Diagnosis and Management of Bacteremic Urinary Tract Infection in Infants

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KEY WORDS
urinary tract infection, bacteremia, serious bacterial infection, hospitalization

ABBREVIATIONS
CI: confidence interval
cfu/mL: colony-forming units per milliliter
CSF: cerebrospinal fluid
hpf: high-powered field
IV: intravenous
LOS: length of stay
OR: odds ratio
SCVMC: Santa Clara Valley Medical Center
UA: urinalysis
UTI: urinary tract infection
VCUG: voiding cystourethrogram
WBC: white blood cell

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abstract

OBJECTIVES: To report the prevalence of bacteremia by age in a sample of infants <1 year of age with urinary tract infections (UTIs), to compare characteristics of infants with UTIs with and without bacteremia, and to describe treatment courses and 30-day outcomes in infants with UTIs with and without bacteremia.

METHODS: We used a retrospective cross-sectional design to determine the prevalence of bacteremia in infants with UTIs at our institution. A double cohort design matching for age and gender was used to compare clinical characteristics and outcomes between infants with bacteremic versus nonbacteremic UTIs.

RESULTS: We identified 1379 UTIs, with blood cultures obtained in 52% of cases. The prevalence of bacteremia was 4.1% (95% confidence interval 3.1%–5.3%) for all UTIs and 8% (95% confidence interval 6.1%–10.2%) for UTIs in which blood culture was obtained. Fifty-five infants with bacteremic UTIs were compared with 110 infants with nonbacteremic UTIs. Except for minor differences in the urinalysis and serum band count, there were no significant differences in clinical presentation between the 2 groups. Bacteremic infants received longer parenteral treatment courses than nonbacteremic infants (mean 6.7 vs 2.4 days, $P < .001$). Treatment courses in the bacteremic group were variable and predicted by age but not severity of illness. No bacteremic infant had recurrent UTI or bacteremia with the same organism within 30 days of discharge.

CONCLUSIONS: Treatment was variable but outcomes were excellent in infants with bacteremic UTIs.

Urinary tract infections (UTIs) are now the most common cause of serious bacterial infection in young children.[1–3] Clinical practice guidelines exist for the diagnosis and management of UTIs in young children[4] but do not include recommendations regarding when to obtain blood cultures in children with suspected UTI or appropriate treatment regimens for infants with UTI and bacteremia, which generates considerable uncertainty over how to manage these infants. Several studies have demonstrated that bacteremia occurs infrequently in children with UTIs[5–9] and that children with bacteremia are difficult to distinguish clinically from children with nonbacteremic UTIs.[5,7,8,10] However, because bacteremic UTI is the most common cause of bacteremia in infants, it is important to examine treatment regimens for this clinical entity and how they relate to clinical outcomes.[11] There is a growing body of evidence suggesting that long courses of intravenous (IV)

antibiotics may not be necessary for even the youngest infants with UTIs.[12–15] However, we are aware of no studies that specifically examine treatment courses and outcomes of infants with bacteremic UTIs. This study aims to report the prevalence of bacteremia by age in a sample of infants <1 year of age with UTIs, to compare characteristics of infants with UTIs with and without bacteremia, and to describe treatment courses and 30-day outcomes in infants with UTIs with and without bacteremia.

METHODS

Study Design

A retrospective cross-sectional design was used to determine the prevalence of bacteremia in infants with UTIs. A retrospective double cohort design was used to compare clinical characteristics and outcomes between infants with bacteremic versus nonbacteremic UTI. A double cohort study samples from 2 cohorts with varying levels of risk factors, in this case presence or absence of bacteremia, and follows outcomes. This differs from a case-control study in which samples are chosen based on presence or absence of a particular outcome.[16]

Setting

Santa Clara Valley Medical Center (SCVMC) is a county hospital and clinic system in Northern California. The pediatric department includes clinics that provide primary and urgent care to >40 000 children per year, a pediatric ward, and NICU and PICU at a tertiary hospital. Urine and blood cultures obtained anywhere within the system are sent to a central hospital laboratory. The SCVMC Institutional Review Board approved this investigation.

Subjects

The SCVMC microbiology database was queried to identify patients <1 year of age who had UTIs between October 1998 and June 2012. UTI was defined as urine culture containing a pathogenic organism with ≥50 000 colony-forming units per milliliter (cfu/mL) by catheterization or ≥100 000 cfu/mL by clean catch or bag. Prevalence of bacteremia in infants with UTIs was analyzed using the entire dataset of UTIs. Some infants with bacteremic UTI had growth of >1 organism in the urine culture. Therefore, infants with urine cultures containing >1 organism were included as long as at least 1 organism met the cfu/mL criteria. Cases from the NICU were excluded because its specialized population is not easily generalizable.

A retrospective double cohort design was performed to compare clinical characteristics and outcomes of UTI with and without bacteremia. The first cohort contained infants with bacteremic UTI, defined as growth from blood culture obtained within 24 hours of the urine culture containing the same pathogen. The second cohort contained infants with UTI (defined by same criteria) with a negative blood culture. Two nonbacteremic infants, age- and gender-matched, were selected for each bacteremic infant.

Data Collection

Medical records of infants with and without bacteremia were reviewed. Comorbidities documented at presentation that may predispose children to UTI and/or bacteremia, such as urologic abnormalities, immunodeficiency, neuromuscular disease, and use of indwelling urinary catheter or central venous catheter were recorded.

Duration of fever (≥38.0°C) after treatment was calculated in the subgroup of hospitalized infants who received their first antibiotic dose in the hospital and compared between bacteremic ($n = 30$) and nonbacteremic ($n = 52$) infants. It was calculated as time from administration of the first antibiotic dose in the hospital until the last documented fever in nursing notes.

Patients were considered ill appearing if there was documentation (in initial clinic, emergency department, or ward physician examination or assessment) of being "lethargic," "toxic," "septic," or "sick." For urinalysis (UA) results, urinary white blood cells (WBCs) were stratified into 5 categories: 0 to 3, 4 to 10, 11 to 20, 21 to 50, and >50 WBCs per high-powered field (hpf). Duration of parenteral antibiotic therapy was calculated as the number of calendar days separating first and last parenteral dose. An additional day was added if the last dose was intramuscular ceftriaxone. For example, a child receiving intramuscular ceftriaxone on Monday and Tuesday morning was recorded as having 2 days of parenteral antibiotics. A long course of parenteral antibiotics was defined as ≥7 days. Length-of-stay (LOS) was an integer for each patient, determined by number of calendar days separating admission and discharge dates. Infants were excluded from analysis of urinary imaging if they had known urologic abnormalities at time of presentation or if notes documented that imaging would be performed elsewhere after discharge. A renal ultrasound was defined as abnormal if the report listed pelviectasis, hydronephrosis/hydroureter, posterior valves, uteropelvic junction obstruction, ureterocele, renal asymmetry/solitary kidney, or renal duplication.

Recurrent UTI and/or bacteremia were defined as a second episode of UTI or bacteremia within 30 days of the initial episode and readmission was defined as rehospitalization for UTI or bacteremia within 30 days of the initial episode.

Statistical Analysis

Calculations were performed using commercially available software (Stata 7; StataCorp LP, College Station, TX). Proportions were compared by using χ^2 analysis and Fisher exact test as appropriate, and continuous variables were compared using Student's *t* test and Wilcoxon rank-sum test as appropriate. To assess frequency of blood culture ordering over time and possible interaction with age, we built a logistic regression model with blood culture ordered (yes/no) as the dependent variable. Independent variables were year (as a linear term, centered on 1998), age (dichotomized at older or younger than 4 months),[17] and interaction of year by age (to assess whether the year-by-year change in blood culture ordering was different for younger versus older patients). The sample of bacteremic infants was a convenience sample based on the date when the microbiology database originated.

RESULTS

Prevalence of Bacteremia in Infants With UTI

A total of 1379 cases of UTI were identified. Blood cultures were obtained in 714 of 1379 of UTIs (52%). The majority of UTIs (55%) were in boys, and blood cultures were ordered more commonly in boys with UTI than girls with UTI (59% vs 42%, $P < .001$). Blood cultures were ordered with decreasing frequency over time (Fig 1). Odds of having a blood culture ordered decreased after 1998 by an average of 11% (odds ratio [OR] 0.89, 95% confidence interval [CI] 0.86–0.92). Compared with patients <4 months, the odds of patients ≥4 months having a blood culture were lower in 1998 (OR 0.34, 95% CI 0.20–0.59) and decreased annually by an additional 8% (interaction term age by year OR 0.92, 95% CI 0.86–0.98).

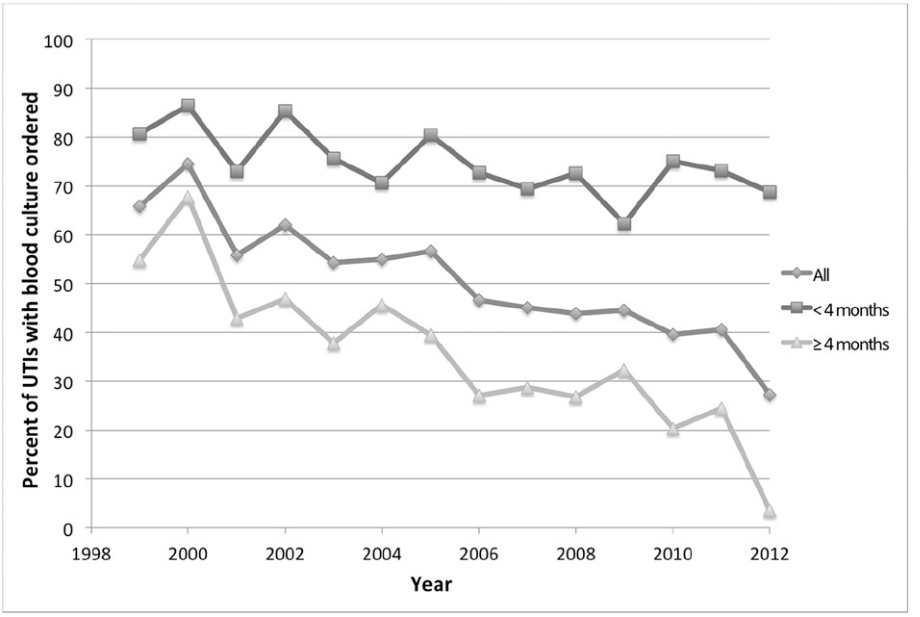

FIGURE 1 Frequency of blood cultures obtained with urine cultures.

Bacterial growth was documented in 101 blood cultures: 41 contaminants (5.7% of all blood cultures obtained; *Staphylococcal* species, non-*aureus* = 39, *Streptococcus viridans* = 1, *Bacillus* species = 1), 3 pathogens that were not present in the urine (*Pseudomonas stutzeri*, *Neisseria meningitidis*, and *Candida* species), and 57 pathogens that were also present in the urine. These 57 infants with bacteremic UTI represented 4.1% (95% CI 3.1%–5.3%) of all infants with UTI and 8% (95% CI 6.1%–10.2%) of infants with UTI in whom blood culture was obtained. Prevalence of bacteremia with UTI decreased with age (Fig 2) but was not significantly different between males and females (data not shown). *Escherichia coli* was the most common organism (84%), followed by *Enterobacter* species (8.8%), *Enterococcus faecalis*, *Staphylococcus aureus*, *Salmonella typhi* type B, and *Stenotrophomonas maltophilia* (1.8% each).

Characteristics of Infants With UTI With and Without Bacteremia

Two of the 57 infants with bacteremic UTIs were excluded from the double cohort analysis because charts were not available. The remaining 55 infants with bacteremic UTIs were compared with 110 age- and gender-matched infants with UTI and a negative blood culture (Table 1). Complete blood counts with differentials were obtained on all bacteremic infants and all but 1 of the non-bacteremic infants. UAs were obtained on the majority of infants, but some components of the UA, especially leukocyte esterase, were performed or reported inconsistently

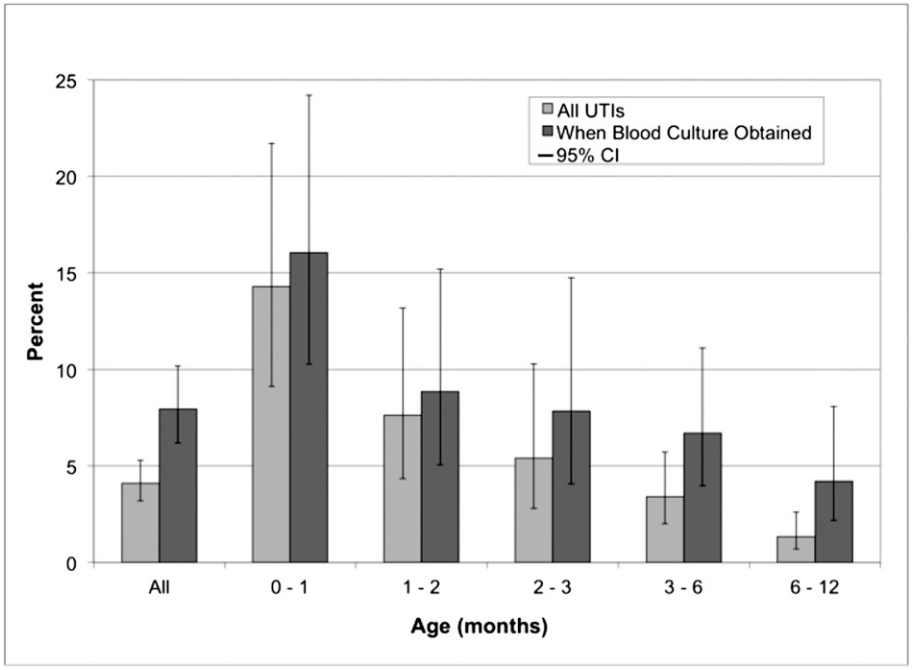

FIGURE 2 Proportion of infants with UTIs who had bacteremia.

(Table 1). Serum percent band count and urinalysis >10 WBCs/hpf and bacteria were higher in infants with bacteremic UTI; otherwise, there were no significant differences between groups on presentation. Subsequent abnormal urinary imaging results were no different between groups, but not all infants received urinary imaging. Imaging was significantly more common in the bacteremic group (Table 2).

Treatment and Outcomes of Infants With Bacteremic UTI

There was substantial variation in duration of parenteral antibiotics (Fig 3) and hospital LOS for infants with bacteremic UTI (data not shown). Distribution of LOS was similar to the duration of parenteral antibiotics, with a slightly lower mean (6.5 days vs 6.8 days), reflecting the fact that some infants were treated as outpatients with intramuscular antibiotics. Infants who received parenteral antibiotic courses ≥7 days were younger than those who received shorter courses (60 vs 101 days, $P = .02$), but there were no other significant differences between these groups in terms of gender, comorbidities, initial laboratory parameters, initial clinical appearance, highest fever before presentation, time to defervescence, or subsequent imaging results (data not shown). Similarly, infants with LOS ≥7 days were younger than those who had shorter hospitalizations or were not hospitalized (mean age 55 vs 111 days, $P = < .001$) but otherwise had no significant clinical or laboratory differences. Even within the youngest group of infants (≤60 days), treatment varied: duration of parenteral therapy was ≤4 days in 7 of 28 (25%), 5 to 7 days in 13 of 28 (46%), and >7 days in 8 of 28 (29%) infants. Most (80%) bacteremic infants who were initially hospitalized had fever durations of <24 hours after antibiotic administration. No infants required ICU transfer, vasopressors, or intubation. One infant with congenital hip dysplasia, bacteremic UTI with *Enterobacter cloacae*, and persistently elevated C-reactive protein was evaluated for possible hip infection and had concerning magnetic resonance imaging findings. Although incision and drainage of the hip and bone biopsy did not reveal pus or bacteria, this infant was treated with IV antibiotics for 42 days total (24 days at home) via central line. No other subjects were discharged from the hospital with an indwelling central venous catheter.

Outpatient encounters within our system after the acute episode were documented for all but 1 bacteremic infant, a 6-week-old who received 7 days of IV antibiotics and had scheduled follow-up with an outside provider. None of the 55 (0%, 97.5% CI 0%–6%) bacteremic infants had a recurrent bacteremic UTI or recurrent UTI with the same species within 30 days of the initial episode. Two infants with bacteremic UTIs had a recurrent UTI with a different species, and 1 of these infants was readmitted. Both infants had vesicoureteral reflux (grade 3 and grade 5). Five infants (4.6%) with a nonbacteremic UTI had a recurrent UTI; 4 (3.6%) were caused by the same organism. Four of these infants had voiding cystourethrogram (VCUG) performed. Of these, 1 infant had ureterocele, and the remaining 3 had normal studies.

Cerebrospinal fluid (CSF) was obtained in 28 of 55 (51%) of the bacteremic infants. Only 1 infant had bacterial growth on CSF culture. *Escherichia coli* was isolated from blood and urine and from the CSF broth only. The lumbar puncture was traumatic (14 315 red blood cells, 59 WBCs), and the primary team suspected that the CSF

TABLE 1 Clinical Characteristics and Laboratory Results of Infants With UTI With and Without Bacteremia

Variable	UTI With Bacteremia ($n = 55$)	UTI With Negative Blood Culture ($n = 110$)	P[a]
Clinical characteristics			
Age, mo (SD)	2.7 (2.4)	2.7 (2.4)	N/A
Age category, mo (%)			N/A
<1	17 (31)	33 (30)	
1–2	11 (20)	22 (20)	
2–3	8 (15)	16 (15)	
3–6	12 (22)	26 (24)	
6–12	7 (13)	13 (12)	
Male gender (%)	34 (62)	68 (62)	N/A
Any comorbidity (%)	3 (5)	6 (5)	1.0
Urologic comorbidity (%)	3 (5)	3 (3)	.40
Highest fever, °C (SD)	39.1 (0.9)	38.9 (0.9)	.48
"Ill-appearing" (%)	3 (5)	1 (1)	.11
WBC count × 10^3 (SD)	17.3 (7.2)	16 (7)	.25
% Band count (SD)	14.9 (10.1)	6.7 (6.9)	<.001
CSF obtained (%)	28 (51)	41 (37)	.09
CSF bacterial growth, if CSF obtained (%)	1 (4)	0 (0)	.22
Urinalysis results[b]			
Urine WBCs/hpf (%)			.01
0–3	4 (8)	24 (24)	
4–10	7 (13)	16 (16)	
11–25	14 (27)	9 (9)	
26–50	5 (10)	13 (13)	
>50	22 (42)	40 (39)	
Urine WBCs >10/hpf (%)	41/52 (75)	62/102 (56)	.02
+ Leukocyte esterase (%)	27/29 (93)	47 (81)	.20
+ Nitrites (%)	26/53 (49)	40/105 (38)	.19
Bacteria (%)			.04
None	0/50 (0)	4/99 (4)	
Few/some	7/50 (14)	28/99 (28)	
Many	43/50 (86)	67/99 (68)	
Location where cultures were obtained			.52
Outpatient clinic (%)	34 (62)	59 (54)	
ED (%)	6 (11)	19 (17)	
Inpatient (%)	15 (27)	32 (29)	

[a] Proportions were compared by using χ^2 analysis and Fisher exact test as appropriate, and continuous variables were compared using Student's t test and Wilcoxon rank-sum test as appropriate.
[b] The denominator for the proportions is the number of infants in whom the specific test results were available.

culture reflected contamination from the blood.

Repeat blood cultures were obtained during the treatment period in 34 of 55 (62%) bacteremic infants, and 11 of 34 (32%) of these infants had ≥2 repeat blood cultures. Only 1 infant had a positive repeat blood culture. This 3-month-old infant was infected with *Stenotrophomonas maltophilia* and had not been receiving appropriate antibiotic coverage for this organism. By the time the repeat blood culture was positive, antibiotics had already been modified based on sensitivities from the original cultures.

Because findings of a positive urine culture but an absence of pyuria on the UA in nonbacteremic infants may reflect asymptomatic bacteruria or contamination rather than true UTI, which in turn may lead to an overestimation of clinical and/or management differences in the bacteremic group, a sensitivity analysis was performed removing all infants with ≤10 WBC/hpf on the UA. The differences between bacteremic and nonbacteremic infants in the serum band count (14.4% vs 7.1%, $P < .001$), the days of parenteral antibiotics (6.6 vs 2.7 days), and the percent hospitalized (95% vs 61%, $P < .001$) remained essentially unchanged.

DISCUSSION

This investigation highlights several important findings about the prevalence of bacteremia in UTIs and clinical characteristics and outcomes of infants with bacteremic UTI. We confirm previous findings that bacteremia is rare in older infants with UTI and that the clinical presentation of infants with bacteremia does not differ substantially from those without bacteremia. We also present the novel finding that although there was a wide range of hospital LOS and duration of parenteral antibiotics for bacteremic infants, outcomes were generally excellent, with prompt defervescence, easy clearance of bacteria from the bloodstream, and no 30-day recurrences or rehospitalizations with the same organism within our medical center system.

Over the study period (1998–2012), providers became more sparing when ordering blood cultures in infants with suspected UTI. Although we have no concrete explanation for this finding, it may reflect decreasing concern about bacteremia in general because routine vaccination against pneumococcus began in 2000 in the United States.[11,18,19] This hypothesis is supported by our demonstration that the decrease was more pronounced in infants aged ≥4 months.

TABLE 2 Clinical Outcomes of Infants With UTI With and Without Bacteremia

Variable	UTI With Bacteremia ($n = 55$)	UTI With Negative Blood Culture ($n = 110$)	P[a]
Clinical outcomes			
Mean duration of parenteral (IV or IM) antibiotics, d (SD)	6.8 (6)	2.4 (2.1)	<.001
Hospitalized (%)	51 (93)	58 (53)	<.001
Mean LOS if hospitalized, d (SD)	6.5 (3.6)	3.8 (2.6)	<.001
Duration of fever after treatment in patients initially hospitalized, h (SD)	12 (22)	6 (14)	.07
Recurrent UTI within 30 d, same organism (%)	0 (0)	4 (3.6)	.30
Recurrent UTI within 30 d, any organism (%)	2 (3.6)	5 (4.6)	1.0
Readmission for UTI or bacteremia within 30 d (%)	1 (1.8)	1 (0.9)	1.0
Imaging			
US obtained (%)	51 (98)	92 (88)	.04
US abnormal, if obtained (%)	18 (35)	28 (30)	.55
VCUG obtained (%)	48 (92)	72 (69)	.001
Abnormal VCUG, if obtained (%)	15 (31)	19 (26)	.56
Grade III-V vesicoureteral reflux, if VCUG obtained (%)	8 (17)	11 (15)	1.0

IM, intramuscular; US, ultrasound.
[a] Proportions were compared by using χ^2 analysis and Fisher exact test as appropriate, and continuous variables were compared by using Student's t test and Wilcoxon rank-sum test as appropriate.

The reported prevalence from previous studies of bacteremic UTIs in children is variable. Our estimate of 8% when blood cultures were obtained in infants with UTI is similar to the 9.3% seen by Bachur et al, which used a similar age range.[6] Other studies have reported lower[8,9] and higher[20,21] probabilities of bacteremia, likely due to differences in age groups and denominators (all UTIs vs UTIs with blood culture). Our finding that the risk of bacteremia with UTI is inverse to age and quite low beyond 6 months confirms previous results.[6,8,20,21]

There are no published recommendations for a threshold pretest probability at which to obtain a blood culture in an infant with suspected UTI. Theoretically, the detection of bacteremia may be beneficial if the extended hospitalizations and courses of parenteral antibiotics prevent a complication such as meningitis or recurrent UTI. However, to our knowledge, there are no data to support this theoretical benefit. Furthermore, there are risks of obtaining blood cultures, including contaminated cultures (almost as common as true pathogens in this cohort), overdiagnosis (ie, detection of bacteremia in an infant leading to additional treatment with no benefit), and patient harm and costs associated with prolonged courses of IV antibiotics.[22–25]

Clinical features of infants with bacteremia were not distinguishable from infants without bacteremia, except for small differences in UA findings and serum band count. This finding confirms previous studies suggesting that children with bacteremic UTI show no major clinical differences from those with nonbacteremic UTI at presentation.[6,9,10,20] Bacteremic infants were no more likely to have abnormal urinary imaging results. However, selective ordering of urinary imaging may have biased this finding. The National Institute for Health and Clinical Excellence (United Kingdom) guidelines suggest that bacteremia alone should prompt a VCUG.[26] These guidelines reference an investigation by Honkinen et al,[10] which found no overall difference in imaging abnormalities between bacteremic and nonbacteremic infants with UTI, but bacteremic infants had a higher risk of high-grade reflux and urinary obstruction. In another investigation involving 33 bacteremic infants,[6] ultrasounds and VCUGs were more likely to be abnormal in infants with bacteremic UTI. However, similar to our study, imaging was selective (VCUG was obtained in 83% of infants). Additional study is needed to determine whether routine VCUGs benefit infants with bacteremic UTI, especially in infants with normal ultrasounds.

There was substantial treatment variability regarding duration of parenteral antibiotics and LOS for bacteremic infants in our institution. Young age was the only significant predictor of a long parenteral course, suggesting that providers did not use treatment response to guide the treatment course. Even within the youngest group (≤60 days), treatment varied significantly, signifying lack of consensus on treatment courses for these infants.

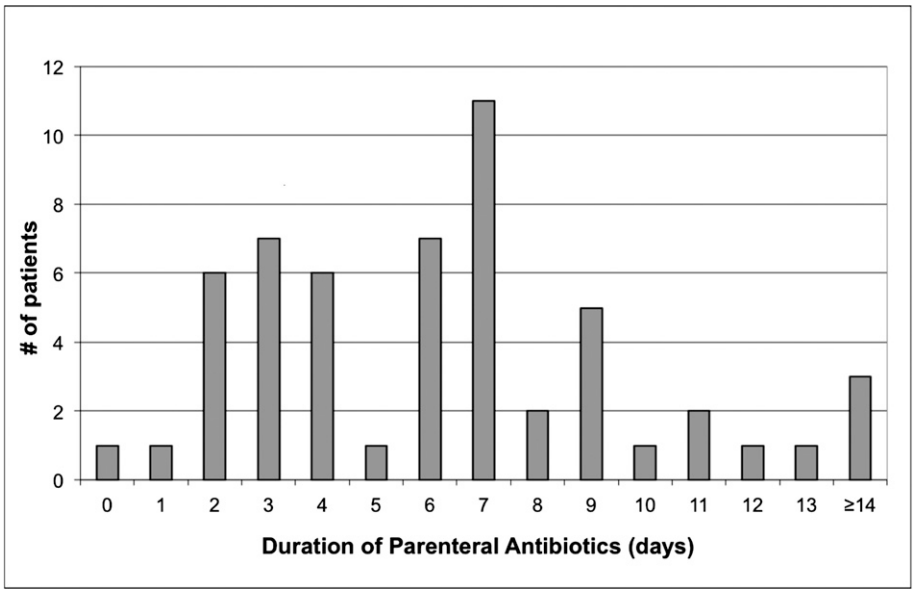

FIGURE 3 Duration of parenteral antibiotics in infants with bacteremic UTI.

Although such treatment variability is well described in young infants with UTI,[15] little is known about treatment of infants with bacteremic UTI, although limited data can be gleaned from existing studies. In a trial of oral cefixime for infants aged 1 to 24 months with UTI, 13 patients had bacteremia; 5 in the oral cefixime only arm and 8 in the IV cefotaxime (3 days) plus oral cefixime (11 days) arm. All 13 patients had clearance of bacteremia within 24 hours and fared well. However, this study had no infants <30 days and only 4 infants between 1 and 2 months of age.[12] Interestingly, this study also reported no renal scarring 6 months later in any of the bacteremic children, suggesting that prevention of scarring should not be justification for prolonged parenteral antibiotic courses. Magin et al described 16 neonates with bacteremic UTI who were treated with IV antibiotics for an average of 7 days, with no recurrent UTIs within 14 days of treatment completion.[14] In a study on IV antibiotic duration in >12 000 infants <6 months with UTI, bacteremia predicted longer parenteral treatment length (55 infants received >3 days and 26 received ≥3 days) but did not predict 30-day readmission.[15] Finally, Honkinen et al reported a mean parenteral antibiotic duration of 6.3 days in patients with bacteremia and 3.8 days in controls (blood culture–negative UTIs) but did not describe readmissions or recurrences.[10] Therefore, although we can extract data describing treatment courses from several existing studies, gaps persist in our understanding of the relationship between treatment courses and outcomes.

Clinical outcomes for patients with bacteremic UTI were excellent in our sample. Most fevers were short-lived (<1 day in 80% of infants initially hospitalized), and no infants required ICU transfer, vasopressors, or intubation. Furthermore, no repeat blood cultures obtained during the acute illness were positive in appropriately treated infants, indicating that bacteria are easily cleared from the bloodstream and follow-up blood cultures are of low yield and may be unnecessary. The positive repeat blood culture in the 1 infant with *Stenotrophomonas* did not change management.

Regardless of LOS and duration of parenteral antibiotics, no infants with bacteremic UTI in our study had recurrent bacteremia or recurrent UTI with the same organism within 30 days, indicating that no infants were undertreated. Although our sample size is modest, to our knowledge it remains the largest study to specifically examine treatment courses and outcomes in infants with bacteremic UTI. That infants who received short courses had excellent outcomes suggests that prolonged hospitalizations and parenteral antibiotic courses are not necessary in many cases.

Our study has several limitations. First, the retrospective design prohibits the conclusion that infants would have fared as well with shorter hospitalizations and courses of parenteral antibiotics. Second, some children may have been rehospitalized elsewhere, although we are encouraged that all but 1 bacteremic infant had at least 1 additional encounter after treatment. Third, by relying on physician documentation to assess clinical appearance and severity of illness, we may have missed some more subtle differences in clinical presentation.

Finally, pyuria was not used as a criterion for our definition of UTI. It is possible that some infants with nonbacteremic UTI had asymptomatic bacteruria rather than true UTI. This potential misclassification could have influenced the differences in serum band count and UA results between groups.

CONCLUSIONS

The prevalence of bacteremia in infants with UTI decreases with age and is low after 6 months of age. Bacteremic UTIs are difficult to distinguish from nonbacteremic UTIs at presentation. There is considerable practice variation in management of bacteremic infants but outcomes are excellent regardless of treatment courses. That infants who received short courses had excellent outcomes suggests that prolonged hospitalizations and parenteral antibiotic courses may not be necessary in many cases. Larger studies are needed to better address when a blood culture should be obtained in infants with possible UTI and how aggressively bacteremic infants should be treated.

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REFERENCES

1. Baker MD, Bell LM, Avner JR. Outpatient management without antibiotics of fever in selected infants. *N Engl J Med*. 1993;329(20):1437–1441.
2. Watt K, Waddle E, Jhaveri R. Changing epidemiology of serious bacterial infections in febrile infants without localizing signs. *PLoS ONE*. 2010;5(8):e12448.
3. Pantell RH, Newman TB, Bernzweig J, et al. Management and outcomes of care of fever in early infancy. *JAMA*. 2004;291(10):1203–1212.
4. American Academy of Pediatrics, Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children aged 2 to 24 months. *Pediatrics*. 2011;128(3):595–610.
5. Bachur R. Nonresponders: prolonged fever among infants with urinary tract infections. *Pediatrics*. 2000;105(5):E59.
6. Bachur R, Caputo GL. Bacteremia and meningitis among infants with urinary tract infections. *Pediatr Emerg Care*. 1995;11(5):280–284.
7. Crain EF, Gershel JC. Urinary tract infections in febrile infants younger than 8 weeks of age. *Pediatrics*. 1990;86(3):363–367.
8. Pitetti RD, Choi S. Utility of blood cultures in febrile children with UTI. *Am J Emerg Med*. 2002;20(4):271–274.
9. Schnadower D, Kuppermann N, Macias CG, et al; American Academy of Pediatrics Pediatric Emergency Medicine Collaborative Research Committee. Febrile infants with urinary tract infections at very low risk for adverse events and bacteremia. *Pediatrics*. 2010;126(6):1074–1083.
10. Honkinen O, Jahnukainen T, Mertsola J, Eskola J, Ruuskanen O. Bacteremic urinary tract infection in children. *Pediatr Infect Dis J*. 2000;19(7):630–634.
11. Greenhow TL, Hung YY, Herz AM. Changing epidemiology of bacteremia in infants aged 1 week to 3 months. *Pediatrics*. 2012;129(3). Available at: www.pediatrics.org/cgi/content/full/129/3/e590.
12. Hoberman A, Wald ER, Hickey RW, et al. Oral versus initial intravenous therapy for urinary tract infections in young febrile children. *Pediatrics*. 1999;104(1 pt 1):79–86.
13. Hewitt IK, Montini G. Pediatric febrile urinary tract infections: the current state of play. *Ital J Pediatr*. 2011;37:57.
14. Magín EC, García-García JJ, Sert SZ, Giralt AG, Cubells CL. Efficacy of short-term intravenous antibiotic in neonates with urinary tract infection. *Pediatr Emerg Care*. 2007;23(2):83–86.
15. Brady PW, Conway PH, Goudie A. Length of intravenous antibiotic therapy and treatment failure in infants with urinary tract infections. *Pediatrics*. 2010;126(2):196–203.
16. Hulley SB, Cummings SR, Newman TB. *Designing Clinical Research*. 4th ed. Philadelphia, PA: Lippincott, Williams, and Wilkins; 2013.
17. Kraemer HC, Blasey CM. Centring in regression analyses: a strategy to prevent errors in statistical inference. *Int J Methods Psychiatr Res*. 2004;13(3):141–151.
18. Stoll ML, Rubin LG. Incidence of occult bacteremia among highly febrile young children in the era of the pneumococcal conjugate vaccine: a study from a Children's Hospital Emergency Department and Urgent Care Center. *Arch Pediatr Adolesc Med*. 2004;158(7):671–675.
19. Herz AM, Greenhow TL, Alcantara J, et al. Changing epidemiology of outpatient bacteremia in 3- to 36-month-old children after the introduction of the heptavalent-conjugated pneumococcal vaccine. *Pediatr Infect Dis J*. 2006;25(4):293–300.
20. Newman TB, Bernzweig JA, Takayama JI, Finch SA, Wasserman RC, Pantell RH. Urine testing and urinary tract infections in febrile infants seen in office settings. *Arch Pediatr Adolesc Med*. 2002;156(1):44–54.
21. Ginsburg CM, McCracken GH Jr. Urinary tract infections in young infants. *Pediatrics*. 1982;69(4):409–412.
22. Goff DA, Larsen P, Brinkley J, et al. Resource utilization and cost of inserting peripheral intravenous catheters in hospitalized children. *Hosp Pediatr*. 2013;3(3):185–191.
23. Jumani K, Advani S, Reich NG, Gosey L, Milstone AM. Risk factors for peripherally inserted central venous catheter complications in children. *JAMA Pediatr*. 2013;167(5):429–435.
24. Owens PLTJ, Elixhauser A, Ryan K. Care of Children and Adolescents in U.S. Hospitals (HCUP Fact Book No. 4; AHRQ Publication No. 04-0004). Rockville, MD: Agency for Healthcare Research and Quality; 2003.
25. Schroeder AR. The never-ending quest to detect bacteremia: time for a culture change. *Hosp Pediatr*. 2014;4(2):85–87.
26. National Institute for Health and Clinical Excellence. Urinary Tract Infection in Children (NICE Clinical Guideline 54). London, England: National Institute for Health and Clinical Excellence; August 2007. Available at: http://www.nice.org.uk/nicemedia/pdf/CG54NICEguideline.pdf. Accessed October 19, 2013.

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