other than UTI indications, i.e. lower urinary tract dysfunction or transplant qualification, were not included in the analysis.

Based on the medical chart retrospective analysis, participants of the study were divided into 3 groups possibly best reflecting one of 3 indications for VCUG in children with UTI recommended by PTNFD in 2021 (recommendation 30, strength of recommendation BI):

Group 1: participants with a history of recurrent UTI. According to PTNFD recommendations, the definition of the recurrent UTI is 2 or more upper UTI, one upper UTI and one lower UTI, and 3 or more lower UTI. In PTNFD recommendations it is stated that in children younger than 2 years it is usually not possible to differentiate between upper and lower UTI. Based on the above, group 1 was composed of children under 2 years old with 2 or more UTIs, children older than 2 years with 2 or more upper UTIs, or at least one upper UTI and one lower UTI or 3 or more lower UTIs. Group 1 comprised 270 children: 199 girls (73.3%) and 71 boys (26.7%). The median age of children in group 1 was 2.5 years, range (0.5–16.17), IQR 4.5 years. The median age for girls was 3.33 years, range (0.5–16.17), IQR 4.78 years, and the median age for boys was 1.08 years, range (0.5–12.75), IQR 1.85 years.

Group 2: participants with a history of one episode of febrile UTI with a septic course. It was composed of children after febrile UTI running with at least 2 signs of organ failure depicting the patient's mental, cardiovascular, and respiratory status, i.e. confusion, hypotension, tachypnoea with elevated inflammatory markers. The median C-reactive protein (CRP) concentration during the course of UTI was 100.4 mg/l, IQR 66.6 mg/l, and the median procalcitonin concentration was 5.5 ng/ml, IQR 2.47 ng/ml. Group 2 comprised 70 children: 35 girls (50%) and 35 boys (50%). The median age in group 2 was 1.08 years, range (0.25–10.75), IQR 2.2 years. The median age for girls was 1.5 years, range (0.25–10.75), IQR 2.17 years, and the median age for boys was 0.75 years, range (0.29–6.25), IQR 0.75 years.

Group 3: participants with a history of 1 episode of UTI and urinary tract abnormalities on ultrasound,

TABLE 1. VUR and other genitourinary tract abnormalities on VCUG in participants of the study

Factor	N	VUR on VCUG n (%)	VCUG normal n (%)	Other abnormalities on VCUG n (%)
Total	366	118 (32.2)	243 (66.4)	5 (1.4)
Girls	245	80 (32.6)	162 (66.1)	3 (1.2)
Boys	121	38 (31.4)	81 (66.9)	2 (1.7)
Group 1	270	90 (33.3)	175 (64.8)	5 (1.8)
Girls	199	65 (32.7)	131 (65.8)	3 (1.5)
Boys	71	25 (35.2)	44 (62.0)	2 (2.8)
Group 2	70	23 (32.8)	47 (67.2)	–
Girls	35	12 (34.3)	23 (65.7)	–
Boys	35	11 (31.4)	24 (68.6)	–
Group 3	26	5 (19.2)	21 (80.8)	–
Girls	11	3 (27.2)	8 (72.8)	–
Boys	15	2 (13.3)	13 (86.7)	–

VUR – vesicoureteral reflux, VCUG – voiding cystourethrography

i.e. hydronephrosis, hydroureter, hydroureteronephrosis, asymmetry of kidney dimensions. Group 3 comprised 26 children: 11 girls (42%) and 15 boys (58%). The median age in group 3 was 1.59 years, range (0.33–11.33), IQR 2.25 years. The median age for girls was 1.75 years, range (0.66–7), IQR 2.25 years, and the median age for boys was 1.25 years, range (0.33–11.33), IQR 3.17 years.

VCUG was performed in every participant. A 5-grade scale established by the International Reflux Study in Children was used to grade patients with VUR [8]. Low-grade VUR was defined as VUR grade 1 and 2, while high-grade VUR was defined as VUR grade 3, 4, and 5 [8]. In case of bilateral refluxes, the grade reflected a more advanced one. The prevalence of VUR, low-grade VUR and high-grade VUR among the 3 groups were compared.

STATISTICAL ANALYSIS

Database management and statistical analysis were performed with the data analysis software system STATISTICA (version 12, StatSoft Inc.). The homogeneity of variance was checked with the Shapiro-Wilk test. Skewed variables were presented as median and IQR values. Continuous variables that were non-normally distributed were compared using the Mann-Whitney *U* test. Categorical variables were described as number and percentage. For the comparison of categorical variables, the χ^2 test or Fisher's exact test were used. The level of significance was set at $p \leq 0.05$.

RESULTS

Within the whole study group, VUR was detected in 118 patients (32.2%). Among the remaining participants, 243 children (66.4%) presented with normal VCUG. However, in 5 children (1.4%) VCUG revealed

abnormalities other than VUR, such as urinary bladder diverticulum or posterior urethral valve.

Within participants with VUR there were 80 females (67.8%) and 38 males (32.2%), comparable to the gender percentage distribution in the entire study group. Among the cohort with VUR, 68 children (57.6%) presented with unilateral reflux, while 50 children (42.4%) presented with bilateral reflux. Noticeably, 39 participants (33.1%) exhibited low-grade reflux and 79 participants (66.9%) exhibited high-grade reflux (Table 1).

In group 1, which comprised children with a history of recurrent UTI, VUR was present in 90 participants (33.3%): in 65 girls (72.2%) and in 25 boys (27.8%), respectively. Out of a cohort with VUR, 50 patients (55.6%) presented with unilateral reflux, while 40 children (44.4%) presented with bilateral reflux. Furthermore, the categorisation based on the severity of reflux revealed low-grade reflux in 29 patients (32.2%), and high-grade reflux in 61 patients (67.8%) (Table 2). In 5 children (1.9%) bladder diverticulum or posterior urethral valve were diagnosed (Table 1).

In Group 2, which included children with a history of febrile UTI with a septic course, VUR was detected in 23 participants (32.9%): in 12 girls (52.2%) and in 11 boys (47.8%). Within this group, 14 children (60.9%) were diagnosed with unilateral reflux, 9 children (39.1%) exhibited bilateral reflux. Further stratification of reflux cases revealed that 10 patients (43.5%) presented with low-grade reflux while 13 patients (56.5%) presented with high-grade reflux (Table 2).

In group 3, which was composed of patients with a first episode of UTI with either hydronephrosis, hydroureter, hydroureteronephrosis, or asymmetry of kidney dimensions detected by ultrasound, VUR was present in 5 participants (19.2%): in 3 girls (60%) and in 2 boys (40%). Within this group, one patient (20%) exhibited bilateral reflux. Furthermore, all patients with detected anomalies presented with high-grade reflux (Table 2).

TABLE 2. VUR localisation and grading in participants of the study

	VUR on VCUG <i>N</i>	Unilateral VUR <i>n</i> (%)	Bilateral VUR <i>n</i> (%)	Low-grade VUR <i>n</i> (%)	High-grade VUR <i>n</i> (%)
Total	118	68 (57.6)	50 (42.4)	39 (33.1)	79 (66.9)
Girls	80	48 (60.0)	32 (40.0)	31 (38.8)	49 (61.2)
Boys	38	20 (52.6)	18 (47.4)	8 (21.1)	30 (78.9)
Group 1	90	50 (55.6)	40 (44.4)	29 (32.2)	61 (67.8)
Girls	65	38 (58.5)	27 (41.5)	25 (38.4)	40 (61.6)
Boys	25	12 (48.0)	13 (52.0)	4 (16.0)	21 (84.0)
Group 2	23	14 (60.9)	9 (39.1)	10 (43.5)	13 (56.5)
Girls	12	8 (66.7)	4 (33.3)	6 (50.0)	6 (50.0)
Boys	11	6 (54.5)	5 (45.5)	4 (36.4)	7 (63.6)
Group 3	5	4 (80.0)	1 (20.0)	0 (0.0)	5 (100.0)
Girls	3	2 (66.7)	1 (33.3)	0 (0.0)	3 (100.0)
Boys	2	2 (100.0)	0 (0.0)	0 (0.0)	2 (100.0)

VUR – vesicoureteral reflux, VCUG – voiding cystourethrography

Comparison between study groups, reflecting certain indications for VCUG in children with a history of UTI, showed no significant differences in the prevalence of VUR and other genitourinary tract abnormalities detected by VCUG, as well as VUR grading, among participants of the survey. The only significant difference was younger age of children with a history of febrile UTI (group 2) when compared to the age of patients with a history of recurrent UTI (group 1), $p < 0.0001$. Similarly to the entire study group, also in group 1, girls outweighed boys, and they were significantly older than boys, $p < 0.00001$. In groups 2 and 3 there were no significant differences in sex and age distributions.

DISCUSSION

In this research, we investigated the detection rate of VUR and other genitourinary tract abnormalities in children with a history of UTI who underwent VCUG in the Division of Paediatric Nephrology in Zabrze, Medical University of Silesia between 2019 and 2022, who and could be considered, in our opinion, as meeting the recommendations of PTNFD established in 2021 [4]. We followed guidelines that had evolved in recent years towards more narrow ones, due to a better knowledge of mechanisms of renal scarring, the role of bladder and bowel dysfunction in children presenting with UTI, the validity of using continuous antibiotic prophylaxis (CAP) in children with VUR, and finally about the lack of an apparent advantage of surgical care over medical treatment of VUR.

It is known that there is a potential risk of renal scarring associated with UTI [1, 9, 10]. Long-term consequences of renal scarring include hypertension and progressive renal failure [4, 5]. The prevalence of kidney scars after UTI in children has been estimated at the level 25–35% [9, 10]. Although, the prevalence of scarring is

higher in children with VUR, renal scars have been detected also in children without reflux [5, 10].

Recent studies have highlighted bowel and bladder dysfunction as a major risk factor of UTI recurrences in children [11, 12]. Thus, all children presenting with UTIs should be evaluated for the presence of bowel and bladder dysfunction and managed accordingly, before any treatment of VUR [13].

CAP was used in children after UTI. In the RIVUR trial, published in 2014, held on children with a history of UTI and VUR, antimicrobial trimethoprim-sulfamethoxazole prophylaxis was associated with a significant reduction in the risk of recurrence, but not in the risk of kidney scarring; moreover, it significantly increased bacterial resistance [11]. According to the current recommendations of the PTNFD on the management of a child with UTI, CAP should not be routinely administered after a first episode of UTI in children who do not have abnormal urinary tract findings on ultrasound, although it might be considered in children with urinary tract abnormalities and recurrent UTI [4]. Moreover, guidelines published by the European Association of Urology and the European Society for Paediatric Urology confirm that CAP may not be required in every VUR patient and state that CAP should be considered until bowel and bladder dysfunction resolution [13].

Based on studies proving no difference between surgical treatment of VUR and CAP in reducing the risk of UTI recurrence or renal deterioration, conservative treatment of VUR has recently been postulated [6, 14]. Conservative therapy of VUR is based on the understanding that it may resolve spontaneously [13, 15]. This approach in VUR includes watchful waiting, intermittent antibiotic prophylaxis or CAP, and bladder and bowel rehabilitation. Immediate antibiotic treatment should be initiated for febrile breakthrough infections [13, 16]. Sur-

gical care should be reserved for CAP noncompliance, breakthrough febrile UTIs despite CAP, and symptomatic VUR that persists during long-term follow-up [15, 16].

Current guidelines of PTNFD on the management of a child with UTI from 2021, set in the context presented above, recommend that VCUG should be performed in children with recurrent UTI, in children after septic UTI, and in children after UTI with urinary tract abnormalities based on ultrasound [4].

The results of our study, held on 366 children with a history of UTI, revealed VUR in 32.2% of the participants and other genitourinary tract abnormalities (bladder diverticulum or posterior urethral valve) in 1.4% participants. Moreover, there was no significant difference in the rate of VUR in children with recurrent UTI (33.3%), children after febrile UTI with a septic course (32.9%), and in children after UTI and ultrasound abnormalities (19.2%). In a Polish study of Kopiczko *et al.* [17] that analysed the results of VCUG in children, performed in the years 2003–2014, i.e. the period preceding the introduction of the recommendations of PTNFD when VCUG was widely used, VUR was present in 21.3% of all patients and in 23.6% of patients who underwent VCUG due to a febrile UTI. Our results indicate a subtle growth in the detection rate of VUR in the era of PTNFD guidelines and reflect data available in the literature. A study by Tullus [1] suggested that as many as 25–40% of children could be affected with VUR. Whereas, according to Sargent [18], the occurrence of VUR was 31.1%, and in research of Venhola *et al.* [19] it was as high as 36% in children with UTI.

Nevertheless, our study showed that 66.4% of children with a history of UTI, who were subjected to VCUG, presented with a normal picture. Taking into account the costs, discomfort, and radiation exposure connected with VCUG as well as contemporary trends towards a more conservative approach to treatment of VUR, it may be reasonable to revise recommendations for VCUG in children again [3, 7]. The guidelines of the American Academy of Paediatrics do not recommend VCUG after the first febrile UTI unless abnormal renal and bladder ultrasound is present [20, 21]. The Italian Society of Paediatric Nephrology recommends VCUG after the second febrile UTI or after the first one with a causative pathogen other than *E. coli* and/or ultrasound abnormalities [22]. Guidelines from the National Institute for Health and Care Excellence in the United Kingdom (NICE) do not advise performing routine imaging to identify VUR [23]. On the other hand, it has been proven that not all malfunctions of the urinary tract are detected when adhering to the guidelines [24]. It should be highlighted that due to the role of bowel and bladder dysfunction as a risk factor of UTI, according to the European Association of Urology and European Society for Paediatric Urology, in case of recurrent UTIs, it is more practical and cost-effective to assess for bowel and bladder dysfunction rather than VUR [13].

CONCLUSIONS

The prevalence of VUR in children with a history of UTI who underwent VCUG, in light of the current recommendations, in children with recurrent UTI, after febrile UTI with a septic course, and after UTI with ultrasound renal and bladder abnormalities, in our study reached 32.2%. The occurrence of genitourinary tract abnormalities other than VUR reached 1.4%. The fact that no aberrations in VCUG were found in nearly two-thirds of children undergoing this procedure may add some relevant arguments for further discussion on the optimisation of the indications for VCUG. However, more research is needed to determine the risks and benefits coming from the possible decrease in early detection of VUR in children.

DISCLOSURES

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