

# Serious Bacterial Infections in Neonates Presenting Afebrile With History of Fever

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abstract

**BACKGROUND:** Infants  $\leq 28$  days of age with fever are frequently hospitalized while undergoing infectious evaluation. We assessed differences in rates of serious bacterial infection (SBI; bacteremia, bacterial meningitis, urinary tract infection) and invasive bacterial infection (IBI; bacteremia, bacterial meningitis) among the following neonates: (1) febrile at presentation (FP), (2) afebrile with history of fever without subsequent fever during hospitalization, and (3) afebrile with history of fever with subsequent fever during hospitalization.

**METHODS:** We performed a single-center retrospective study of neonates evaluated for SBI during emergency department evaluation between January 1, 2006, and December 31, 2017. Patients were categorized into FP, afebrile with no subsequent fever (ANF), and afebrile with subsequent fever (ASF) groups. We compared rates of SBI and IBI between groups using logistic regression and assessed time to fever development using time-to-event analysis.

**RESULTS:** Of 931 neonates, 278 (29.9%) were in the ANF group, 93 (10.0%) were in the ASF group, and 560 (60.2%) were in the FP group. Odds of SBI in neonates ANF were 0.42 (95% confidence interval [CI] 0.23–0.79) compared with infants FP, although differences in IBI were not statistically significant (0.52, 95% CI 0.19–1.51). In infants ASF, median time to fever was 5.6 hours (interquartile range, 3.1–11.4). Infants ASF had higher odds of SBI compared to infants FP (odds ratio 1.93, 95% CI 1.07–3.50).

**CONCLUSIONS:** Neonates with history of fever who remain afebrile during hospitalization may have lower odds for SBI and be candidates for early discharge after an observation period.



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**WHAT'S KNOWN ON THIS SUBJECT:** One-third of neonates who are evaluated in emergency departments for serious infection with reported fever are afebrile on initial presentation. These infants are presumed to have the same risk of infections compared with those febrile at presentation.

**WHAT THIS STUDY ADDS:** Neonates with historical fever who are afebrile on both initial presentation and during hospitalization are at lower risk of serious bacterial infections compared with those who develop fever and may be candidates for a shorter period of hospitalization.

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The management of febrile infants  $\leq 28$  days of age is an important clinical challenge in pediatric medicine. Rates of serious bacterial infections (SBIs; urinary tract infection [UTI], bacteremia, and bacterial meningitis) in febrile neonates are as high as 14%.<sup>1-3</sup> A number of clinical and laboratory criteria are used in pediatric institutions to identify low-risk groups<sup>4-7</sup> with the aim of identifying those infants who can forego empirical antibiotics. Improved understanding of the risk factors for SBI or invasive bacterial infection (IBI; bacteremia and bacterial meningitis) could shorten hospitalizations and treatment.

The majority of neonates evaluated in emergency departments (EDs) due to reported or documented fever are admitted.<sup>8</sup> In a review of 37 pediatric EDs between the years 2011 and 2013, researchers identified that 78% of neonates evaluated for fever were subsequently admitted to the hospital.<sup>9</sup> These admissions typically last 24 to 48 hours.<sup>10</sup> These evaluations are overwhelming for families<sup>11</sup> and expose neonates to the risk of hospital-acquired infections. Strategies to reduce the duration of admission would mitigate these risks and simultaneously lower the cost of care.

Well-appearing neonates with historical fever who are afebrile in the ED present a particular challenge. These infants constitute approximately one-third of those who are evaluated for SBI.<sup>12,13</sup> Although some studies suggest that these infants are at a lower risk of SBI,<sup>14,15</sup> others have suggested a smaller risk reduction: 1 evaluation among 2470 infants  $< 90$  days old revealed that rates of IBI between afebrile and febrile infants were similar.<sup>12</sup> Researchers for another report derived from a multicenter North American study identified lower rates of SBI in afebrile versus febrile neonates (12.0% versus 17.4%,

respectively) but with limited risk reduction.<sup>13</sup>

Previous evaluations of afebrile infants with history of fever have been limited by only considering initial temperature. If infants with only historical fever who remain afebrile during hospitalization were at lower risk for SBI, they may be eligible for discharge after a brief period of observation. This may allow for shorter hospitalizations and reduced need for empirical antimicrobial therapy. To date, it has not been definitively established if infants who remain afebrile after serial temperature measurements despite a reported history of fever have lower odds of SBI compared with those who are febrile during evaluation.

In this study, we evaluate a population of infants  $\leq 28$  days of age with reported fever who underwent an evaluation for SBI. We aim to describe the rates of SBI or IBI for those who are persistently euthermic and for those who develop a fever and compare this to those who are febrile on admission. Better understanding of the infectious risk of these infants could limit unnecessary periods of hospitalization. We also aim to identify typical time to fever onset in initially afebrile patients and to report outcomes on afebrile infants who presented to the ED after receiving antipyretics.

## METHODS

### Setting

We performed a single-center retrospective study of neonates (defined as infants  $\leq 28$  days of age) presenting with a documented or historical fever and who underwent an evaluation for SBI. In our institution, all neonates with a fever (documented or historical) undergo a routine evaluation to identify those at low risk of SBI.<sup>6</sup> This includes

urinalysis, urine culture, complete blood count with differential, blood culture, cerebrospinal fluid (CSF) cytology, glucose and protein evaluation, and CSF culture. Patients are admitted for an observation period ranging from 24 to 48 hours. Before data collection, institutional review board approval was obtained with a waiver of informed consent.

### Sample Size Estimation

Previous evidence suggests that 1 in 3 neonates evaluated in EDs with a historical fever are afebrile on assessment<sup>12-14</sup> and that  $\sim 20\%$  of these infants develop a fever.<sup>16</sup> The incidence of SBI for all neonates evaluated for SBI in multicenter studies is  $\sim 12\%$ .<sup>9</sup> We estimated that inclusion of 554 febrile neonates and 277 neonates with history of fever only would allow us to detect a 50% difference in the rate of SBI between these 2 groups. Statistical power was set at 80% and 2-sided type I error was set at 0.05.<sup>17</sup> In a preliminary data search at our institution, we identified 231 febrile neonates presenting to the ED who received CSF cultures over a 34-month period. We collected data over a 12-year time period to achieve appropriate sample size.

### Patient Acquisition

Eligible patients were identified from a search of an institutional data repository of electronic medical records (EMRs). Records of patients  $\leq 28$  days of age presenting to the ED between January 1, 2006, and December 31, 2017, and who obtained any culture were included for initial review. From these records, charts were reviewed to ensure eligibility for inclusion and to identify neonates with either a historical fever (afebrile in ED group) or a documented fever in the ED (febrile in ED group).

### Patient Exclusion

Charts of all eligible patients were reviewed for inclusion eligibility.

Patients were excluded from the study if (1) blood, urine, and CSF cultures were not all obtained at our institution; (2) parenteral antibiotics were administered before acquisition of any culture; (3) no temperature was documented; (4) records were missing; or (5) there was a well-defined local infection in the presence of a fever or historical fever. Charts of afebrile patients were additionally excluded if they received an evaluation for SBI in the absence of a historical fever or if there was documentation of antipyretic administration before hospital arrival. We reported on outcomes of these infants who received antipyretics before arrival separately. Given previously published evidence demonstrating the inability of ED physicians to accurately determine which infants are at risk for serious infections on both structured and unstructured physical examination,<sup>18</sup> we did not include or exclude infants on the basis of their examination characteristics.

### Study Definitions

Fever was defined as a temperature  $\geq 38.0^{\circ}\text{C}$  measured by any method in the prehospital setting. We included patients with all means of temperature measurement in this study because nonrectal temperatures generally correlate with rectal means of temperature measurement<sup>19</sup> and because this method adheres to a fever inclusion criteria used by a large multicenter prospective cohort study of infants who were evaluated for SBI.<sup>20</sup> SBI was defined as the presence of UTI, bacteremia, or bacterial meningitis. IBI was defined as the presence of bacteremia or bacterial meningitis. On the basis of clinical characteristics, patients were classified into 3 groups: historically febrile neonates who were afebrile at presentation with no subsequent fever during hospitalization, historically febrile neonates who were afebrile at presentation with subsequent fever

during hospitalization, and neonates who were febrile at presentation (FP).

### Data Abstraction

For eligible patients, an EMR-based query was used to identify demographics (sex, age in days, race, ethnicity), temperatures from vital sign assessments, method of temperature assessments, laboratory results (complete blood cell counts with differentials and urinalyses), culture times and results, times of preliminary positive blood culture results, and dosing and administration times of antibiotics and antipyretics.

### Study Outcomes

Primary outcomes were SBI and IBI. Bacteremia and bacterial meningitis were defined as growth of a single organism from blood culture and CSF culture. Organisms including *Bacillus non-cereus/non-anthraxis*, diphtheroids, *Lactobacillus*, *Micrococcus*, and viridans group streptococci were considered contaminants. UTI was defined as growth of  $\geq 50\,000$  colony forming units/mL from a catheterized specimen of a known pathogen or growth of 10 000 to 50 000 colony forming units/mL of pathogenic organism from a catheterized specimen with positive urinalysis. A positive urinalysis finding was determined by (1) trace or greater for leukocyte esterase or nitrate on dipstick or laboratory-based urinalysis or (2)  $>5$  white blood cells per high-powered field or per microliter on a centrifuged or uncentrifuged urine specimen.<sup>21</sup> In ambiguous cases, an infectious disease specialist (L.W.W. and A.J.N.) reviewed results blinded to the clinical context of the patient to determine if a culture result was consistent with a true infection.

Our secondary outcomes were the proportion with and time to development of fever in initially afebrile neonates during subsequent

hospitalization and outcomes (fever development, time to fever, and rates of infections) of infants afebrile at presentation who had received antipyretic before presentation. All vital signs from hospital presentation to discharge were assessed. Time to fever onset was defined as the interval from first temperature assessment recorded in the EMR to first recorded temperature  $\geq 38.0^{\circ}\text{C}$ .

### Analysis

Descriptive statistics for categorical variables were summarized with proportions of patients. For continuous variables, we calculated means with SDs or medians with interquartile ranges (IQRs). We compared differences in continuous variables with respect to laboratory and assessment data with box plots. Data were compared with  $\chi^2$  tests (for categorical data), Wilcoxon rank sum tests (for continuous data), comparing the afebrile with no subsequent fever (ANF) and afebrile with subsequent fever (ASF) groups to the FP group. We compared rates of SBI and IBI between the 3 groups using univariate binomial logistic regression, with the population of neonates FP as a reference group. Findings were reported as odds ratios (ORs) with 95% confidence intervals (CIs). We reported the proportion of infants who were initially afebrile that developed fever after admission. To understand the time of fever onset after admission among those patients who developed a fever, we reported the median time to fever onset with IQR and performed a time-to-event (survival) analysis to identify time to fever development among neonates in the ASF group. Discharges or dosing of acetaminophen were considered as right-censored data. Analysis was done by using the survival (version 2.43) package<sup>22</sup> in R version 3.5.0 (<https://www.R-project.org/>; R Foundation for Statistical Computing, Vienna, Austria).

## RESULTS

### Patient Inclusion and Demographics

Of 2356 encounters of infants  $\leq 28$  days who received cultures in the ED during the inclusion period, 931 (mean age 18.1 days  $\pm$  SD 7.3, 507 boys [54.5%]) met inclusion criteria (Fig 1). Of them, 560 (60.2%) had fever on initial assessment. Of the remaining 371 (39.8%), 93 of 371 (25.1%) developed a fever during hospitalization and 278 of 371 (74.9%) remained afebrile. In total, 15 817 temperature measurements were obtained. Statistically significant differences were noted in the counts of temperatures, durations between temperature assessments, length of stay, and laboratory parameters between the FP and ANF group. These distributions appeared similar when demonstrated in box plots (Supplemental Fig 2). Of the 371 patients

afebrile but with history of fever, temperatures before hospital arrival were measured as follows: rectal in 254 (68.5%), axillary in 29 (7.8%), temporal in 14 (3.8%), otic in 5 (1.3%), oral in 1 (0.3%), and not stated in 68 (18.3%). Patient demographics, summarized laboratory values, and treatment and assessment characteristics are provided in Table 1.

### Development of SBI

Of 560 in the FP category, 58 (10.4%) had SBI, including 19 (3.4%) with an IBI. Of 93 in the ASF category, 17 (18.3%) had SBI, including 4 (4.3%) with an IBI. Of 278 in the ANF category, 13 (4.7%) developed SBI, including 5 (1.8%) with an IBI (Table 2). The odds of neonates ANF having SBI was lower than neonates FP. Infants ASF had higher odds of SBI compared with infants FP. The odds

of IBI was not significantly different between these groups (Table 3).

### Time to Fever

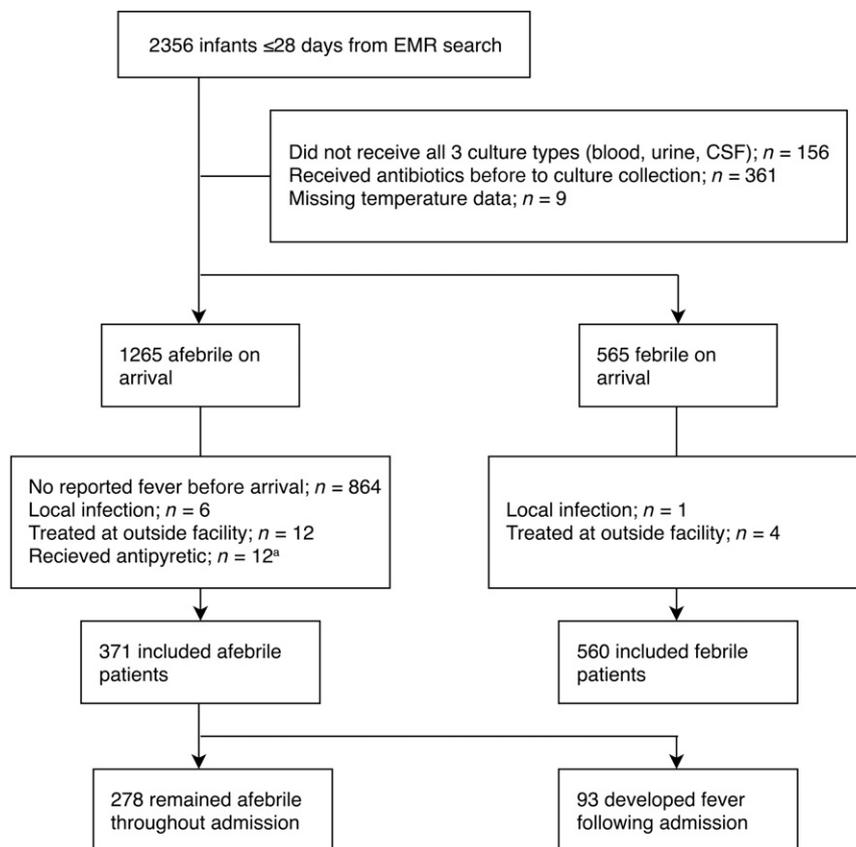
Of 371 patients with history of fever, 93 patients (25.1%) developed a fever during hospitalization. Median first elevated temperature was 38.2°C (IQR, 38.0–38.5). Median time to first elevated temperature was 5.6 hours (IQR, 3.1–11.4 hours). At 24 hours, the proportion of patients in the ASF group who had developed fever was 0.88 (95% CI, 0.79–0.93) (Table 4). A Kaplan Meier curve demonstrating time-related development of fever in neonates in the ASF group is presented in Supplemental Fig 3.

### Outcomes of Infants Given Antipyretics

Twelve patients afebrile on presentation were excluded from the primary analysis due to antipyretics before arrival. Of these, 7 of 12 (58.3%) developed a fever during subsequent hospitalization. Median time to fever was 5.2 hours (IQR, 4.5–7.0). Of these patients, 1 infant was diagnosed with *Escherichia coli* UTI and bacteremia.

## DISCUSSION

We investigated the risk of SBI and IBI in neonates who were afebrile on presentation to the ED on the basis or presence or absence of fever during hospitalization. Neonates with historical fever and who remained afebrile had lower odds of SBI. Infants who were initially afebrile but who developed a fever during hospitalization had higher odds of SBI. Rates of IBI between the groups were not statistically different. One-fourth of afebrile neonates with historic fever developed a fever during hospitalization. Findings from this study suggest that a subset of initially afebrile infants tested for SBI who remain afebrile may be candidates for earlier discharge after a shorter observation period.



**FIGURE 1** Study patient inclusion. <sup>a</sup> Patients' outcomes reported as a secondary analysis.

**TABLE 1** Demographics, Laboratory Values, and Hospitalization Characteristics From Included Patients in Study Subgroups

Patient Demographics	ANF Group	P <sup>a</sup>	ASF Group	P <sup>a</sup>	FP Group
No.	278	—	93	—	560
No. males (%)	153 (55.0)	.86	51 (54.8)	.99	303 (54.1)
Mean age, d ± SD	17.9 ± 7.6	.30	20.8 ± 7.3	.22	18.9 ± 7.2
Race		.23		.55	
White	210 (75.5)		68 (73.1)		414 (73.9)
African American	45 (16.2)		21 (22.6)		105 (18.8)
Other	7 (2.5)		3 (3.2)		22 (3.9)
Unknown	16 (5.8)		1 (1.1)		19 (3.4)
Ethnicity		.22		.60	
Hispanic/Latino	6 (2.2)		2 (2.2)		6 (1.1)
Not Hispanic/Latino	225 (80.9)		80 (86.0)		476 (85.0)
Not stated	47 (16.9)		11 (11.8)		78 (13.9)
Historical characteristics					
Term gestation		.08		.29	
≥36 wk	273 (98.2)		91 (97.8)		556 (99.3)
<36 wk	4 (1.4)		1 (1.1)		1 (0.2)
Not stated	1 (0.4)		1 (1.1)		3 (0.5)
Laboratory characteristics					
Median white blood cell count, 10 <sup>9</sup> /L (IQR)	11.3 (9.5–13.9)	<.001	11.0 (8.6–14.0)	.26	10.4 (7.4–14.1)
Median absolute neutrophil count, 10 <sup>9</sup> /L (IQR)	3.46 (2.28–4.90)	<.001	4.22 (3.01–6.44)	.88	4.42 (2.77–6.91)
Median absolute band count, 10 <sup>9</sup> /L (IQR)	0.00 (0.00–0.20)	<.001	0.30 (0.00–0.7)	.90	0.29 (0.06–0.83)
Hours to positive preliminary blood culture results (IQR)	20.2 (19.3–23.9)	.81	16.7 (13.8–19.0)	.14	20.2 (16.4–25.8)
Time characteristics					
Median time difference between temperature assessments, min (IQR)	240 (202–300)	<.001	240 (178–277)	.004	240 (150–284)
Median No. temperature assessments per patient (IQR)	11 (8–14)	<.001	14 (11–17)	.40	14 (11–18)
No. temperatures measured as rectal (%)	2002/3226 (62.1)	.02	1046/1457 (71.8)	<.001	6643/11 134 (59.7)
Hospitalization data					
Median length of stay, h (IQR)	43.0 (33.5–51.1)	<.001	47.4 (42.6–61.0)	.87	47.5 (40.3–62.2)
Given antibiotics	210 (75.5)	<.001	77 (82.8)	.41	485 (86.6)

—, not applicable.

<sup>a</sup> Pairwise comparisons (between the ANF group and FP group and between the ASF group and FP group) by  $\chi^2$  or Wilcoxon rank sum tests as appropriate.

The majority of research evaluating SBI in infants presenting with only history of fever has been limited to the initial assessed temperature. Whether these infants are at the same risk of SBI as those who have a measured fever at presentation remains controversial. Although in several earlier studies suggest that the rate of SBI in this population is lower compared with their febrile counterparts,<sup>14,15</sup> recent studies with larger populations have suggested that the rates of SBI in this group may not be substantially reduced.<sup>12,13</sup> The findings from these studies suggest that initial temperature in infants with a reported history of fever is not adequate to determine which infants require evaluation for an SBI.

In contrast, little has been reported on the outcomes of afebrile neonates after hospital admission. In 1990, Bonadio et al<sup>16</sup> reported on 244

infants <60 days of age who presented with a reported fever measured rectally. Of 40 patients without a fever on initial vital signs, 8 (20%) developed a fever after subsequent admission, similar to the figure reported in our study. Rates of SBI among those who remained afebrile through the course of their hospitalization were not reported in this study.<sup>16</sup> The results of our study, using a large cohort of consecutive patients and analyzing only neonates who are at higher risk of SBIs, suggest that the subpopulation of neonates who are only historically febrile and who remain euthermic have lower odds of SBI as compared with those with a measured fever during their hospitalization.

Based on the results from this and other studies evaluating rates of SBI on the basis of fever at time of ED presentation,<sup>12,13</sup> we do not advocate

for decreased testing in afebrile infants with history of fever only. Given we found that a substantial proportion of initially afebrile infants ultimately were diagnosed with an SBI, a prolonged period of observation of these infants without testing or empirical antimicrobial treatment may result in missed or delayed treatment of infections. However, in the select population of infants who are low risk based on initial laboratory evaluation and persistently afebrile after a longer period of observation, our findings suggest that these infants may be candidates for discharge before 24 hours. This is particularly pertinent because the majority of preliminary culture results are available by this time. In our study, the median time to positive culture results in infants in the ANF group was 20.2 hours. These times to positive culture results are generally

**TABLE 2** Types of SBI and IBI Identified in Patient Population Divided Into 3 Groups

Group	Notes
Group 1: ANF group (n = 278)	
No. SBI (%)	13 of 278 (4.7)
No. IBI (%)	5 of 278 (1.8)
UTI	<i>E coli</i> (3), <i>Klebsiella pneumoniae</i> (1), group B <i>Streptococcus</i> (1), <i>Escherichia Fergusonii</i> (1), <i>Enterococcus faecalis</i> (1), <i>Enterbacter cloacae</i> (1)
Bacteremia	<i>Staphylococcus aureus</i> (2), <i>Acinetobacter anitratus</i> (1)
Meningitis	<i>E coli</i> (1), <i>E faecalis</i> (1)
Group 2: ASF group (n = 93)	
No. SBI (%)	17 of 93 (18.3)
No. IBI (%)	4 of 93 (4.3)
UTIs	<i>E coli</i> (6), <i>E faecalis</i> (3), <i>K pneumoniae</i> (2), group B <i>Streptococcus</i> (1), <i>E cloacae</i> (1)
Bacteremia	Group B <i>Streptococcus</i> (2)
Multiple	<i>E coli</i> bacteremia and UTI (2)
Group 3: FP group (n = 560)	
No. SBI (%)	58 of 560 (10.4)
No. IBI (%)	19 of 560 (3.4)
UTI	<i>E coli</i> (30), group B <i>Streptococcus</i> (2), <i>Klebsiella oxytoca</i> (2), <i>S aureus</i> (1), <i>Citrobacter freundii</i> (1), <i>E cloacae</i> (1), <i>E faecalis</i> (1), <i>K pneumoniae</i> (1)
Bacteremia	Group B <i>Streptococcus</i> (4), <i>Acinetobacter Iwoff/johnsonii</i> (1), <i>Enterococcus faecium</i> (1), <i>S aureus</i> (1), <i>Streptococcus mitis</i> (1), <i>Moraxella catarrhalis</i> (1), <i>Streptococci, β hemolytic</i> , not group A, B, C, F or G (1)
Meningitis	<i>E coli</i> (1)
Multiple	<i>E coli</i> bacteremia and UTI (6), <i>E coli</i> bacteremia and meningitis (1), <i>Haemophilus influenzae</i> bacteremia and meningitis (1)

consistent with data from multicenter studies.<sup>10</sup> Therefore, the critical events that would increase the risk of bacterial infection (a positive culture or development of fever) would be expected to occur within the 24-hour observation time period. Of those afebrile infants that developed fever, the majority did so within 6 hours, and by 24 hours this figure approached 90%. Management decisions must also take into consideration the statistically higher rate of SBI in infants initially euthermic at presentation but who developed fever during admission. The decision to discharge after a period of observation must therefore take into consideration the clinical appearance of the child, the total time the infant remained

afebrile, any preliminary positive culture results, the provision of empirical antibiotics before discharge, and the ability of the treating physician to reach the caregiver in the event of a positive result.

The results of this study are subject to limitations of retrospective chart review. The decision to perform testing for SBI was at the discretion of the treating provider, and therefore some afebrile infants may have not been evaluated disproportionately on this basis. However, rates of afebrile infants and febrile infants from this study are similar to the 2 previously mentioned large studies evaluating outcomes in these groups.<sup>12,13</sup> In our institution, the management of febrile

neonates is driven by a practice guideline that requires blood, urine, and CSF testing for all infants ≤28 days old with a fever (historical or documented). Although some infants may not have received any testing, this would have been a rare event. Incomplete testing was probably not a significant limitation: of 156 infants excluded for this reason, only 19 would have otherwise met inclusion criteria (2% of the included cohort). Although we were unable to report on the outcomes of patients who did not receive any testing for SBI, rates of SBI in this study are similar to those presented in other studies, suggesting that this was not a major confounder.<sup>1-3</sup> The effect of antimicrobial therapy on subsequent fever development is a potential confounder, although we found that greater numbers of patients who were febrile received antibiotics. Because there is no consensus method to identify if a true pathogen is causative or merely associated with fever, we were unable to confirm if a suspected true-positive pathogen was causative of fever for patients. Additionally, although initial

**TABLE 3** OR, 95% CIs, and P Value of SBI and IBI of Infants (1) Infants ANF and (2) Infants ASF Compared With Infants FP

	SBI		IBI	
	OR (95% CI)	P	OR (95% CI)	P
ANF group	0.42 (0.23–0.79)	.006	0.52 (0.19–1.51)	.20
ASF group	1.93 (1.07–3.50)	.03	1.28 (0.43–3.85)	.66
FP group	Reference	—	Reference	—

—, not applicable.

**TABLE 4** Summarization of Time-To-Event Analysis Statistics of 93 Neonates in the ASF Subgroup

Time (h)	Number at Risk for Fever	Total Number With Fever (%)	95% CI
0	93	0 (0.0)	n/a
6	45	49 (52.7)	41.4–61.8
12	22	71 (76.3)	65.9–83.6
18	13	80 (86.0)	76.9–91.6
24	11	82 (88.2)	79.4–93.2
30	8	85 (91.4)	83.3–95.6
36	0	93 (100.0)	n/a

n/a, not applicable.

temperatures obtained in the ED are always obtained by rectal temperature, serial measurements were conducted with a combination of rectal or axillary temperature measurements. Finally, although infants afebrile at the time of culture collection are hypothesized to have a greater proportion of false-negative results, this remains unestablished.<sup>23</sup>

## CONCLUSIONS

Afebrile neonates with historical fever only who remain afebrile during hospitalization are at lower odds of SBI compared with those with a fever at presentation. Infants who develop a fever have higher odds of SBI. Rates of IBI were similar between groups. One-fourth of neonates with a history of fever but afebrile on presentation

to the ED developed a fever during their hospitalization. Infants with history of fever alone who remain afebrile after an observation period may be candidates for earlier hospital discharge.

## ABBREVIATIONS

ANF: afebrile with no subsequent fever  
 ASF: afebrile with subsequent fever  
 CI: confidence interval  
 CSF: cerebrospinal fluid  
 ED: emergency department  
 EMR: electronic medical record  
 FP: febrile at presentation  
 IBI: invasive bacterial infection  
 OR: odds ratio  
 SBI: serious bacterial infection  
 UTI: urinary tract infection

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