Urinary Tract Infection in Outpatient Febrile Infants Younger than 30 Days of Age: A 10-year Evaluation

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Background: To determine the prevalence of outpatient-diagnosed urinary tract infection (UTI) in consecutive febrile neonates ≤30 days of age and correlate demographic, laboratory and radiographic imaging results with infectious etiology.

Methods: Review of medical records of consecutive febrile infants ≤30 days of age presenting to an urban pediatric emergency department during a 10-year period, whose policy is to perform a sepsis evaluation (urine culture obtained by bladder catheterization) and hospitalize for parenteral antibiotic therapy pending culture results.

Results: Of 670 febrile neonates ≤30 days of age evaluated for sepsis, urine culture was obtained in 651 cases (97%). Of 100 patients with UTI (15.4%), 73% were male; the most common uropathogens were *Escherichia coli* (71%), *Enterococcus* (10%) and *Klebsiella* sp. (10%). In all, 39% had a maximum documented fever ≥102°F, and 40% had CBC total white blood cells count ≥15,000/mm^3. Urine dipstick test was positive for leukocyte esterase or nitrite in 79%. Renal ultrasound performed in 95 patients (95%) showed anatomic abnormalities in 47%; 5/26 (24%) with hydronephrosis had vesicoureteral reflux on voiding cystourethrogram. Four patients had urosepsis; none had bacterial meningitis and no patients died.

Conclusions: UTI affects approximately 1 in 6 febrile neonates ≤30 days of age. Males are affected 2.5-times greater than females. *E. coli* continues to be the predominant uropathogen. Clinical parameters like height of fever, CBC total white blood cell count and urine dipstick test lack sensitivity in identifying UTI risk in the outpatient setting. Only 4 infants had urosepsis (4%). Nearly half of neonates with UTI have a radiographically identified anatomic abnormality. All febrile young infants should receive performance of a urine culture; those with UTI require imaging.

Key Words: febrile young infant, serious bacterial infection, urinary tract infection, hydronephrosis, urosepsis

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The febrile young infant is a common pediatric problem presenting for outpatient evaluation. Prior studies have delineated relatively high risk for serious bacterial infection (SBI) when compared with older febrile children.[1,2] A variety of potential host deficiencies can contribute to these youngest infants being susceptible to invasive bacterial infection. In addition, their neurologic immaturity can confound accurately grading patient clinical appearance.[3] It is widely recommended that all febrile infants <1 month of age receive a comprehensive sepsis evaluation and hospitalization for empiric antibiotic therapy pending culture results.

The most common SBI in febrile young infants is urinary tract infection (UTI). Delayed diagnosis and treatment theoretically increases risk for renal scarring and possible urosepsis, each with potentially serious consequences.

A recent consensus report by the American Academy of Pediatrics on UTI excluded making recommendations for infants 0–2 months of age, citing a paucity of data defining UTI risk in these patients.[4] The purpose of this study is to define the characteristics and outcomes of a large consecutive group of consecutive febrile infants aged ≤30 days with UTI who received an emergency department (ED) sepsis evaluation.

METHODS

The study was approved by the Institutional Review Board of Maimonides Medical Center. A retrospective review of medical records of consecutive febrile (rectal temperature ≥38.0°C measured by healthcare provider or ≥100.4°F measured by caretaker within 24 hours of ED visit) infants aged ≤30 days evaluated in the pediatric ED of Maimonides Medical Center from 2004 to 2013 was performed. As per protocol, all febrile infants ≤30 days of age receive a comprehensive sepsis evaluation (lumbar puncture [LP], complete blood count [CBC] and blood culture [BC], urinalysis [UA] and urine culture [UC] obtained by bladder catheterization) and are hospitalized for parenteral antibiotic therapy pending culture results. Pyuria was present with either dipstick positive for leukocyte esterase or urinalysis microscopy with ≥10 white blood cells (WBC) per high-powered field. UTI was present with UC positive for a single bacterial pathogen isolated from a bladder catheterized-obtained sample with a colony count of either: (1) ≥50,000 CFU/mL or (2) 10,000–50,000 colony forming units per mL (CFU/mL) with associated pyuria.[5–7] We included the latter criteria to maximize inclusion of all "treatment-indicated" cases, avoiding misclassifying neonates with fever, pyuria and UC isolation of a single uropathogen at lower colony counts as "asymptomatic bacteruria" or "contaminant". Urine dipstick test was positive when manifesting either + leukocyte esterase or + nitrite. Urosepsis occurred with simultaneous isolation of an identical bacterial pathogen in urine and blood.

All radiographic studies were interpreted by a pediatric radiologist. Ultrasound diagnosis of pelviectasis was made when there was isolated linear fullness of the collecting system. Ultrasound diagnosis of hydronephrosis was made when there was distention proximal to the collecting system—graded as "mild" if distal to the renal calyces and either "moderate" or "severe" if involving the renal calyces. Voiding cystourethrogram (VCUG) diagnosis of vesicoureteral reflux (VUR) was graded per the International System of Radiographic Grading of Vesicoureteral Reflux criteria.[8]

RESULTS

A total of 670 febrile infants ≤30 days of age presented to the ED during the 10-year study period; 19 medical records (3%) did not give urine culture results and these cases were excluded. Table 1 shows clinical characteristics of the 651 study patients. All had bladder catheterized-collected UC performed; of the 100 infants meeting the criteria for UTI, 87 had a urine dispstick test performed and 95 had RUS performed before hospital discharge. No patient received antibiotics before ED evaluation. All patients

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TABLE 1. Characteristics of 100 Febrile Infants ≤30 Days of Age With UTI

Male gender	73 (73%)
Mean patient age	23.3 days
Mean patient age with hydronephrosis on RUS	25.2 days
Mean patient age with normal RUS	22.6 days
Mean maximum measured rectal temperature	101.9°F
Maximum measured rectal temperature ≥102°F	39 (39%)
Mean CBC total WBC count	14,400 /mm^3
CBC total WBC count ≥15,000/mm^3	40 (40%)
Positive urine dipstick test for leukocyte esterase or nitrite	69/87 (79%)
Negative urine dipstick test for leukocyte esterase or nitrite	18/87 (21%)
Urosepsis (bacteremia with UTI)	4 (4%)
Bacterial meningitis	0
Deaths	0

had a rectal temperature measurement, LP with CSF analysis and CBC/blood culture performed.

Urine cultures were positive for the following bacterial pathogens: *Escherichia coli* (71), *Enterococcus* (10), *Klebsiella neumoniae* (7), *Klebsiella oxytoca* (3) *Enterobacter cloacae* (3), Group B *Streptococcus* (1), *Pseudomonas aeruginosa* (1), *Staphylococcus aureus* (1), *Staphylococcus* coagulase-negative (1), *Serratia marcescens* (1) and viridans streptococci (1). The distribution of urine culture colony counts with UTI were 10–20,000 CFU/mL (5), 20–49,000 CFU/mL (17), 50–75,000 CFU/mL (39) and ≥100,000 CFU/mL (39). All 4 cases of urosepsis had *E. coli* UTI and bacteremia.

Of 95 patients who had renal ultrasound (RUS) imaging, 45 (47%) had a renal anatomic abnormality, including 19 with pelviectasis and 26 with hydronephrosis (graded as mild in 12 cases and moderate in 14 cases). A VCUG was performed in 21/26 patients with hydronephrosis; 5 (24%) were positive for VUR (*E. coli* in 1 case, *Enterobacter* sp. in 2 cases and *Klebsiella* sp. in 2 cases); of these, 1 was grade II, 2 were grade III, 1 was grade IV and 1 was grade V.

DISCUSSION

A recent American Academy of Pediatrics consensus statement[4] on pediatric UTI excluded infants 0–2 months of age from consideration due to insufficient published data characterizing this group. Prior analyses estimated the prevalence of UTI in febrile young infants within the context of larger age groups: ages 0–2 months (10–13.6%)[7,9,10] and ages 0–3 months (7–9%).[11,12] Among febrile infants ages 0–3 months, 7.5% of girls had UTI; whereas UTI was present in 2.4% of circumcised and up to 20% of uncircumcised boys.[11]

Few prior studies examining outpatient-evaluated febrile neonates specifically analyzed UTI; several series examining +SBI rates reported UTI prevalence < 5%.[1,2] By contrast, we found a much greater overall UTI rate of 15.4% in these very young febrile infants (approximately 1 in 6 cases). This higher rate may be due in part to more comprehensive criteria we used to diagnose UTI. No ideal microbiologic standard has been devised to accurately define UTI in this age group. Although nearly 80% of positive urine cultures in our series grew a uropathogen at a concentration ≥50,000 CFU/mL, we sought to maximize inclusion of all "treatment-indicated" cases by diagnosing the infection whenever a febrile neonate with pyuria had a positive UC for a single uropathogen at colony counts ≥10,000 CFU/mL.[5–7]

A prior prospective study[7] applying similar microbiologic criteria for diagnosing UTI showed 11% of febrile outpatient-evaluated neonates had UTI. Being an offshoot of a bronchiolitis study, UTI sampling only occurred during peak respiratory season (between October through March), which precluded an accurate assessment of prevalence; and limited their conclusions due to skewed proportions analyzed. A relative strength of our analysis is that hospital protocol dictated a stereotyped evaluation of each patient (complete sepsis evaluation) which captured for analysis 97% of all febrile neonates who presented to our ED during the 10-year study period; providing a more comprehensive annual prevalence rate.

In accord with other series[7,13–16] we documented, *E. coli* was the predominant uropathogen (71%) and UTI was more common in males (73%) vs. females.[9,15,17] Similarly consistent with prior series of febrile young infants with +SBI, higher degrees of fever (≥102°F) were absent in nearly two-thirds of febrile neonates with UTI.[1,2,16]

Prior studies[9,13–15] documented prevalence rates of associated bacteremia in infants with UTI ranging as high as 16–31%. By contrast, our results showed only 4% of neonates had urosepsis (none had bacterial meningitis), which accords with other studies documenting relatively lower rates ranging from 0 to 6%.[18–20]

Outpatient evaluation variables were relatively insensitive for identifying UTI risk. Only 39% of patients had peripheral blood leukocytosis (CBC total WBC count ≥15,000/mm^3). A urine dipstick test positive for leukocyte esterase or nitrite was only 79% sensitive, lower than previously reported for relatively older children (up to 90–100%).[4,21] Reliance on urine dipstick test results to determine whether to perform a urine culture would have resulted in missed diagnosis of 21% of UTI cases in our cohort. Similarly, microscopic urinalysis was relatively insensitive at identifying those with underlying UTI. Our laboratory uses standard technique for urinalysis; perhaps usage of enhanced urinalysis technique would have improved detection of pyuria in these patients.[21] These findings reiterate that outpatient tools to identify UTI risk in febrile young infants are imperfect[7] and emphasizes the need to culture the urine in all cases.[22]

There is little published data establishing specific rates of RUS abnormalities in febrile neonates with UTI.[14,20,23–26] Such abnormalities in relatively older children ages 2–24 months with a first UTI are identified in approximately 12–15% of cases.[4,24] Some prior neonatal UTI series performing renal imaging were limited by surveying only those in a neonatal intensive care unit,[16,26] examining a select (nonconsecutive) group of neonates with UTI[15,20] or reporting neonatal statistics as a subset within the context of wider age ranges surveyed.[20,23,24]

Several studies specifically reported RUS findings in outpatient-evaluated young infants with UTI. One[15] examining 45 selected males aged 0–8 weeks with UTI showed hydronephrosis in 24%. Another[20] examining 64 selected neonates with UTI found 20% with abnormal RUS findings and 20% with VCUG-diagnosed VUR.

By contrast, our study of consecutive outpatient-evaluated febrile neonates (95% had RUS performed) found nearly half with UTI had a renal anatomic abnormality; specifically, pelviectasis (20%) and hydronephrosis (27%). Although the finding of isolated pelviectasis usually requires no intervention and has a high rate of spontaneous resolution,[27] recognizing this underlying abnormality identifies those who require close urologic monitoring and evaluation for UTI with repeat febrile illnesses. Of patients with hydronephrosis who had a VCUG performed, nearly one-fourth had VUR; of microbiologic interest is that in 80% with VUR, the uropathogen was a non-*E. coli* Gram-negative organism (*Klebsiella* or *Enterobacter*).

CONCLUSIONS

UTI is present in 1 of 6 febrile neonates presenting for outpatient evaluation. Nearly 50% have a radiographic anatomic

abnormality and one-fourth with hydronephrosis have VUR. All febrile young infants should receive performance of a urine culture; those with UTI require RUS imaging. Those with hydronephrosis should have further evaluation for VUR. The purpose of renal imaging is to detect urologic abnormalities that require additional management, such as further radiographic studies or subspecialty consultation. Identifying abnormalities is important to determine prognosis and establish appropriate follow up and monitoring so as to maximize renal function.

REFERENCES

1. Bonadio WA, Webster H, Wolfe A, et al. Correlating infectious outcome with clinical parameters of 1130 consecutive febrile infants aged zero to eight weeks. *Pediatr Emerg Care*. 1993;9:84–86.
2. Bonadio WA, Romine K, Gyuro J. Relationship of fever magnitude to rate of serious bacterial infections in neonates. *J Pediatr.* 1990;116:733–735.
3. Bonadio WA, Hennes H, Smith D, et al. Reliability of observation variables in distinguishing infectious outcome of febrile young infants. *Pediatr Infect Dis J*. 1993;12:111–114.
4. American Academy of Pediatrics. Practice parameter: the diagnosis, treatment, and evaluation of the initial urinary tract infection in febrile infants and young children. Committee on Quality Improvement, Subcommittee on Urinary Tract Infection. *Pediatrics* 2011;128:595–610.
5. Hoberman A, Wald ER. Urinary tract infections in young febrile children. *Pediatr Infect Dis J*. 1997;16:11–17.
6. Hoberman A, Wald ER, Reynolds EA, et al. Pyuria and bacteruria in urine specimens obtained by catheter from young children with fever. *J Pediatr.* 1994;124:513–519
7. Zorc JJ, Levine DA, Platt SL, et al.; Multicenter RSV-SBI Study Group of the Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics. Clinical and demographic factors associated with urinary tract infection in young febrile infants. *Pediatrics*. 2005;116:644–648.
8. Lebowitz RL, Olbing H, Parkkulainen KV, et al. International system of radiographic grading of vesicoureteric reflux. International Reflux Study in Children. *Pediatr Radiol*. 1985;15:105–109.
9. Lin DS, Huang SH, Lin CC, et al. Urinary tract infection in febrile infants younger than eight weeks of Age. *Pediatrics*. 2000;105:E20.
10. Morley EJ, Lapoint JM, Roy LW, et al. Rates of positive blood, urine, and cerebrospinal fluid cultures in children younger than 60 days during the vaccination era. *Pediatr Emerg Care*. 2012;28:125–130.
11. Shaikh N, Morone NE, Bost JE, et al. Prevalence of urinary tract infection in childhood: a meta-analysis. *Pediatr Infect Dis J*. 2008;27:302–308.
12. Ismaili K, Lolin K, Damry N, et al. Febrile urinary tract infections in 0- to 3-month-old infants: a prospective follow-up study. *J Pediatr.* 2011;158:91–94.
13. Ginsburg CM, McCracken GH Jr. Urinary tract infections in young infants. *Pediatrics*. 1982;69:409–412.
14. Wang SF, Huang FY, Chiu NC, et al. Urinary tract infection in infants less than 2 months of age. *Zhonghua Min Guo Xiao Er Ke Yi Xue Hui Za Zhi*. 1994;35:294–300.
15. Goldman M, Lahat E, Strauss S, et al. Imaging after urinary tract infection in male neonates. *Pediatrics*. 2000;105:1232–1235.
16. Barton M, Bell Y, Thame M, et al. Urinary tract infection in neonates with serious bacterial infections admitted to the University Hospital of the West Indies. *West Indian Med J*. 2008;57:101–105.
17. Kanellopoulos TA, Salakos C, Spiliopoulou I, et al. First urinary tract infection in neonates, infants and young children: a comparative study. *Pediatr Nephrol*. 2006;21:1131–1137.
18. Crain EF, Gershel JC. Urinary tract infections in febrile infants younger than 8 weeks of age. *Pediatrics*. 1990;86:363–367.
19. Krober MS, Bass JW, Powell JM, et al. Bacterial and viral pathogens causing fever in infants less than three months old. *Am J Dis Child*. 1985;139:889–892
20. Downs SM: Technical report: urinary tract infections in febrile infants and young children. *Pediatrics*. 1999;103:e54
21. Hoberman A, Wald E, Penchansky L, et al. Enhanced urinalysis as a screening tool for urinary tract infection. *Pediatrics* 1993;91;1196
22. Baraff LJ, Bass JW, Fleisher GR, et al. Practice guideline for the management of infants and children 0 to 36 months of age with fever without source. Agency for Health Care Policy and Research. *Ann Emerg Med*. 1993;22:1198–1210.
23. Hoberman A, Charron M, Hickey RW, et al. Imaging studies after a first febrile urinary tract infection in young children. *N Engl J Med*. 2003;348:195–202.
24. Preda I, Jodal U, Sixt R, et al. Value of ultrasound in evaluation of infants with first urinary tract infection. *J Urol.* 2010;183:1984–1988.
25. Krause C, Eisenstein B. Davidovits M. Prevalence of vesicoureteral reflux in neonatal urinary tract infection. *Clin Pediatr* 2004;43:619–625.
26. Sastre JB, Aparicio AR, Cotallo GD, et al.; Grupo de Hospitales Castrillo. Urinary tract infection in the newborn: clinical and radio imaging studies. *Pediatr Nephrol*. 2007;22:1735–1741.
27. Cheng AM, Phan V, Geary DF, et al. Outcome of isolated antenatal hydronephrosis. *Arch Pediatr Adolesc Med*. 2004;158:38–40.