RESEARCH ARTICLE

Clinical Predictors for Abnormal Renal Bladder Ultrasound in Hospitalized Young Children With a First Febrile Urinary Tract Infection

Sowdhamini S. Wallace, DO, MS,[c] Kathryn Ban, MD,[c] Amrita Singh, MD,[c] Karen Lui, MD,[c] Imgard Carolina Molleda, MD,[c] Robert C. Orth, MD, MPH, PhD,[b] Stacy B. Pierson, MD,[c] Lauren Hess, MD,[c] Huay-ying Lo, MD,[c] Chester J. Koh, MD,[a,d] Lauren Walker, MD,[c] Hannah Neubauer, MD,[c] Charles G. Macias, MD, MPH[e]

ABSTRACT

BACKGROUND: Physicians often obtain a routine renal bladder ultrasound (RBUS) for young children with a first febrile urinary tract infection (UTI). However, few children are diagnosed with serious anatomic anomalies, and opportunity may exist to take a focused approach to ultrasonography. We aimed to identify characteristics of the child, prenatal ultrasound (PNUS), and illness that could be used to predict an abnormal RBUS and measure the impact of RBUS on management.

METHODS: We conducted a single-center prospective cohort study of hospitalized children 0 to 24 months of age with a first febrile UTI from October 1, 2016, to December 23, 2018. Independent variables included characteristics of the child, PNUS, and illness. The primary outcome, abnormal RBUS, was defined through consensus of a multidisciplinary team on the severity of ultrasound findings important to identify during a first UTI.

RESULTS: A total of 211 children were included; the median age was 1.0 month (interquartile range 0–2), and 55% were uncircumcised boys. All mothers had a PNUS with 10% being abnormal. *Escherichia coli* was the pathogen in 85% of UTIs, 20% (n = 39 of 197) had bacteremia, and 7% required intensive care. Abnormal RBUS was found in 36% (n = 76 of 211) of children; of these, 47% (n = 36 of 76) had moderately severe findings and 53% (n = 40 of 76) had severe findings. No significant difference in clinical characteristics was seen among children with and without an abnormal RBUS. One child had Foley catheter placement, and 33% received voiding cystourethrograms, 15% antibiotic prophylaxis, and 16% subspecialty referrals.

CONCLUSIONS: No clinical predictors were identified to support a focused approach to RBUS examinations. Future studies should investigate the optimal timing for RBUS.

[a]Division of Pediatric Urology, Department of Surgery, [b]Department of Pediatric Radiology, Texas Children's Hospital and [c]Section of Pediatric Hospital Medicine, Department of Pediatrics and [d]Scott Department of Urology, Baylor College of Medicine, Houston, Texas; and [e]Division of Pediatric Emergency Medicine, Rainbow Babies and Children's Hospital and Case Western Reserve University, Cleveland, Ohio

www.hospitalpediatrics.org
DOI:https://doi.org/10.1542/hpeds.2019-0240

Address correspondence to Sowdhamini S. Wallace, DO, MS, Texas Children's Hospital, 1102 Bates Ave, FC 1860, Houston, TX 77030. E-mail: swallace@bcm.edu

HOSPITAL PEDIATRICS (ISSN Numbers: Print, 2154-1663; Online, 2154-1671).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

Urinary tract infections (UTIs) occur in 5% to 8% of febrile infants and frequently result in emergency department (ED) visits and hospitalizations.[1–3] Renal scarring occurs in 15% of this population, and in the presence of genitourinary tract anomalies or high-grade vesicoureteral reflux (VUR), the risk is two fold.[4] For this reason, the 2011 American Academy of Pediatrics guideline for first febrile UTI in children 2 to 24 months recommends screening for genitourinary anomalies with routine renal bladder ultrasound (RBUS)[5] and further affirmed this recommendation in the 2016 guideline.[6] The purpose of routine RBUS examinations is to identify signs of genitourinary anomalies or high-grade VUR that may require further radiologic testing, surgery, or subspecialty referral.[5] This recommendation, however, is supported by low-quality evidence from observational studies,[5] and it is unclear whether the benefits of routine testing outweigh the risks.

Approximately one-third of children have abnormal RBUS findings; however, few children are ultimately diagnosed with obstructive genitourinary tract anomalies that require timely intervention at the time of first febrile UTI.[7–11] Thus, the benefit may be small but nevertheless important for the 1% of the population affected by serious genitourinary tract anomalies.[3] The risks of routine RBUS testing may include exposing a greater number of infants to subsequent imaging tests, and these risks may be higher when the RBUS examination is performed in the presence of acute pyelonephritis and inflamed kidneys. Certain findings, such as increased renal size, urothelial thickening, and pelviectasis, may be present both in the setting of acute pyelonephritis and VUR.[12–15]

A targeted approach to performing RBUS may allow for a more judicious use of resources to identify infants at higher risk of having serious genitourinary anomalies. A targeted approach may be especially important in the hospital setting where children are still recovering from an acute UTI. We aimed to identify clinical predictors of abnormal RBUS examinations in hospitalized young children with first febrile UTI. We hypothesize that abnormal prenatal ultrasound (PNUS),[16–18] male sex,[19] young age, and high illness severity could be associated with abnormal RBUS. Secondly, we sought to specifically identify clinical predictors for the most severe abnormalities on RBUS knowing that provider perspectives regarding which abnormalities merit detection during the first febrile UTI may vary. Last, we aimed to measure the acute impact of routine RBUS on subsequent medical and surgical interventions in these young children.

METHODS

We conducted a prospective cohort study of hospitalized children 0 to 24 months of age with a first febrile UTI from October 2016 to December 2018 at a large quaternary-care children's hospital in the southern United States. Data for covariates and outcomes were collected by interview of caregivers, chart review, and phone calls 6 weeks after discharge. The local institutional review board approved the study protocol before study commencement.

Study Population

We identified potential participants via a daily report that queried the electronic medical record for hospitalized children with receipt of a urine culture. We focused on children in the hospital setting to enable complete capture of RBUS results.

Children 0 to 24 months of age were eligible if they had fever and a laboratory-confirmed UTI. Fever was defined as temperature of ≥100.4°F by caregiver history or during the ED visit or hospitalization. Urine specimens had to be collected by either catheterization or suprapubic aspiration. For children 2 to 24 months of age, UTI was defined as ≥50 000 colony-forming units (CFUs) of bacteria plus urinalysis with pyuria.[5] Pyuria was defined as either a positive leukocyte esterase result and/or ≥5 white blood cell per high-power field.[5] For infants <2 months of age, UTI was defined on the basis of previous literature for this age group; infants could either have ≥50 000 CFUs of bacteria on urine culture regardless of the urinalysis result or ≥10 000 CFUs of bacteria with pyuria on urinalysis.[13,20]

Children were excluded if they had a history of a previous UTI, postnatal diagnosis of genitourinary anomalies, previous postnatal imaging of the genitourinary tract, genitourinary tract instrumentation, or a history of neurogenic bladder.

Covariates

The data for all covariates were collected by interview of the caregiver by using a standardized data collection form and through review of the electronic medical record. Covariates included characteristics of the participant, illness, and PNUS history. Definitions for less familiar covariates are listed in Table 1. Comorbidities were defined according to previous studies of young children with UTIs.[20] The uropathogen grown on urine culture was categorized as *Escherichia coli* or non–*E coli* because of the known association between non–*E coli* uropathogens and VUR.[13] Variables related to the illness severity included ICU stay, positive pediatric systemic inflammatory response syndrome (SIRS) criteria,[21] and bacteremia (excluding contaminants[22]). We recorded variables related to PNUS examinations because the ability to identify abnormal findings in utero might be influenced by the timing of ultrasound and the quality of the study.[5] Variables related to PNUS included the number of ultrasounds during pregnancy, trimester of last ultrasound, general PNUS result, and, specifically, PNUS genitourinary tract anomalies. PNUS characteristics were measured by parent report because this was considered the most feasible in real-world clinical settings.

Outcomes

The primary outcome was an abnormal RBUS with clinically important abnormalities that require detection at the time of a first febrile UTI. As part of clinical care, pediatric radiology staff read each RBUS examination. Because of varying physician thresholds in deeming findings on RBUS as clinically important, we defined abnormal RBUS in 3 categories on the basis of the severity of findings similar to 2 recently published studies.[12,23] An RBUS was categorized as abnormal within 1 of the 3 thresholds on the basis of the most severe finding found on the report (Table 2).

TABLE 1 Definitions of Select Covariates

Category	Covariate	Definition
Participant characteristics	Prematurity	Gestational age <37 wk
	Comorbidities	Congestive heart failure, chronic lung disease, immunodeficiency, malignancy, diabetes mellitus, HIV, sickle cell disease, chronic neurologic problems
	Family history	History of kidney disease, nephrolithiasis, genitourinary tract anomalies, and VUR in an immediate family member
Illness characteristics	Uropathogen	*E coli* or non–*E coli* Common contaminants were excluded[a]
	Pediatric SIRS	≥2 criteria, but 1 criterion must be abnormal temperature or leukocyte count Four criteria Temperature >38.5°C or <36.0°C Tachycardia or bradycardia by using age-specific parameters Tachypnea or initiation of mechanical ventilation Abnormal leukocyte count or >10% bands
	Bacteremia	Growth of any bloodborne pathogen Contaminants were excluded[b]
PNUS characteristics	PNUS result	General result of last PNUS performed in pregnancy by caregiver report; classified as either normal or abnormal
	PNUS genitourinary abnormalities	Of those with abnormal PNUS, abnormalities specifically related to the kidney, ureter, or bladder by caregiver report

[a] Contaminants on urine culture: coagulase-negative *Staphylococcus*, *Lactobacillus*, *Micrococcus*, *Diphtheroids*, and *Bacillus* species.[20]

[b] Contaminants on blood culture: coagulase-negative *Staphylococcus*, *Micrococcus*, viridans group *Streptococcus* or α *Streptococcus*, *Corynebacterium*, and *Bacillus* were considered contaminants.[22]

Because radiologists may report hydronephrosis using varying terminology, the Society of Fetal Urology (SFU) grading system was used to objectively define the severity of hydronephrosis for each RBUS examination in a standard way. The SFU grading system is similar to other scoring systems for hydronephrosis, such as the urinary tract dilation classification system.[24] A multidisciplinary panel of 9 members was convened to reach consensus on the lowest threshold of abnormalities that should be deemed important to identify at the time of first febrile UTI. The investigative team anchored each threshold to a clinical meaning to assist the panel. The panel included 3 pediatric hospitalists, 2 outpatient pediatricians, 2 pediatric urologists, 1 radiologist, and 1 pediatric emergency medicine physician. Consensus was obtained by sending an electronic survey to the panel for anonymous polling. The stop criterion was set with a target goal of 80% consensus and was achieved after 1 round of surveys. Eighty-nine percent (8 of 9) panel members chose threshold B (moderately severe abnormalities) to be the lowest clinically important threshold to identify at the time of first febrile UTI. On the basis of this result, abnormal RBUS was defined as thresholds B and C. Threshold A and normal RBUS reports were considered a normal RBUS. Knowing that the perspective on the threshold of abnormalities for detection with the first UTI may vary among providers, we also evaluated whether any predictors existed in association with the most severe abnormalities, threshold C, as a secondary outcome.

Additional secondary outcomes were chosen to measure the impact of RBUS on subsequent medical or surgical interventions. These secondary outcomes were measured via review of the electronic medical record and by phone calls to parents 6 weeks after discharge. The follow-up period of 6 weeks was chosen to capture interventions or new diagnoses made that could have occurred as a result of obtaining the RBUS test. Secondary outcomes included the following tests, treatments, or procedures: medical or surgical interventions for decompression of the bladder (eg, Foley catheter), other surgical interventions, voiding cystourethrograms (VCUGs), antibiotic prophylaxis, and subspecialty referrals. We also measured the number of children diagnosed with VUR by VCUG.

Data Analysis

Sample size was estimated by the rule of 10 (or 1-in-10 rule) for logistic regression with an estimate of including 5 variables in our final model. Thus, we needed ≥50 patients with an abnormal RBUS within the sample. By using an estimate from previous literature of 25% of the population with an abnormal RBUS,[23,25] the sample size was calculated to be 200 children. Descriptive statistics were used to describe measures of central tendency and dispersion for covariates. Univariable analysis was used to look for associations between independent and dependent variables. For variable selection for the multivariable model, statistical significance was set with an $\alpha < .20$. Independent variables found to have a statistically significant association with abnormal RBUS were selected for multivariable analysis to identify independent predictors. Multivariable logistic regression analysis was used to build a prediction model for abnormal RBUS. R package version 3.3.2 software was used for the analysis.

RESULTS

Initial screening identified 3721 children with a urine culture, 378 children met criteria for febrile UTI, and after exclusion criteria, 211 children remained in the final study population (Fig 1). The median age was 1.0 month (interquartile range [IQR] 0–2) with 65% ($n = 137$) being <2 months of age. The majority of children were male (60%), Hispanic (61%), and had public insurance (66%) (Table 3). The median gestational age of infants was 39.0 weeks (range 29–42) with 87% ($n = 184$) at term gestation. Five percent ($n = 11$) of children

TABLE 2 Definition of Abnormal RBUS by Using Thresholds of Severity for Ultrasound Findings

	Normal RBUS Finding		Abnormal RBUS Finding	
	Normal	Threshold A[a]	Threshold B[a]	Threshold C[a]
Collecting system dilation	None	Any dilation without hydronephrosis (prominence, fullness, extrarenal pelvis)	Mild hydronephrosis (pelviectasis, caliectasis)	Moderate to severe hydronephrosis
	SFU 0[b]	SFU 1[b]	SFU 2[b]	SFU 3–4[b]
Ureter	Normal	Normal	Normal	Any ureteral dilation (hydroureter)
Urothelial thickening	None	None	Present	Present
Parenchyma	Normal	Simple cyst	Solitary kidney, duplication, size discrepancy, renal ectopia	Stone, dysplasia, cortical thinning or scar, abnormal corticomedullary differentiation and/or echogenicity, multicystic or polycystic
Bladder	Normal	Bladder debris	Bladder wall thickening or diverticulum	Ureterocele, dilated posterior urethra, bladder trabeculation

[a] Our multidisciplinary panel created a clinical meaning to anchor to each threshold of abnormalities. Threshold A findings were mild abnormalities that could be incidental findings or related to the UTI itself. Threshold B findings were moderate abnormalities that could lead to medical interventions, further testing or need for subspecialty involvement. Threshold C findings were considered to be severe abnormalities for which close subspecialty follow-up and possible future surgical interventions might be needed.

[b] The SFU grading system was used to objectively define the severity of hydronephrosis for each RBUS examination.

had comorbidities, which included genetic syndromes, malignancy, or cardiac or neurologic conditions. Of the 127 male children, 91% (n = 115) were uncircumcised. Eight percent (n = 16) had a positive family history. *E coli* was the predominant uropathogen found in 85% (n = 180) of UTIs, and 7% (n = 15) of UTIs were due to *Klebsiella* species. Of the 197 children who had blood cultures obtained, 20% (n = 39) had bacteremia. All 39 children had the same pathogen in their blood and urine cultures except for 1 child. Although 69% met criteria for SIRS after presentation to the ED, only 7% (n = 15) received treatment in the ICU.

All mothers had a PNUS performed during pregnancy; 84% (n = 176/210) had ≥3 ultrasounds, and 84% (n = 171/204) had their last ultrasound during their third trimester. When being interviewed, 10% (n = 22) of mothers reported that the last PNUS was abnormal and of those women, 2 reported genitourinary tract abnormalities on PNUS. One infant had "fluid on the kidneys" and another infant had discrepancy in kidney size with 1 kidney appearing small.

RBUS was performed on all 211 children during hospitalization; 36% (n = 76) had an abnormal RBUS result. Of the 76 abnormal RBUS tests, 47% (n = 36) had moderately severe abnormalities (threshold B) and 53% (n = 40) had severe abnormalities (threshold C). After univariable analysis, only gestational age and genitourinary abnormalities on PNUS were found to be possibly associated with abnormal RBUS with a P value <.20 (Table 3). Multivariable logistic regression revealed that increased gestational age minimally increased the odds of having an abnormal RBUS (odds ratio [OR] 1.21; 95% confidence interval [CI] 1.01–1.46), whereas the OR for abnormal genitourinary findings on PNUS was inconclusive because only 2 infants were affected (OR 1.0; 95% CI ∞–∞). Of the 2 infants with abnormal genitourinary findings on PNUS, the RBUSs revealed (1) focal hyperechogenicity of the renal parenchyma of 1 kidney and (2) hydroureteronephrosis later confirmed to be grade III VUR by VCUG. Overall, in terms of the timing of RBUS, RBUSs obtained while children were still febrile were more often abnormal than if obtained ≥1 day after fever resolution (45% [n = 45 of 99] vs 26% [n = 27 of 103], respectively; P value = .004).

When examining the association between covariates and the most severe threshold C abnormalities, abnormal genitourinary findings on PNUS and non–*E coli* organisms had possible associations (Table 4). Multivariable logistic regression revealed no statistically significant predictors of threshold C severe abnormalities; non–*E coli* uropathogen had an OR of 2.10 (95% CI 0.85–4.92), and abnormal PNUS genitourinary findings had an OR of 1.0 (95% CI ∞–∞).

One child required additional acute hospital intervention after the RBUS. She was a 3-month-old healthy girl who presented to the PICU in septic shock. She had a Foley catheter placed to decompress the bladder because of severe bilateral hydronephrosis and hydroureter with a duplicated right-sided collecting system with obstructing ureterocele. The Foley catheter was removed after 24 hours when clinical improvement was seen; subsequently, the infant voided spontaneously with normal

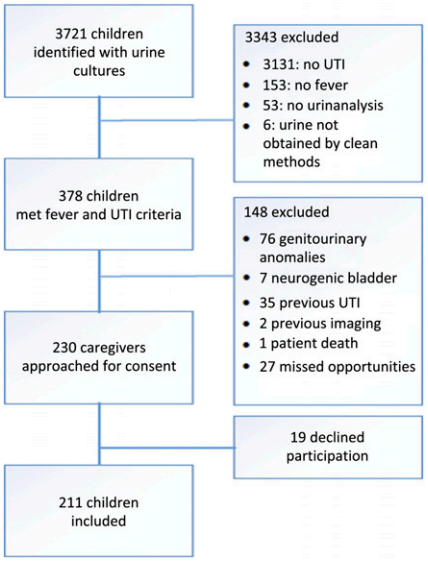

FIGURE 1 Flow diagram of study participants.

TABLE 3 Characteristics of 211 Young Children With First Febrile UTI

Characteristic	Total Population ($N = 211$)	Normal RBUS ($n = 135$)	Abnormal RBUS ($n = 76$)	P
Median age, mo (IQR)	1.0 (0–2)	1.0 (0–2)	1.0 (0–3)	.528[a]
Sex, *n* of *N* (%)				.970[b]
Male	127 of 211 (60)	81 of 135 (60)	46 of 76 (61)	—
Female	84 of 211 (40)	54 of 135 (40)	30 of 76 (39)	—
Ethnicity, *n* of *N* (%)				.424[b]
Non-Hispanic	79 of 202 (39)	54 of 130 (42)	25 of 72 (35)	—
Hispanic	123 of 202 (61)	76 of 130 (58)	47 of 72 (65)	—
Race, *n* of *N* (%)				.883[c]
White	155 of 193 (80)	101 of 126 (80)	54 of 67 (81)	—
African American	24 of 193 (12)	15 of 126 (12)	9 of 67 (13)	—
Asian American	14 of 193 (7)	10 of 126 (8)	4 of 67 (6)	—
Insurance, *n* of *N* (%)				.964[c]
Private	65 of 211 (31)	42 of 135 (31)	23 of 76 (35)	—
Public	139 of 211 (66)	88 of 135 (65)	51 of 76 (67)	—
Self-pay	7 of 211 (3)	5 of 135 (4)	2 of 76 (3)	—
Median gestational age, mo (IQR)	39.0 (29–42)	38.0 (37–39)	39.0 (38–39)	.052[a]
Circumcision, *n* of *N* (%)				1.0[c]
Uncircumcised	116 of 127 (91)	74 of 81 (91)	42 of 46 (91)	—
Circumcised	11 of 127 (9)	7 of 81 (9)	4 of 46 (9)	—
Family history, *n* of *N* (%)				.762[b]
Negative	193 of 209 (92)	120 of 134 (90)	73 of 75 (97)	—
Positive	16 of 209 (8)	14 of 134 (10)	2 of 75 (3)	—
E coli versus non–*E coli*, *n* of *N* (%)				.954[b]
Non–*E coli*	31 of 211 (15)	20 of 135 (15)	11 of 76 (14)	—
E coli	180 of 211 (85)	115 of 135 (85)	65 of 76 (86)	—
ICU stay, *n* of *N* (%)				1.0[c]
No	196 of 211 (93)	125 of 135 (93)	71 of 76 (93)	—
Yes	15 of 211 (7)	10 of 135 (7)	5 of 76 (7)	—
SIRS, *n* of *N* (%)				.970[b]
Yes	143 of 207 (69)	92 of 133 (69)	51 of 74 (69)	—
No	64 of 207 (30)	41 of 133 (31)	23 of 74 (31)	—
Bacteremia, *n* of *N* (%)				1.0[c]
No	158 of 197 (80)	103 of 128 (80)	55 of 69 (80)	—
Yes	39 of 197 (20)	25 of 128 (20)	14 of 69 (20)	—
PNUS done in pregnancy, *n* of *N* (%)	211 of 211 (100)	135 of 135 (100)	76 of 76 (100)	NA
Median quantity of PNUS (IQR)	3.0 (3–3)	3.0 (3–3)	3.0 (3–3)	.829[a]
1 PNUS, *n* of *N* (%)	5 of 210 (2)	3 of 135 (2)	2 of 75 (3)	—
2 PNUS, *n* of *N* (%)	29 of 210 (14)	20 of 135 (15)	9 of 75 (12)	—
≥3 PNUS, *n* of *N* (%)	176 of 210 (84)	112 of 135 (83)	64 of 75 (85)	—
Trimester of last PNUS				1.0[c]
First trimester, *n* (%)	0 (0)	0 (0)	0 (0)	—
Second trimester, *n* of *N* (%)	33 of 204 (16)	22 of 133 (17)	11 of 71 (16)	—
Third trimester, *n* of *N* (%)	171 of 204 (84)	111 of 133 (83)	60 of 71 (85)	—

TABLE 3 Continued

Characteristic	Total Population ($N = 211$)	Normal RBUS ($n = 135$)	Abnormal RBUS ($n = 76$)	*P*
PNUS result, *n* of *N* (%)				.787[b]
Normal	189 of 211 (90)	122 of 135 (90)	67 of 76 (88)	—
Abnormal	22 of 211 (10)	13 of 135 (10)	9 of 76 (12)	—
PNUS genitourinary anatomy result, *n* of *n* (%)				.129[c]
Normal	20 of 22 (91)	135 of 135 (100)	74 of 76 (97)	—
Abnormal	2 of 22 (9)	0 of 135 (0)	2 of 76 (3)	—

NA, not available; —, not applicable.
[a] Wilcoxon rank test.
[b] χ^2 test.
[c] Fisher's exact test.

urine output. Urology recommended outpatient VCUG and diuretic renal scan for further evaluation.

To measure the subsequent impact of RBUS testing after discharge, 194 of 211 (92%) caregivers were reached by phone call, and 4 additional children had VCUG results available through medical record review. Sixty-six of 198 children (33%) had a subsequent VCUG test, and of these, 22 had a normal RBUS. Reasons for obtaining VCUGs in these 22 children are described in Supplemental Table 5. Of the 66 children with VCUG, 25 (38%) were diagnosed with VUR. Sixteen children (64% of children with VUR) had dilating grade III ($n = 4$), IV ($n = 7$), or V ($n = 5$) VUR. Of the 194 children, 29 (15%) received antibiotic prophylaxis. None of the 194 children had surgical interventions performed within 6 weeks of hospital discharge. Review of the medical records revealed that 33 of 211 (16%) had subspecialty referrals to a nephrologist or urologist because of an abnormal RBUS result (24 consults during hospitalization and 9 referrals by the pediatrician after discharge). The majority of recommendations in the hospital setting involved nonurgent VCUG after resolution of the acute illness and antibiotic prophylaxis.

DISCUSSION

In our prospective cohort of hospitalized children with first febrile UTI, we found no clinical characteristics of PNUS testing, the child, or presenting illness that were associated with clinically important abnormalities on RBUS. This also holds true for the most severe abnormalities seen on RBUS, although further exploration of whether an association exists between non–*E coli* pathogens and severe abnormalities on RBUS is warranted for future research. RBUS examinations in this cohort of hospitalized children infrequently resulted in the need for acute medical or surgical interventions during hospitalization but did result in a substantial proportion of children receiving VCUG testing, antibiotic prophylaxis, and subspecialty referrals. Overall, we were unable to identify clinical predictors for abnormal RBUS to support a focused approach to RBUS examinations at the time of first febrile UTI in hospitalized children.

Our findings are similar to other studies that report the impact of RBUS and continued need for routine examinations at the time of first febrile UTI. Giorgi et al[8] studied a population of infants using a "bottom to up" approach in which VCUG was performed before RBUS. They found that even with a normal VCUG, RBUS studies identified findings of obstruction, duplication, and cystic kidney disease. Approximately 4% of their population received alterations in management, including surgical interventions or subspecialty referrals. Authors of 2 additional retrospective studies and 1 prospective study of predominantly infants and young children with first UTI found 10% to 16% had important findings on RBUS.[10,26,27] In our population, approximately one-third of participants received further testing or subspecialty referrals on the basis of the RBUS result. However, we must be cautious when interpreting these results because additional testing may not always equate to benefit for the patient. In some cases, spurious findings on 1 test could cascade to multiple future interventions that could have been avoidable.[28,29] In our population, 40 children had a normal VCUG, and it is possible that some of this testing could have been performed as a result of acute inflammatory changes seen on RBUS. In contrast to our study findings, several other studies that included older populations with a female predominance found less utility in RBUS examinations with low prevalence of detection of genitourinary anomalies or alterations in management.[9,11,30] Thus, on the basis of our findings and previous literature, RBUS is needed at the time of first UTI in hospitalized populations of children <2 years of age, but the utility is questionable in older children.

To avoid the cascade effect of additional testing driven by inflammatory changes seen on early RBUS examinations, the timing of RBUS may warrant further exploration in future studies. The American Academy of Pediatrics clinical practice guideline for first febrile UTI recommends obtaining an RBUS after resolution of the acute illness.[5] This may be especially important to note because RBUS abnormalities attributable to the acute illness, such as urothelial thickening, can be seen in both acute infection and VUR.[14] Although we cannot discern which RBUS findings resolved after acute illness in our study, we did find that abnormal RBUS was more frequent among children while still febrile. In addition, our findings support the lack of urgency in performing RBUS because acute procedures, such as bladder decompression, were uncommon as a result

TABLE 4 Comparison of Characteristics of Young Children With First Febrile UTI by Threshold C RBUS Severe Findings

Characteristic	Non–Threshold C (n = 171)	Threshold C (n = 40)	P
Median age, mo (IQR)	1.0 (0–2)	1.0 (0.5–3)	.455[a]
Sex, *n* of *N* (%)			.836[b]
Female	67 of 171 (39)	17 of 40 (43)	—
Male	104 of 171 (61)	23 of 40 (58)	—
Ethnicity, *n* of *N* (%)			.928[b]
Non-Hispanic	63 of 163 (39)	16 of 40 (40)	—
Hispanic	100 of 163 (61)	23 of 40 (58)	—
Race, *n* of *N* (%)			.573[c]
White	128 of 157 (82)	27 of 36 (75)	—
African American	18 of 157 (11)	6 of 36 (17)	—
Asian American	11 of 157 (7)	3 of 36 (8)	—
Insurance, *n* of *N* (%)			.565[c]
Private	53 of 171 (31)	12 of 40 (30)	—
Public	111 of 171 (65)	28 of 40 (70)	—
Self-pay	7 of 171 (4)	0 of 40 (0)	—
Median gestational age, mo (IQR)	39.0 (37–39)	39.0 (38–39)	.532[a]
Circumcision, *n* of *N* (%)			1.0[c]
Uncircumcised	94 of 103 (91)	21 of 23 (91)	—
Circumcised	9 of 103 (9)	2 of 23 (9)	—
Family history, *n* of *N* (%)			.510[b]
Negative	156 of 170 (92)	37 of 39 (95)	—
Positive	14 of 170 (8)	2 of 39 (5)	—
E coli versus non–*E coli*, *n* of *N* (%)			.193[b]
Non–*E coli*	22 of 171 (13)	9 of 40 (23)	—
E coli	149 of 171 (87)	31 of 40 (78)	—
ICU stay, *n* of *N* (%)			.742[c]
No	158 of 171 (92)	38 of 40 (95)	—
Yes	13 of 171 (8)	2 of 40 (5)	—
SIRS, *n* of *N* (%)			.579[b]
No	50 of 168 (30)	14 of 39 (36)	—
Yes	118 of 168 (70)	25 of 39 (64)	—
Bacteremia, *n* of *N*(%)			.253[c]
No	131 of 160 (82)	27 of 37 (73)	—
Yes	29 of 160 (18)	10 of 37 (27)	—
Quantity PNUS (IQR)	3.0 (3–3)	3.0 (3–3)	.829[a]
Trimester of last PNUS, *n* of *N* (%)			.633[c]
First	0 of 166 (0)	0 of 38 (0)	—
Second	26 of 166 (16)	7 of 38 (18)	—
Third	140 of 166 (84)	31 of 38 (82)	—
PNUS result, *n* of *N* (%)			.849[b]
Normal	154 of 171 (90)	35 of 40 (88)	—
Abnormal	17 of 171 (10)	5 of 40 (13)	—
PNUS genitourinary anatomy result, *n* of *N* (%)			.0352[c]
Normal	171 of 171 (100)	38 of 40 (95)	—
Abnormal	0 of 171 (0)	2 of 40 (5)	—

—, not applicable.
[a] Wilcoxon rank test.
[b] χ^2 test.
[c] Fisher's exact test.

of RBUS. The decision to perform RBUS during hospitalization or after discharge should also take into account the reliability of the caregivers and their preferences. Researchers have shown that follow-up rates can be lower for VCUG when performed as an outpatient.[31] In future studies, researchers should also investigate the association between non–*E coli* uropathogens and severe RBUS findings because this could be 1 potential parameter that could help risk stratify which children should have RBUS more urgently without deferring to the outpatient setting. Physicians could also consider asking about prenatal history because both infants with genitourinary abnormalities on PNUS had abnormal RBUS.

We have several limitations to our study. First, we focused on hospitalized children to fully capture RBUS examinations as the primary outcome. With the focus on hospitalized children, however, the age of our population could be younger, and the illness severity could be higher than in children with UTI cared for in the outpatient setting. Thus, our findings may not be generalizable to children seen in the outpatient setting. Second, knowing that 22 children with normal RBUS examinations had a VCUG, the practice of obtaining VCUGs may have differed in our cohort compared to other institutions (Supplemental Table 5). Third, all RBUS examinations were performed during the acute phase of illness in the hospital setting. Our results may have been different had a large proportion of RBUS examinations been performed after the acute illness when inflammatory changes would have resolved. Previous reports, however, indicate that most centers perform RBUS on children before discharge, making these findings generalizable to most hospital settings.[9,11,32] Last, we used a single-center design, in which all mothers had receipt of at least 1 PNUS. The prenatal care received by this population could impact the results,[26] and it would be prudent to replicate the study in other centers to confirm the findings.

CONCLUSIONS

Given the lack of clinical predictors identified for abnormal RBUS, we are unable to develop a focused imaging strategy for RBUS examinations at the time of first febrile UTI for hospitalized children ages 0 to 24 months. Further studies are needed to evaluate the optimal timing for RBUS testing and whether postponing RBUS until after fever resolution or hospital discharge is associated with any benefits or harms. Additionally, future studies could explore whether an association exists between non–*E coli* uropathogens and severe abnormalities on RBUS.

Dr Wallace conceptualized the study question and design, led the study team, participated in data collection and review of renal ultrasound reports, performed data analysis, and wrote the initial draft of the manuscript; Drs Ban and Singh contributed to the study design, determined the threshold of severity of findings on renal ultrasound reports, collected data, and critically revised the manuscript; Dr Lui contributed to the study design, substantially contributed to data collection, critically revised the manuscript, and participated in the consensus panel for the primary outcome; Dr Molleda contributed to the study design, substantially contributed to data collection, and critically revised the manuscript; Dr Orth contributed to the study design, participated on the consensus panel for the primary outcome, determined the Society of Fetal Urology scores for hydronephrosis in renal ultrasound examinations, and critically revised the manuscript; Drs Pierson, Hess, Lo, and Neubauer contributed to the study design, collected data, and critically revised the manuscript; Drs Koh and Walker contributed to the study design, collected data, critically revised the manuscript, and participated on the consensus panel for the primary outcome; Dr Macias provided guidance for the study design and data analysis, participated in the consensus panel for the primary outcome, and critically revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Hospital Pediatrics 2020;10;392
DOI: 10.1542/hpeds.2019-0240 originally published online April 17, 2020;

Hospital Pediatrics®

AN OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

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