Journal of Pediatric Urology (xxxx) xxx xxx

Risk of urinary tract infection in patients with hydroureter: An analysis from the Society of Fetal Urology Prenatal Hydronephrosis Registry

Sarah A. Holzman [a,b,*], Luis H. Braga [c], Rebecca S. Zee [d], C.D. Anthony Herndon [d], Carol A. Davis-Dao [a,b], Nora G. Kern [e], Joshua D. Chamberlin [a,f], Melissa McGrath [c], Kai-wen Chuang [a,b], Heidi A. Stephany [a,b], Elias J. Wehbi [a,b], Tiffany T. Nguyen [a,b], Anne G. Dudley [g], Valre W. Welch [d], Gina M. Lockwood [h], Walid A. Farhat [i], Antoine E. Khoury [a,b]

[a]CHOC Children's, Division of Pediatric Urology, Orange, CA, USA

[b]University of California, Irvine, Department of Urology, Irvine, CA, USA

[c]McMaster University, Faculty of Health Sciences, Hamilton, Ontario, Canada

[d]Children's Hospital of Richmond at Virginia Commonwealth University, Department of Urology, Richmond, VA, USA

[e]University of Virginia, Charlottesville, VA, USA

[f]Loma Linda University, Department of Pediatric Urology, Loma Linda, CA, USA

[g]Division of Urology, Department of Research, Connecticut Children's Medical Center, Hartford, CT, USA

[h]Department of Urology, The University of Iowa, Iowa City, IA, USA

[i]Department of Urology, University of Wisconsin School of Medicine, Madison, WI, USA

* Correspondence to: Sarah A. Holzman, 505 S. Main Street Suite 100, Orange, CA 92675, USA, Tel.: +714 509 3919, Fax: +714 509 3915
saholzma@hs.uci.edu (S.A. Holzman)

Keywords
Megaureter; Hydronephrosis; Vesicoureteral reflux; Urinary tract infection

Abbreviations
CAP, Continuous antibiotic prophylaxis; PNH, Prenatal Hydronephrosis; SFU, Society for Fetal Urology; UVJ, Ureterovesical junction; UPJO, Ureteropelvic junction obstruction; UTI, Urinary tract infection; VCUG, Voiding cystourethrogram; VUR, Vesicoureteral reflux

Received 23 April 2021
Revised 27 August 2021
Accepted 1 September 2021
Available online xxx

Summary

Background
Prenatal hydronephrosis is one of the most common anomalies detected on prenatal ultrasonography. Patients with prenatal hydronephrosis and ureteral dilation are at increased risk of urinary tract infection (UTI) and continuous antibiotic prophylaxis (CAP) is recommended. However, current guidelines do not define the minimum ureteral diameter that would be considered a dilated ureter in these patients.

Objective
We evaluate the definition of clinically relevant hydroureter, its association with UTI, and the impact of CAP.

Study design
Patients with prenatal hydronephrosis from seven centers were enrolled into the Society for Fetal Urology Prenatal Hydronephrosis Registry from 2008 to 2020. Patients with ureteral measurement on ultrasound were included. Patients with ureterocele, ectopic ureter, neurogenic bladder, posterior urethral valves, horseshoe or solitary kidney, known ureteropelvic junction obstruction, or follow-up less than one month were excluded. Primary outcome was UTI. Analyses were performed using Cox regression.

Results
Of the 1406 patients enrolled in the registry, 237 were included. Seventy-six percent were male, ureteral diameter ranged from 1 to 34 mm, and median follow-up was 2.2 years. Patients with ureters 7 mm or greater had nearly three times the risk of UTI adjusting for sex, circumcision status, antibiotic prophylaxis and hydronephrosis grade (HR = 2.7, 95% CI: 1.1–6.5, $p = 0.03$; Figure). In patients who underwent voiding cystourethrogram (VCUG; 200/237), ureteral dilation of 7 mm or more identified patients at increased UTI risk controlling for sex, circumcision status, vesicoureteral reflux and hydronephrosis grade (HR = 2.3, 95% CI: 0.97–5.6, $p = 0.06$). CAP was significantly protective against UTI (HR = 0.50 (95% CI: 0.28–0.87), $p = 0.01$). Among patients who underwent VCUG and did not have vesicoureteral reflux, ureteral dilation 7 mm or greater corresponded with higher UTI risk compared to ureteral diameter less than 7 mm on multivariable analysis (HR = 4.6, 95% CI: 1.1–19.5, $p = 0.04$).

Conclusions
This is the first prospectively collected, multicenter study to demonstrate that hydroureter 7 mm or greater identifies a high-risk group for UTI who benefit from antibiotic prophylaxis. In contrast, patients with prenatal hydronephrosis and non-refluxing hydroureter less than 7 mm may be managed more conservatively.

https://doi.org/10.1016/j.jpurol.2021.09.001

Please cite this article as: Holzman SA et al., Risk of urinary tract infection in patients with hydroureter: An analysis from the Society of Fetal Urology Prenatal Hydronephrosis Registry, Journal of Pediatric Urology, https://doi.org/10.1016/j.jpurol.2021.09.001

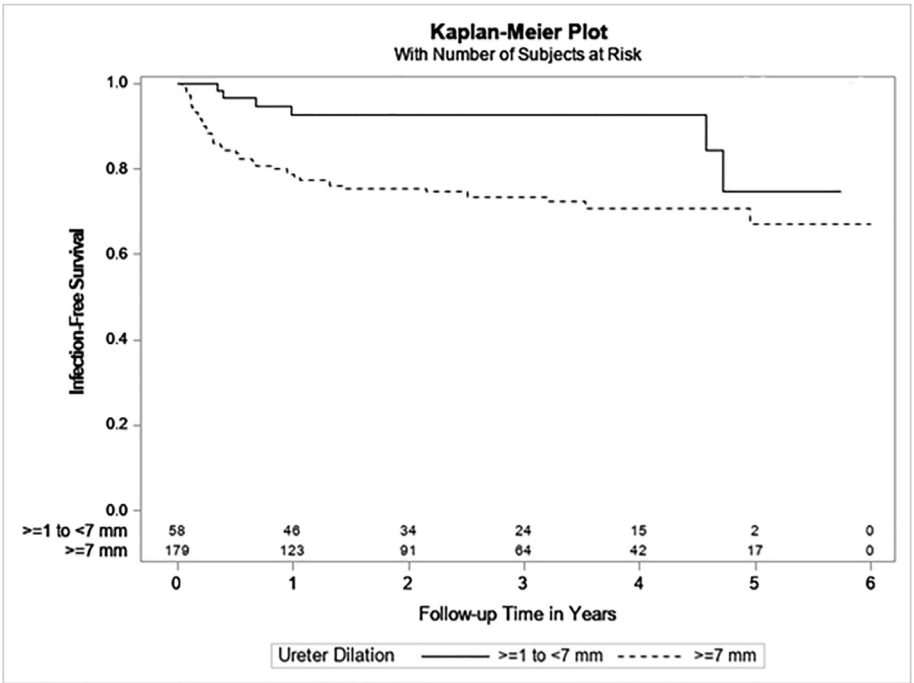

Figure UTI-free probability stratified by <7 mm and ≥7 mm ureteral dilation.

Introduction

Prenatal hydronephrosis (PNH) is one of the most common anomalies detected on prenatal ultrasonography and is reported in up to five percent of pregnancies [1]. The etiology of PNH can include transient or physiologic hydronephrosis, ureteropelvic junction obstruction, and vesicoureteral reflux. Ureteral dilation occurs in 5–10% of antenatal hydronephrosis cases [1]. Currently, nearly 79% of patients with hydroureteronephrosis present on perinatal ultrasound while the minority of patients present after a febrile urinary tract infection (UTI) [2]. Most patients with ureteral dilation will resolve spontaneously on postnatal follow-up and can be managed conservatively [3,4].

Patients with ureteral dilation are at increased risk for UTI and thus continuous antibiotic prophylaxis (CAP) is recommended [5–9]. However, the literature is inconsistent with regard to the ureteral diameter threshold that appears to be clinically relevant. The British Association of Paediatric Urologists consensus statement recommends a threshold of 7 mm as utilized previously for primary non-refluxing megaureter [5,10]. A recent prospective study on patients with prenatal hydronephrosis found that patients with non-refluxing primary megaureter (defined as ureteral diameter 7 mm or greater) had almost an 11 times higher risk of UTI [8]. Conversely, Hodhod et al. (2018) demonstrated an increased UTI risk in prenatal hydronephrosis patients with hydroureter greater than 4 mm [9].

Previously reported risk factors for UTI in patients with ureteral dilation include lack of CAP and intact prepuce [10–12]. The purpose of this study is to analyze our prospective multi-institutional registry of PNH patients with ureteral dilation to determine a ureteral diameter threshold associated with increased UTI risk. We hypothesize that patients with ureteral dilation greater than 7 mm are at greater risk of developing a UTI.

Materials and methods

Setting and population

Seven medical centers enrolled patients into the Society for Fetal Urology (SFU) Prenatal Hydronephrosis Registry between 2008 and 2020. Children were eligible for the registry if they were diagnosed with PNH based on *in utero* imaging and presented at a participating center with prenatal imaging records available. The patients were followed prospectively through the fifth year of life. Clinical variables collected included imaging results, CAP use, and the development of UTI based on urinalysis, urine culture and antibiotic treatment. Data on demographics, circumcision status, and other diagnoses were collected. All centers obtained individual Institutional Review Board (IRB) approval (coordinating center IRB # HM20007783).

Inclusion and exclusion criteria

Patients with PNH and a ureteral diameter measurement recorded on ultrasound at any visit were considered for inclusion in the study. For patients with ureteral diameters recorded at multiple visits, the largest ureteral diameter recorded was used for analysis. Children with the following were excluded: ureterocele, bladder diverticulum,

Please cite this article as: Holzman SA et al., Risk of urinary tract infection in patients with hydroureter: An analysis from the Society of Fetal Urology Prenatal Hydronephrosis Registry, Journal of Pediatric Urology, https://doi.org/10.1016/j.jpurol.2021.09.001

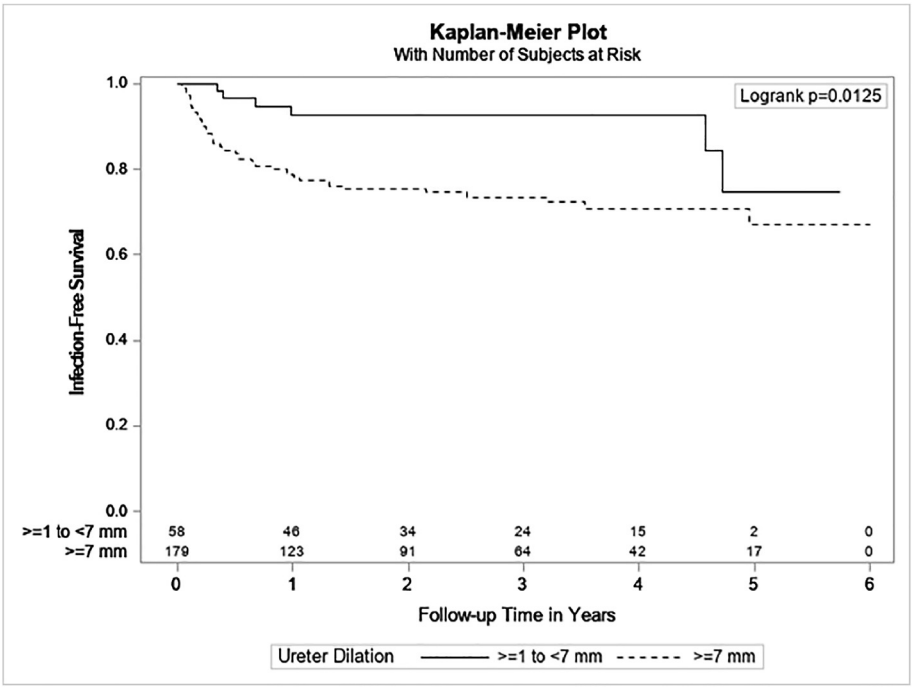

Fig. 1 Kaplan–Meier curves displaying UTI-free probability for all 237 patients stratified by <7mm and ≥7 mm ureter dilation.

posterior urethral valves, urethral atresia, neurogenic bladder, prune belly syndrome, nephrolithiasis, horseshoe kidney, multicystic dysplastic kidney, solitary kidney, suspected ureteropelvic junction obstruction and/or history of pyeloplasty (Supplemental Fig. 1). Patients with missing data and those with less than one month of follow-up were also excluded. Children who were diagnosed with hydronephrosis following a UTI in the postnatal setting were not eligible for enrollment in the registry.

Primary outcome and covariates

The primary outcome was development of the first UTI during follow-up. UTI was strictly defined as positive pyuria (urinalysis with positive leukocyte esterase and/or greater than five white blood cells per high-power field) with a urine culture containing a single-organism with greater than 50,000 CFU/mL collected on a mid-stream clean-catch or catheterized specimen depending on patient age and toilet training status [13]. All UTIs were reviewed by a senior investigator to confirm that these criteria were met.

The use of CAP was assessed in all children during follow-up. Patients placed on CAP at any time point after establishing urologic care were defined as receiving CAP. However, patients without prior CAP exposure who were only prescribed antibiotics in response to a UTI were not defined as receiving CAP. Hydronephrosis grade was defined using the SFU hydronephrosis grading system, based on the first postnatal ultrasound. High grade hydronephrosis was defined as SFU grades 3–4 and low grade hydronephrosis was defined as SFU grades 1–2. For patients with bilateral hydronephrosis, the highest SFU grade was reported. A voiding cystourethrogram (VCUG) was obtained at the discretion of the treating center and vesicoureteral reflux (VUR) status was determined based on the initial VCUG. Since this was an observational study, use of CAP and testing for suspected UTIs were also at clinician discretion. Study data were collected and managed using REDCap (Research Electronic Data Capture, Vanderbilt University, Nashville, TN) [14].

Statistical analysis

Univariate analyses were conducted using Chi-square and Kruskal–Wallis tests. Multivariable Cox regression analysis estimated the UTI risk adjusting for key risk factors including sex, circumcision status, CAP, and hydronephrosis

Table 1 Characteristics of prenatal hydronephrosis patients with dilated ureter

Patient Characteristics N (%)	n = 237
Sex	
Males circumcised	89 (38)
Males uncircumcised	90 (38)
Females	57 (24)
Missing circumcision status	1
Median follow-up time (in years, IQR)	2.1 (0.83–3.9)
Median age at first visit (in months, IQR)	1.1 (0.42–3.2)
Median ureter width (in mm, IQR)	8.5 (5.9–11)
High Grade Hydronephrosis (Grades 3–4)	145 (61)
VCUG	200 (84)
VUR (Grades I–V)	81 (41)
High grade VUR (Grades IV–V)	65 (80)
CAP	155 (65)
UTI	53 (22)
Median time to UTI (in months, IQR)	4.4 (2.3–11)

Please cite this article as: Holzman SA et al., Risk of urinary tract infection in patients with hydroureter: An analysis from the Society of Fetal Urology Prenatal Hydronephrosis Registry, Journal of Pediatric Urology, https://doi.org/10.1016/j.jpurol.2021.09.001

grade. Hazard ratios and 95% confidence intervals were estimated for each variable in the model. Kaplan–Meier curves were used to calculate the probability of developing a UTI, with follow-up defined as time from birth to most recent clinical encounter or UTI event. Number needed to treat for the effectiveness of CAP in preventing UTI was estimated from the multivariable Cox regression model [15]. All statistical tests were two-tailed with p value less than 0.05 considered to be significant. Analyses were performed using SAS Statistical Software (Version 9.4, Cary, NC).

Results

Patient characteristics

Of the 1406 enrollees in the SFU registry, 237 were included in the study. Seventy-six percent (180/237) were male and 50% (90/180) of male patients were circumcised. Patients were enrolled at a median age of 1.1 months (IQR 0.43–3.2). Patients were followed for a median of 2.2 years (IQR 0.95–4.0). Median ureteral diameter was 8.5 mm (range 1.0–34). A large proportion of patients had high grade hydronephrosis (grades 3 and 4) (62%, 145/237). In addition, the majority of patients (84%, 200/237) had a VCUG and among those 41% (81/200) had VUR. Most patients with VUR were high grade (grades IV and V) (80%, 65/81). CAP was prescribed for 65% of patients (155/237) during urology follow-up. Twenty two percent (53/237) had a UTI during the study period (Table 1) and 91% (48/53) had a febrile UTI; the remaining five patients with UTI did not have fever but were symptomatic with pyuria and a positive culture.

Hydroureter analysis

Ureteral dilation of 7 mm was a significant threshold to distinguish patients at higher risk of UTI (Fig. 1). Fifty-eight patients had ureteral diameter measurements between 1 and 6 mm, and 179 patients had ureteral dilation of 7 mm or larger. In patients with dilation less than 7 mm, 0/28 circumcised males, 2/15 (13%) uncircumcised males and 4/15 (27%) females developed a UTI. Comparing different thresholds for ureteral dilation in the multivariable Cox regression model (4 mm, 5 mm, 6 mm, 7 mm, 8 mm, 9 mm and 10 mm), the results for less than 7 mm compared with 7 mm or greater ureteral dilation produced the most highly significant and largest effect estimate for UTI risk. Patients with ureteral dilation 7 mm or greater had almost three times the risk of UTI adjusting for sex, circumcision status, CAP, and hydronephrosis grade (HR = 2.7, 95% CI: 1.13–6.45, $p = 0.03$). We also found that threshold diameters of 8, 9 and 10 mm were also significant predictors of UTI on Cox regression analysis (HR 2.2, 2.3 and 1.9 respectively), however the highest hazard ratio of 2.7 was found with 7 mm threshold ureteral diameter. In the cohort who underwent VCUG (200/237), ureteral diameter of 7 mm or greater identified patients at increased UTI risk controlling for sex, circumcision status, VUR, and hydronephrosis grade (HR = 2.3, 95% CI:0.97–5.6, $p = 0.058$) although this was just outside the level of statistical significance.

UTI analysis

On multivariable analysis the following were identified as independent risk factors for UTI development: ureteral dilation 7 mm or greater, intact prepuce, female sex, and lack of CAP (Table 2). CAP was found to be protective against UTI in patients with ureteral diameter 7 mm or greater (HR = 0.50, 95% CI:0.28–0.87, $p = 0.01$; Table 2) and extremely protective when controlling for VUR in the 200 patients who underwent VCUG (HR = 0.30, 95% CI: 0.16–0.55, $p < 0.0001$). However, CAP was not associated with reduced UTI risk in the subset of patients with ureteral diameter less than 7 mm (58/237) (HR = 1.1, 95% CI: 0.20–6.0).

Table 2 Univariable and multivariable analysis of UTI risk among children with dilated ureters and prenatal hydronephrosis.

	No. UTI (%)	Univariable p value	Multivariable model	
			HR (95% CI)	p value
Overall	53 (22)			
Ureter dilation				
≥1 and < 7 mm	6 (10)		1.0 (Ref)	
≥7 mm	47 (26)	0.01	2.7 (1.1–6.5)	0.03
Males circumcised	7 (8.0)		1.0 (Ref)	
Males uncircumcised	27 (30)	0.0001	4.0 (1.7–9.2)	0.001
Females	19 (33)	0.02	5.1 (2.1–12)	0.0003
Missing circumcision status	1			
Hydronephrosis Grade				
Low grade	18 (20)		1.0 (Ref)	
High grade	35 (24)	0.41	1.1 (0.63–2.0)	0.67
Missing grade				
CAP				
No	23 (28)		1.0 (Ref)	
Yes	30 (19)	0.13	0.50 (0.28–0.87)	0.01

Please cite this article as: Holzman SA et al., Risk of urinary tract infection in patients with hydroureter: An analysis from the Society of Fetal Urology Prenatal Hydronephrosis Registry, Journal of Pediatric Urology, https://doi.org/10.1016/j.jpurol.2021.09.001

Based on the full cohort of all 237 patients with dilated ureter, we estimate that 9 patients need to be treated with CAP to prevent one UTI at one year of follow-up. Among the subset of patients with dilated ureter 7 mm or greater (179/237), the corresponding number needed to treat was 7.

VUR analysis

Among patients with ureteral diameter 7 mm or greater who underwent VCUG, there was no difference in UTI development for refluxing versus non-refluxing patients (HR = 1.4, 95% CI: 0.76–2.7, $p = 0.27$; Fig. 2). In patients who underwent VCUG and did not have VUR (119 patients), those with ureteral dilation 7 mm or greater had a significantly higher UTI risk compared to patients with ureteral dilation less than 7 mm (HR = 4.6, 95% CI: 1.1–19.5, $p = 0.04$). Conversely, in patients with VUR, ureteral diameter greater than 7 mm did not predict increased UTI risk on multivariable analysis (HR = 1.1, 95% CI: 0.31–3.6, $p = 0.93$). The presence of high grade hydronephrosis did not predict patients at higher UTI risk (HR = 1.1, 95% CI: 0.62–2.1, $p = 0.69$).

Discussion

Herein, we present the results of over 1400 patients prospectively enrolled in the SFU prenatal hydronephrosis registry focusing on 237 patients with concomitant dilated ureter. Our study confirmed that a ureteral diameter of 7 mm or greater identified patients who were at higher risk of UTI development during follow-up on multivariable analysis controlling for multiple known risk factors. Interestingly, we found that patients with dilation 7 mm or greater were at increased risk of UTI regardless of the presence of VUR. Furthermore, among non-refluxing patients, ureteral diameter of 7 mm or larger identified patients at higher UTI risk likely secondary to increased urinary stasis in the more dilated ureters. We found that CAP was strongly protective for patients with hydroureter over 7 mm, providing a fourfold decrease in UTI risk (Table 2). Antibiotic prophylaxis was also extremely protective in patients with non-refluxing megaureter 7 mm or greater.

While prenatal hydronephrosis with hydroureter has been established as risk factor for UTI development previously [6], there was not a clear-cut definition of the minimum ureteral diameter to define hydroureter. In our study we found that 7 mm was a highly significant threshold to define patients at risk of developing a UTI. Similarly, ureteral diameters greater than 8 and 9 mm were also significant predictors of UTI risk but 7 mm was the minimum significant threshold with the highest hazard ratio. In our series, lower thresholds under 7 mm were not found to be significant to define patients at increased UTI risk. We found that patients with ureteral dilation less than 7 mm and confirmed VUR had a higher UTI rate (21%) compared to patients with dilation under 7 mm and no VUR (8%). We also found a relatively low number needed to treat of seven patients to prevent one UTI in patients with PNH and ureteral dilation 7 mm or greater. In this case, prescribing CAP is especially important as many patients presented under two months of age when a fever would prompt a neonatal sepsis admission. However, our study only had a small subset of patients with ureteral dilation under 7 mm with confirmed VUR (n = 19). Numerous prior studies identified patients with ureteral diameters greater than 10 mm as at risk for non-spontaneous resolution but were not focused on UTI risk [11,16]. Furthermore, ureteral diameter 13 mm

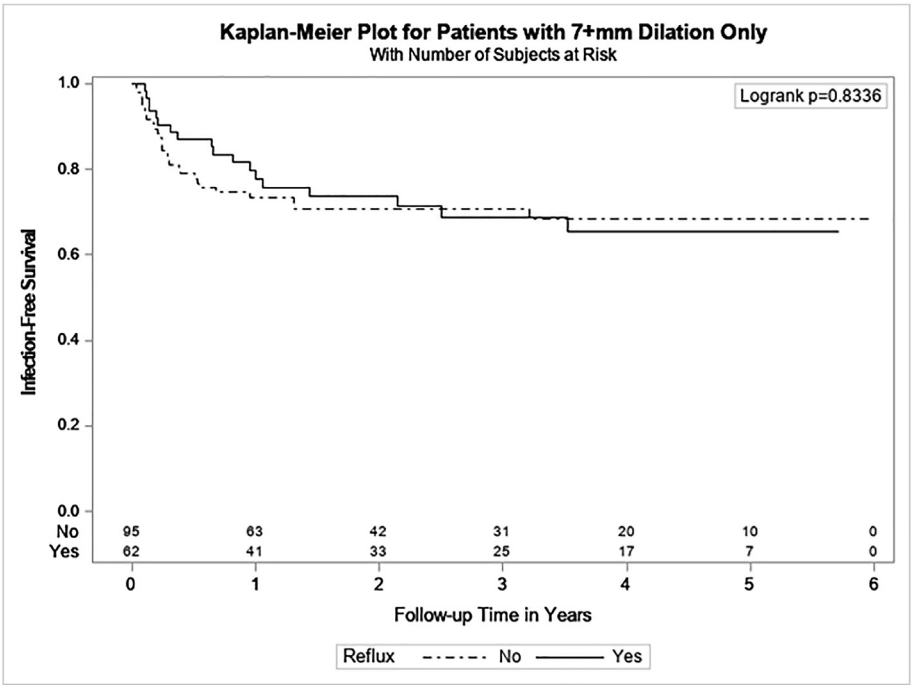

Fig. 2 Kaplan–Meier curves for subset of patients with only ≥7 mm dilated ureter showing no difference between patients with and without VUR (among those with VCUG performed, n = 157).

Please cite this article as: Holzman SA et al., Risk of urinary tract infection in patients with hydroureter: An analysis from the Society of Fetal Urology Prenatal Hydronephrosis Registry, Journal of Pediatric Urology, https://doi.org/10.1016/j.jpurol.2021.09.001

or greater has been established previously as having a significantly higher probability of requiring surgical intervention [10,17].

The increased UTI rate noted in our patients with hydroureteronephrosis is consistent with prior studies on congenital dilated ureter with published UTI rates between 19 and 50% [8,10,12]. PNH with ureteral dilation has been identified previously as an independent risk factor for UTI [6,8,9,18,19]. Similarly, CAP has been shown to be highly protective for patients with PNH and ureteral dilation >11 mm [6]. Our study also identified uncircumcised males and female sex as independent risk factors for UTI development, which has been demonstrated previously within the SFU registry database and in the literature [8,10,20,21]. Braga et al. (2016) found that CAP was also highly protective in primary non refluxing megaureter patients with a number needed to treat of three patients [10]. However, their study was limited to patients with non-refluxing megaureter while our study included both non refluxing and refluxing dilated ureters and included ureteral diameters under 7 mm. Indeed, CAP is recommended for any patient with prenatal hydroureteronephrosis in the Canadian guidelines of antenatally detected hydronephrosis [22].

Our results were interesting with regard to the effect of reflux in this population with dilated ureter. Contrary to prior studies, in examining only those who had VCUG, neither high grade hydronephrosis nor the presence of VUR were significant predictors of UTI risk in patients with ureteral diameter 7 mm or greater (HR 1.2, $p = 0.64$ for high grade hydronephrosis and HR 1.4, $p = 0.27$ for reflux). We found that in dilated ureter patients with VUR, 7 mm was not a significant threshold to determine UTI risk. Dilating VUR has been demonstrated previously to be a risk factor for UTI and this may explain why we did not see an increased risk in patients with ureteral dilation greater than 7 mm who also had underlying reflux [23,24]. Conversely, in patients without reflux, ureteral dilation 7 mm or greater was a strong predictor of UTI risk (HR 4.6, $p = 0.04$).

Strengths of our study include the prospective and multicenter design with seven included pediatric urology centers. We also present the largest cohort to date on prenatal hydronephrosis with concomitant dilated ureter. Our study examined children with lower diameter dilated ureters that have not been included in most prior studies [10]. However, our study is not without limitations. CAP use was analyzed as having ever versus never been prescribed during urology follow-up. Due to the multicenter nature of data collection, the precise length of time on CAP was not known for all patients and we were unable to assess CAP compliance. Given the young age of our included patients, we were not able to evaluate the effect of bladder and bowel dysfunction, which is a well-established UTI risk factor [25]. Finally, two of the more common etiologies of dilated ureter, primary obstructive megaureter and VUR, are known to resolve spontaneously as children age and patients with dilated ureters less than 7 mm may have been more likely to resolve and not develop a UTI during the study period [10]. Given our study design of including patients with any dilated ureter measurement following enrollment, patients with resolved dilation would be followed when they no longer had increased UTI risk. Furthermore, the majority of patients did not undergo diuretic renography therefore we cannot evaluate primary obstructive megaureter and its effects on UTI risk in this study.

Conclusions

This is the first prospectively collected, multi-center study to demonstrate that ureteral diameter 7 mm or greater identifies patients at higher risk of UTI who appear to benefit from CAP administration. Additionally, ureteral diameter 7 mm or greater predicted higher UTI risk regardless of the status of VUR. In contrast, patients with non-refluxing hydroureter less than 7 mm were not at increased risk of UTI and thus may be managed more conservatively. Based on our study results, we recommend that patients with dilated ureter should be followed closely. When the ureteral dilation is 7 mm or greater, CAP is warranted, particularly when the patient has other risk factors for UTI, including female sex and intact prepuce.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest

The authors have no conflicts of interest to report.

Acknowledgements

The authors would like to thank Mr. John Irby for management and coordination of the registry database. We would also like to thank all of the personnel involved at each participating center.

References

[1] Nguyen HT, Herndon CD, Cooper C, Gatti J, Kirsch A, Kokorowski P, et al. The society for fetal urology consensus statement on the evaluation and management of antenatal hydronephrosis. J Pediatr Urol 2010;6:212—31.
[2] Rubenwolf P, Herrmann-Nuber J, Schreckenberger M, Stein R, Beetz R. Primary non-refluxive megaureter in children: single-center experience and follow-up of 212 patients. Int Urol Nephrol 2016;48:1743—9.
[3] McLellan DL, Retik AB, Bauer SB, Diamond DA, Atala A, Mandell J, et al. Rate and predictors of spontaneous resolution of prenatally diagnosed primary nonrefluxing megaureter. J Urol 2002;168:2177—80. discussion 80.
[4] Dekirmendjian A, Braga LH. Primary non-refluxing megaureter: analysis of risk factors for spontaneous resolution and surgical intervention. Front Pediatr 2019;7:126.
[5] Farrugia MK, Hitchcock R, Radford A, Burki T, Robb A, Murphy F, et al. British association of paediatric urologists consensus statement on the management of the primary obstructive megaureter. J Pediatr Urol 2014;10:26—33.

[6] Herz D, Merguerian P, McQuiston L. Continuous antibiotic prophylaxis reduces the risk of febrile UTI in children with asymptomatic antenatal hydronephrosis with either ureteral dilation, high-grade vesicoureteral reflux, or ureterovesical junction obstruction. J Pediatr Urol 2014;10:650—4.
[7] Castagnetti M, Cimador M, Esposito C, Rigamonti W. Antibiotic prophylaxis in antenatal nonrefluxing hydronephrosis, megaureter and ureterocele. Nat Rev Urol 2012;9:321—9.
[8] Braga LH, Farrokhyar F, D'Cruz J, Pemberton J, Lorenzo AJ. Risk factors for febrile urinary tract infection in children with prenatal hydronephrosis: a prospective study. J Urol 2015;193:1766—71.
[9] Hodhod A, Capolicchio JP, Jednak R, El-Sherif E, El-Doray AE, El-Sherbiny M. Influence of postnatal hydroureter in determining the need for voiding cystourethrogram in children with high-grade hydronephrosis. Arab J Urol 2018;16:238—44.
[10] Braga LH, D'Cruz J, Rickard M, Jegatheeswaran K, Lorenzo AJ. The fate of primary nonrefluxing megaureter: a prospective outcome analysis of the rate of urinary tract infections, surgical indications and time to resolution. J Urol 2016;195:1300—5.
[11] Gimpel C, Masioniene L, Djakovic N, Schenk JP, Haberkorn U, Tonshoff B, et al. Complications and long-term outcome of primary obstructive megaureter in childhood. Pediatr Nephrol 2010;25:1679—86.
[12] Song SH, Lee SB, Park YS, Kim KS. Is antibiotic prophylaxis necessary in infants with obstructive hydronephrosis? J Urol 2007;177:1098—101. discussion 101.
[13] Subcommittee on urinary tract infection. Reaffirmation of AAP clinical practice guideline: the diagnosis and management of the initial urinary tract infection in febrile infants and young children 2-24 Months of age. Pediatrics 2016;138.
[14] Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377—81.
[15] Austin PC. Absolute risk reductions and numbers needed to treat can be obtained from adjusted survival models for time-to-event outcomes. J Clin Epidemiol 2010;63:46—55.
[16] Ranawaka R, Hennayake S. Resolution of primary non-refluxing megaureter: an observational study. J Pediatr Surg 2013;48:380—3.
[17] Chertin B, Pollack A, Koulikov D, Rabinowitz R, Shen O, Hain D, et al. Long-term follow up of antenatally diagnosed megaureters. J Pediatr Urol 2008;4:188—91.
[18] Lee JH, Choi HS, Kim JK, Won HS, Kim KS, Moon DH, et al. Nonrefluxing neonatal hydronephrosis and the risk of urinary tract infection. J Urol 2008;179:1524—8.
[19] Silay MS, Undre S, Nambiar AK, Dogan HS, Kocvara R, Nijman RJM, et al. Role of antibiotic prophylaxis in antenatal hydronephrosis: a systematic review from the European association of urology/European society for paediatric urology guidelines panel. J Pediatr Urol 2017;13:306—15.
[20] Ellison JS, Dy GW, Fu BC, Holt SK, Gore JL, Merguerian PA. Neonatal circumcision and urinary tract infections in infants with hydronephrosis. Pediatrics 2018;142.
[21] Zee RS, Herbst KW, Kim C, McKenna PH, Bentley T, Cooper CS, et al. Urinary tract infections in children with prenatal hydronephrosis: a risk assessment from the society for fetal urology hydronephrosis registry. J Pediatr Urol 2016;12:261 e1—7.
[22] Capolicchio JP, Braga LH, Szymanski KM. Canadian urological association/pediatric urologists of Canada guideline on the investigation and management of antenatally detected hydronephrosis. Can Urol Assoc J 2018;12:85—92.
[23] Nordenstrom J, Sjostrom S, Sillen U, Sixt R, Brandstrom P. The swedish infant high-grade reflux trial: UTI and renal damage. J Pediatr Urol 2017;13:146—54.
[24] de Bessa Jr J, de Carvalho Mrad FC, Mendes EF, Bessa MC, Paschoalin VP, Tiraboschi RB, et al. Antibiotic prophylaxis for prevention of febrile urinary tract infections in children with vesicoureteral reflux: a meta-analysis of randomized, controlled trials comparing dilated to nondilated vesicoureteral reflux. J Urol 2015;193:1772—7.
[25] Dias CS, Silva JM, Diniz JS, Lima EM, Marciano RC, Lana LG, et al. Risk factors for recurrent urinary tract infections in a cohort of patients with primary vesicoureteral reflux. Pediatr Infect Dis J 2010;29:139—44.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpurol.2021.09.001.

Please cite this article as: Holzman SA et al., Risk of urinary tract infection in patients with hydroureter: An analysis from the Society of Fetal Urology Prenatal Hydronephrosis Registry, Journal of Pediatric Urology, https://doi.org/10.1016/j.jpurol.2021.09.001