

BRIEF REPORT

Urinary Tract Infection in Young Infants: Practice Patterns in Evaluation and Treatment

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OBJECTIVES: No clear guidelines exist for the management of infants ≤ 60 days old with urinary tract infection (UTI), although this condition represents a significant percentage of serious bacterial infection in this age group. We examined patterns of UTI management in infants ≤ 60 days at a tertiary care children's hospital and hypothesized that younger infants would be hospitalized longer.

METHODS: We reviewed electronic health records of infants age ≤ 60 days with diagnostic codes of UTI or fever hospitalized from January 2013 to January 2017 with urine culture obtained and UTI diagnosis documented. Outcomes were duration of parenteral antibiotic therapy, length of stay (LOS), and hospital readmission.

RESULTS: One hundred ninety-three infants met criteria. Median age at admission was 37 days (interquartile range [IQR]: 22–48). Median duration of parenteral antibiotics was 59 hours (IQR 43–114) and median LOS was 71 hours (IQR 57–127). Infants age ≤ 28 days, with fever duration ≥ 24 hours, irritability or lethargy on initial examination, and bacteremia received longer parenteral therapy and had longer LOS. In multivariate analysis, age, irritability or lethargy, and presence of bacteremia remained independently related to parenteral therapy duration and LOS.

CONCLUSIONS: In young infants with UTI, patients aged ≤ 28 days had longer duration of IV antibiotic therapy and LOS, independent of other clinical characteristics of their illness. The duration of parenteral therapy and LOS was relatively short, although significant variability still existed.

ABSTRACT

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Infants aged ≤ 60 days with urinary tract infection (UTI) present a management challenge for pediatric hospitalists. Despite UTI being the most common serious bacterial infection in febrile neonates, the American Academy of Pediatrics guidelines for pediatric UTI exclude infants aged 0 to 2 months.^{1,2} Parenteral therapy durations of 5 to 22 days are reported in infants aged ≤ 30 days.³ In a multicenter study of infants aged ≤ 6 months hospitalized for treatment of UTI, the proportion of children receiving parenteral therapy for ≥ 4 days ranged from 15% to 87%. Despite differences in treatment duration, no association with readmission rate was found.⁴ In a survey with a clinical vignette of a 2-week-old with UTI, the preferred duration of parenteral antibiotics varied strikingly across different subspecialties.⁵

In this study, we examined patterns of management of febrile infants aged ≤ 60 days hospitalized with UTI at a tertiary care children's hospital. We suspected that younger age, bacteremia, ill appearance, prolonged fever, abnormal urinary tract anatomy, and prematurity would be predictive of the duration of parenteral antibiotic therapy.

METHODS

Using the electronic health record, we identified infants aged ≤ 60 days with UTI who were hospitalized at a tertiary care children's hospital from January 1, 2013 through May 7, 2018. The study was approved by the institutional review board; informed consent was waived for a retrospective study. We used encounter diagnosis codes to identify all patients 0 to 60 days old who had fever or UTI. Of these, we only included patients who were hospitalized, had a urine culture obtained, and had a final discharge diagnosis of UTI. Laboratory and/or microbiologic evidence of UTI was not required for inclusion. Exclusion criteria included treatment of a separate source of infection requiring antibiotic therapy (eg, bacterial meningitis), chronic severe systemic disease (including neuromuscular disorder, congenital or acquired immunodeficiency, malignancy, quadriplegia

or paraplegia, hydrocephalus or neurologic malformations, or organ transplant), infants in whom urinary tract foreign body exposure might have introduced infection (indwelling genitourinary devices, genitourinary tract instrumentation, or surgical intervention within the previous 7 days), or a diagnosis of hospital-acquired UTI.⁶ Data were included from the first admission and not subsequent admissions for readmitted patients.

Variables were extracted from the participant's chart by reviewing documentation in notes from the admission history and physical and the emergency medicine provider's documentation (Supplemental Fig 1). Four pediatric hospitalists performed the chart reviews. Questions about data extraction were settled by group consensus; interrater reliability was not assessed. For the purposes of analysis, an undocumented subjective variable in the history or physical examination was considered a negative response. Vital signs were recorded on the basis of the first data documented. Antibiotic therapy was abstracted from the medication administration record.

Demographic and clinical variables were described by using counts (proportions) and medians (interquartile range [IQRs]). Primary outcome was duration of parenteral therapy. Secondary outcomes were length of stay (LOS) and readmission rate. LOS was determined by subtracting the time of the first vital sign from the time of discharge order placement in hours. Duration of parenteral therapy was calculated by subtracting the time of administration of last dose of intravenous antibiotic from the time of the first dose in hours. Readmission rate was calculated on the basis of any admissions within 30 days of the initial admission that had UTI as a clinical diagnosis.

Associations between demographic and clinical characteristics and outcomes were evaluated. Age was categorized as ≤ 28 days and 29 to 60 days; duration of fever was categorized as ≥ 24 and < 24 hours;

bacteremia was categorized as either present or absent. A χ^2 test or Fisher exact test was used for categorical variables, and the Mann-Whitney test was used for continuous variables. We used a generalized linear model to explore whether duration of antibiotic therapy and LOS were associated with age, duration of fever, irritability, lethargy, and presence of bacteremia because these variables were significantly associated with 1 or both outcomes in the univariable analysis.

RESULTS

One hundred ninety-three subjects were included in this study (Supplemental Fig 2). Sixty-nine (35.8%) infants were ≤ 28 days. Participants were 54.4% male; 59.6% were white, 18.7% were African American, and 21.7% were other or unspecified race. The median duration of parenteral antibiotic therapy was 59 (IQR: 43–114) hours. The median duration of total antibiotic therapy was 13 (IQR: 10–14) days. The median LOS was 71 (IQR: 57–127) hours (Table 1).

Univariable analysis did not reveal a statistically significant relationship between age and either duration of fever or presence of bacteremia (Supplemental Tables 4 and 5). Younger patients (age ≤ 28 days) and patients with bacteremia had longer durations of parenteral antibiotics and LOS ($P < .0001$ for all associations) (Table 2). Lethargy on initial examination was associated with LOS and duration of antibiotics. Irritability and duration of fever were associated with LOS only. Prematurity, other signs of ill appearance on initial examination (poor capillary refill or poor tone), and abnormal imaging (including renal ultrasound and/or voiding cystourethrogram) were not associated with either LOS or duration of parenteral therapy.

In multivariable analysis, age, presence of bacteremia, irritability, and lethargy, but not duration of fever, were independently associated with the duration of parenteral antibiotic therapy and LOS (Table 3). Patients ≤ 28 days had longer duration of parenteral antibiotic (mean duration was 1.65 times that of older patients, $P < .0001$) and longer LOS (mean duration was

TABLE 1 Description of Study Cohort

Demographics	<i>n</i> (%) or median (IQR)
Total infants	193
Age at admission, d, median (IQR)	37 (22–48)
Age ≤28 d, <i>n</i> (%)	69 (35.8)
Male sex, <i>n</i> (%) ^a	105 (54.4)
Race, <i>n</i> (%)	
White	115 (59.6)
African American	36 (18.7)
Other ^b	30 (15.5)
Unknown	12 (6.2)
Ethnicity, <i>n</i> (%)	
Hispanic or Latino	55 (28.5)
Not Hispanic or Latino	134 (69.4)
Unknown	4 (2.1)
Season, <i>n</i> (%)	
Winter: December to February	43 (22.3)
Spring: March to May	48 (24.9)
Summer: June to August	62 (32.1)
Fall: September to November	40 (20.7)
Abnormal urinary anatomy, <i>n</i> (%)	57 (29.5)
Duration of fever ≥24 h, <i>n</i> (%)	35 (18.1)
Presence of bacteremia, <i>n</i> (%)	29 (15.0)
Antibiotic therapy	
Duration of parenteral therapy, h, median (IQR)	59 (43–114)
Total therapy, d, median (IQR)	13 (10–14)
Outcomes	
LOS, h, median (IQR)	71 (57–127)

^a Percentages may not sum to 100 because of rounding.

^b Including American Indian, Alaskan native, Asian, Native Hawaiian, Pacific Islander, Hispanic, and multiple race.

The presence of irritability or lethargy on initial examination is suggestive of a more ill infant, which would reasonably lead to a longer duration of parenteral therapy and therefore LOS. However, we also found that age group, independent of other clinical considerations, led practitioners to prolong parenteral therapy. There is no evidence that a longer duration of parenteral antibiotic therapy is needed for treatment of UTI in infants ≤28 days of age. For older infant populations, shorter durations of parenteral antibiotics are not associated with treatment failure.^{4,8} Authors of a retrospective study of infants age ≤60 days admitted for UTI showed that the use of parenteral antibiotics for ≥4 days decreased from 50% to 19% from 2005 to 2015, with no impact on readmission rate.⁹ Researchers of a multicenter retrospective study of infants age ≤60 days with bacteremic UTIs also demonstrated no advantage to long-course parenteral antibiotics (>7 days) with respect to recurrence or readmission.¹⁰ The importance of bacteremia in the setting of UTI is debated; researchers in multiple studies have suggested that the clinical symptoms and outcomes are not significantly different in bacteremic UTIs.^{11,12} Duration of fever, although often used to approximate a response to therapy, has not been shown to be predictive of any difference in clinical course in young children with UTI.¹³

There are several limitations to our study. This was a single-center study at an academic institution, and our sample size was small. Some of the variables were dependent on documentation practices and therefore possibly inaccurate. Readmissions could have occurred at hospitals outside of our system. It is possible that infants 29 to 60 days with UTI could have been managed as outpatients, although we anticipate this would be a small number because the typical practice in our hospital is admission of all infants ≤60 days requiring antibiotics according to institutional clinical practice guidelines. Because we were most interested in the practices of providers after diagnosing a UTI, we did not limit our cohort with regard to urinalysis or microbiologic

1.60 times that for older patients, $P < .0001$). Clinical findings of bacteremia, lethargy, and irritability on initial examination were also found to be independently predictive of both duration of parenteral therapy and LOS.

Nine infants (4.6%) were readmitted within 30 days, and 5 (2.6%) of these readmissions were for UTI recurrence. Four of the readmissions for recurrent UTI were due to the same organism causing the initial admission, 3 had concomitant bacteremia on initial admission, and 3 had abnormal genitourinary anatomy. There was no association found between the duration of parenteral antibiotics in readmitted and non-readmitted infants (estimated ratio of means: 1.23, 95% confidence interval: 0.68–2.22).

DISCUSSION

In this single-center retrospective analysis of UTI management in young infants, age ≤28 days, presence of bacteremia, irritability, or lethargy on initial examination, and fever duration ≥24 hours were all associated with longer parenteral antibiotic therapy and/or LOS, whereas urinary tract abnormalities and prematurity were not. Although there was variability, the duration of parenteral therapy and LOS was generally short (median 59 hours and <3 days, respectively). This is consistent with recommendations published for UTI treatment in infants aged <1 month because it is approximately the amount of time it would take for blood and cerebrospinal fluid cultures to result.⁷

TABLE 2 Duration of Parenteral Antibiotics and LOS by Age, Duration of Fever, Bacteremia, Lethargy, and Irritability (*N* = 193)

	Total, <i>n</i>	Duration Parenteral Antibiotic, h, Median (IQR)	<i>P</i>	LOS, h, Median (IQR)	<i>P</i>
Age, d					
≤28	69	87.6 (51.7–165.8)	<.0001	109.5 (65.4–171.4)	<.0001
29–60	124	54.3 (41.4–76.4)	<.0001	65.2 (52.1–87.9)	<.0001
Fever duration, h					
≥24	35	59.9 (49.3–108.4)	.14	87.4 (64.8–132.5)	.036
<24	158	56.5 (42.4–117.1)	.14	68.6 (52.9–123.8)	.036
Bacteremia					
No	164	54.7 (42.4–78.6)	<.0001	67.0 (53.3–98.5)	<.0001
Yes	29	118.4 (78.2–168.1)	<.0001	135.3 (94.7–179.2)	<.0001
Lethargy					
No	189	58.8 (42.9–108.3)	.019	70.5 (56.5–123.8)	.02
Yes	4	245.9 (137.1–301.6)	.019	264.6 (153.7–317.4)	.02
Irritability					
No	180	58.6 (42.7–108.2)	.18	69.5 (56.0–118.5)	.029
Yes	13	78.0 (54.9–138.7)	.18	132.5 (77.7–173.7)	.029

data, and it is possible that some of the infants did not have a UTI.

Without clear guidelines for management of hospitalized young infants with UTIs, age remains a driving factor in the duration of parenteral antibiotic treatment and LOS in our hospital. The risks

associated with prolonging hospitalization need to be weighed with the risk of transitioning to oral antibiotics earlier. With our findings, we provide further support for relatively short durations of parenteral intravenous therapy in young infants with UTI.

TABLE 3 Multivariable Analysis

Outcome and Clinical Group	Estimated Ratio of Mean Outcome ^a	95% Confidence Interval
Duration parenteral antibiotics		
Age ≤28 d	1.65	1.40–1.95
Fever ≥24 h	1.12	0.91–1.37
Bacteremia	1.87	1.50–2.32
Lethargy	2.30	1.31–4.02
Irritability	1.51	1.10–2.08
LOS		
Age ≤28 d	1.60	1.38–1.86
Fever ≥24 h	1.12	0.94–1.35
Bacteremia	1.68	1.38–2.04
Lethargy	2.06	1.26–3.39
Irritability	1.54	1.16–2.04

The model included all variables with a univariate association with duration of parenteral antibiotics or LOS with *P* < .10. Variables with *P* > .10 in univariate analysis (and therefore not included in the model) were: prematurity, other signs of ill appearance on initial examination (poor capillary refill or poor tone), and abnormal imaging (including renal ultrasound and/or voiding cystourethrogram).

^a The estimated ratio of means for outcome is the exponential of the estimated difference in logs of the expected outcome variable from the generalized linear model. The estimated ratio of mean outcome in shown clinical groups is relative to the reference group (eg, ratio of mean LOS in infants ≤28 d relative to mean LOS in infants 29–60 d), similar to an odds ratio.

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