Outcome of Febrile Infants ≤3 Months of Age Admitted to the Emergency Department of a Belgian Tertiary Pediatric Hospital

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Keywords

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Abstract

Background: Fever in infants under 3 months of age is a frequent cause for visits to the pediatric emergency department. Most children present with fever without a source and undergo multiple medical examinations to rule out serious bacterial infection (SBI), which often results in hospitalization. This study aimed to document fever outcomes in newborns and infants under 3 months old based on hospitalization data. The goal was to find a prediction rule that would enable healthcare professionals to identify febrile infants at risk for SBI.

Methods: A single-center retrospective study was conducted, covering the period from January 2016 to December 2022. In total, 150 infants aged up to 3 months old were admitted for fever without a source at the emergency department of Cliniques Universitaires Saint-Luc in Brussels, Belgium. The patient's medical history, clinical presentation, and complementary test results were analyzed to identify predictors of SBI.

Results: The results showed a significant increase in C-reactive protein levels (CRP=12.8mg/L in SBI cases; 5.5mg/L in viral infection cases, p-value=0.04) and neutrophil numbers in BI cases in children under 4 weeks old. No anamnestic or clinical factors were found to effectively differentiate febrile children aged less than 3 months at risk of developing SBI.

Conclusion: Further investigations are necessary to identify infants at risk for SBI using new biological parameters, including procalcitonin levels. The management protocol for these children must be re-evaluated to determine which complementary tests should be performed, whether hospitalization is necessary, and which patients are eligible for admission.

Introduction

Fever in infants, defined as a rectal temperature ≥38°C, is a common reason for Emergency Department (ED) visits in infants under 3 months old (1–3). These patients often present with fever without a clear diagnosis despite medical history, physical exams, and blood tests, resulting in a diagnosis of fever without a source (FWS). Infants in this age group are at a higher risk of serious bacterial infection (SBI), due to perinatal exposure and limited immunity compared to older children (4–7).

Differentiating simple viral infections (VI) from SBI based solely on medical history and clinical criteria is challenging. The main cause of SBI is urinary tract infections (UTI), while instances of meningitis and bacteremia have markedly declined over the past three decades due to herd immunity from vaccination (6). However, it is important to keep in mind that these conditions can be life-threatening (8,9). This challenge often results in additional tests, empirical antibiotics, and preventive hospitalizations. Therefore, it is critical to strike a balance between minimizing risks for patients and managing the time and costs of testing (10).

Although algorithms exist to differentiate between low- and high-risk infants, their inconsistent use in practice leads to unnecessary hospitalizations and procedures (3,11–15). Many febrile infants under three months are hospitalized to rule out SBI, resulting in discharges without a definite diagnosis (i.e., probable viral infections (VI)). Invasive investigations and antibiotics are frequently initiated in all infants, even those without SBI, potentially increasing the risk of adverse effects, complications, and antibiotic resistance(16,17).

Therefore, it is crucial to evaluate the usefulness of a panel of complementary tests in febrile infants and establish an optimal management strategy. This descriptive retrospective study aims to document the outcomes of infants under 3 months who were admitted for fever without a source (FWS) at the emergency department (ED) of Cliniques Universitaires Saint-Luc in Brussels. The objective is to identify clinical or biological markers that can predict SBI in order to reduce unnecessary tests, antibiotic use, and hospitalizations for low-risk infants. Management and diagnostic procedures in infants under 3 months were assessed, and their characteristics and clinical presentations at ED admission were compared to enhance care quality and cost-effectiveness.

Methods

Study design and settings

This is a retrospective, descriptive, single-center study that utilized historical data collected from the medical records of pediatric patients aged 0 to 3 months who presented with a rectal temperature of ≥38°C, as reported by their caregiver, at the pediatric ED of Cliniques Universitaires Saint-Luc clinics, a Belgian tertiary hospital, from January 2016 to December 2022. The exclusion criteria for this study included a known diagnosis at admission that could account for the presence of fever, prior hospitalization in neonatal or pediatric intensive care units, and comorbidities predisposing to increased infection risks, such as cancer, primary or secondary immunosuppression, extreme prematurity (i.e., less than 28 weeks of gestation), congenital heart disease, or asplenia (18). Only children who had been hospitalized were considered for this study. The hospital's ethics committee (ethics committee of Cliniques Universitaires Saint-Luc, N° 2023/02MARS/11) approved the study. Informed consent was not required due to the study's retrospective design.

For assessment purposes, patients were categorized into subgroups based on age and infection type. The subgroups included newborns under

4 weeks old, young infants aged 1 to 3 months old, and infections caused by either viruses or bacteria (19). According to our in-house guidelines, the management of fever in infants under 4 weeks old should include a full septic work-up, including systematic blood analysis such as a full blood count and CRP. For patients under 1 month old, physicians perform a series of tests including blood cultures, urinalysis (clean-catch, urinary catheterization or suprapubic puncture), and lumbar punctures (LP). For patients between 1 and 3 months old, physicians only perform a LP based on biological criteria (WBC >15 000/mm^3, WBC <500/mm^3 and/or CRP >40mg/L), as well as the infant's clinical assessment and general condition (i.e., sepsis or clinical signs suggestive of meningitis such as irritability or bulging anterior fontanel) (20). The threshold for determining positivity in urine culture varies depending on the method employed. For bags or clean-catch, the threshold is greater than 100,000 CFU. For urinary catheterization, the threshold is greater than 50,000 CFU. For suprapubic punctures, the detection of more than one germ is necessary.

All data were collected in a secure Excel document restricted to authorized personnel only. The data collected included obstetrical and neonatal history, such as intrapartum infection, premature rupture of membranes, vaginal smear results for group B *Streptococcus*, delivery route, birth weight and height, and prenatal jaundice. Patient characteristics, such as gender, age, and comorbidity, were also recorded, along with presenting symptoms at admission, duration and degree of fever, diagnostic test results, and antimicrobial treatments administered, including antibiotic or antiviral therapy. Hospitalization and rehospitalization within 30 days were also noted.

Table 1: Description of the total population.

	N=150
Age (mean [SD]), w	4.9 [2.5]
Fever duration (median [IQR]), h	8.00 [2.00; 24.00]
Peak fever (median [IQR]), °C	38.50 [38.20; 39.00]
Comorbidities, n/N (%)	14/150 (9,3)
Heart disease	2/150 (1,3)
Endocrinological problem	1/150 (0,67)
Uro-nephrologic pathology	4/150 (2,66)
Digestive disorder	3/150 (2)
Hematological pathology	3/150 (2)
ENT disorder	1/150 (0,67)
No comorbidities, n/N (%)	136/150 (90,7)
Symptoms beyond fever, n/N (%)	
Rhinitis	46/150 (30,7)
Cough	38/150 (25,3)
Skin rash	23/150 (15,3)
Diarrhea	27/150 (18)
Vomiting	18/150 (12)
Abdominal pain	25/150 (16,7)
Decreased appetite	52/150 (34,7)
No other symptoms, n/N (%)	23/150 (15.3)
Good general condition, n/N (%)	87/150 (58)
Notion of contagion, n/N (%)	92/150 (61,3)
Blood biology (CRP, WBC, neutrophil), n/N (%)	148/150 (98.7)
Urine analysis, n/N (%)	138/150 (92)
Nasal swab, n/N (%)	124/150 (82.7)
LP, n/N (%)	62/150 (41.3)
Antibiotic administration, n/N (%)	85/150 (56.7)

Numbers of individuals within the overall population exhibiting diverse study parameters, encompassing epidemiological characteristics, complementary tests, and initial therapeutic management

(w=weeks; h=hours; CRP=C-reactive protein; WBC=white blood cells; SD=standard deviation).

Statistical analysis

The study presented demographic and clinical data using standard statistical measures. Continuous variables were expressed as mean ± standard deviation, non-continuous variables as median followed by interquartile range, and categorical variables as numbers and proportions. Linear regression was used for continuous variables. Normality was tested using the Shapiro-Wilk test, and depending on the distribution of the variables, either a Student's t-test or Wilcoxon test was performed for continuous or categorical variables, respectively. The Pearson's chi-squared test was used to analyze the associations between categorical variables. Our research team conducted all statistical analyses using R software (R. Coreteam 2021). A significance level of 5% was set for all analyses.

Results

Analysis of the whole cohort

A total of 150 individual ED attendances were recorded during the study period. Table 1 summarizes the epidemiological characteristics, complementary tests, and initial therapeutic management. The mean age of the children was 4.9 weeks, and all presented with FWS for less than 24 hours. Blood testing was performed in 98.7% of cases, while urinalysis and nasal swab were performed in 92% and 82.7% of cases, respectively, regardless of the children's age. In the study, 41.3% of infants underwent LP, and 56.7% received intravenous antibiotics.

The study population was divided into two subgroups based on infection type: viral or bacterial. Of the total population, 17 cases of SBI were identified (11.3%), with eight cases in infants under four weeks old and nine cases in infants between one and three months old. The remaining 133 infants had VI (see Figure 1).

Of the infants diagnosed with SBI, 47% were male and 53% were female. In our cohort, UTI was the primary cause of SBI, accounting for 50% of infected cases in children under four weeks old, compared to 77% in the older subgroup. The most frequently identified pathogens were: *Klebsiella pneumoniae* (33%), *Pseudomonas aeruginosa* (16,7%), *Escherichia coli* (16,7%), *Citrobacter koseri* (16,7%), and *Enterococcus faecalis* (16,7%).

Regarding the complementary laboratory tests performed, the median CRP level (7.00mg/l [1.50; 12.60]) and the urine white blood cell count (WBC) (26.00 x10^3/µL [8.00; 116.00]) were higher in bacterial than viral diseases (1.20mg/l [0.80; 5.00] and 4.00 x10^3/µL [1.50; 14.00], respectively), with statistically significant between-group differences (Table 2).

Our analysis revealed that rehospitalizations were more common within 30 days in SBI cases than in VI cases. Overall, the clinical presentation upon ED admission was quite similar between both groups, without any real between-group differences noted. In terms of contagion, 53% of patients were in the SBI group and 62.4% were in the VI group (p-value 0.26). In summary, no statistically significant clinical or anamnestic criteria were found to predict patients at high risk of developing SBI.

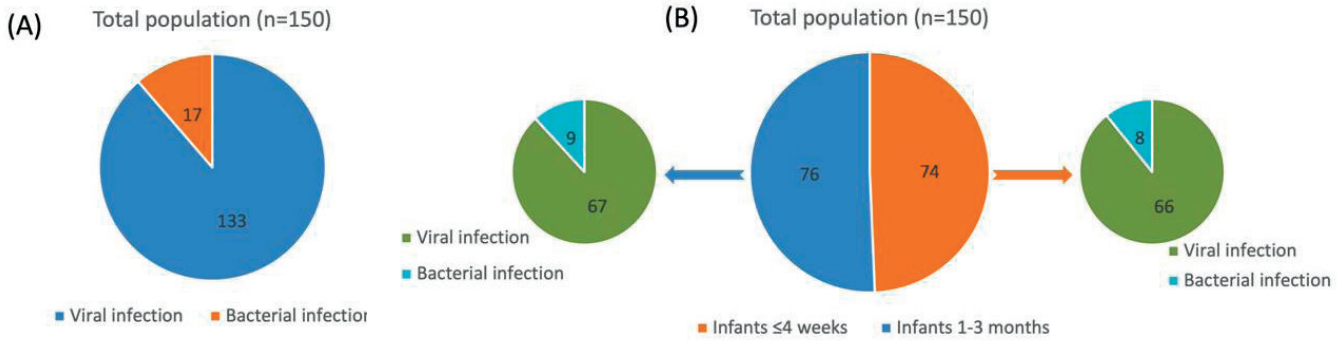
Subgroups of infants less than four weeks old based on infection type

In the second step, the study population was divided into two subgroups based on age: 74 infants under four weeks old and 76 between 1 and 3 months old (see to Figure 1 and Table 3). Children less than 4 weeks old accounted for 49% of our sample, of which 10.8% were diagnosed with SBI. In over half of the cases, no clinical symptoms other than fever were present upon ED admission. However, infants with SBI had a higher CRP level (10.45mg/L in SBI vs. 1.00mg/L in VI, p-value=0.004) and a higher neutrophil count (47.75 x10^3/µL in SBI vs. 31.90 x10^3/µL in VI, p-value=0.02) upon ED admission (Table 3).

Figure 1: Distribution of study population groups

(A) Pie chart depicting the distribution of diagnosed infections among patients admitted at ED for FWS within the study population.

(B) Nested diagram representing the distribution of the study population according to age, then according to the diagnosis made following their emergency admissions for FWS.



As LP is a standard part of the management protocol for febrile infants under 4 weeks old, it was routinely performed in these cases (21). Yet, no difference were noted in the results from LP in terms of neutrophil numbers, protein levels, and glucose levels between VI versus SBI.

Subgroups of infants between one and three months old based on infection type

Children aged from one to three months represented 51% of our sample, including 11.8% diagnosed with SBI. Compared to younger children, no statistically significant differences in CRP levels (3.60mg/L in SBI vs. 1.60mg/L in VI, p-value=0.36), WBC counts (10.77 x103/µL in SBI vs. 9.26 x103/µL, p-value=0.25), and neutrophil numbers (37.00 $x10^3$/µL in SBI vs. 31.20 $x10^3$/µL, p-value=0.62) were observed (Table 3). When LP was performed, a higher protein level was found in VI cases (45.50mg/dL in VI vs. 25.00mg/dL in SBI, p-value=0.03). However, none of the studied parameters were able to predict SBI.

Discussion

This retrospective study evaluated the management and outcome of infants less than three months old admitted for FWS at the ED of a Belgian tertiary care pediatric hospital. Overall, 11.3% of the children exhibited a SBI, which is consistent with published data reporting SBI rates reported ranging from 5 to 15% (6,22,23). This number is rather relevant and helps to understand the practice of conducting routine complementary tests in young febrile infants . As previously mentioned, UTI was the primary cause of SBI. However, urine was mostly collected using an Urinocol collection bag or via the midstream technique. Sample contamination resulting in a false diagnosis cannot be excluded. Therefore it is important to search for UTI in a sterile manner, using urinary catheterization or suprapubic puncture.

Our study aimed to identify biomarkers that can predict low-risk SBI patients. We analyzed thoroughly anamnestic, clinical, and biological criteria, as currently applied at Cliniques Universitaires Saint-Luc. However, we were unable to reliably identify children at low-risk of SBI who could be discharged without close monitoring and empirical antibiotics, thereby saving time and costs. The clinical presentations of the two groups, SBI and VI, on ED admission were similar. Children with SBI did not exhibit altered general conditions or states of shock more commonly than those with VI. Accurate diagnosis was complicated as those with simple VI could also be irritable upon febrile peaks. It is worth noting that febrile children under 3 months old tended to visit the emergency department more frequently within the first 24 hours of fever onset, allowing for better follow-up regarding disease progression. Surprisingly, lumbar puncture was only performed in 55% of infants under 4 weeks old. This figure is unexpected, as most international guidelines recommend lumbar puncture in febrile infants under four weeks old (21). This may be due to the clinical presentation and the decision to monitor with hospitalization. In literature reports, cerebrospinal fluid

Table 2: Baseline characteristics of patients, stratified by the type of infection.

	VI (N=133)	BI (N=17)	p-value
Terms, weeks of pregnancy	39.00 [38.00; 40.00]	39.00 [38.00; 40.00]	0.75[b]
BH, cm	49.89 ± 2.26	48.92 ± 0.79	0.0036[a]
BW, kg	3.3 ± 0.47	3.14 ± 0.43	0.2 [a]
BMI	14.55 ± 1.7	14.42 ± 1.27	0.82 [a]
HC, cm	34.66 ± 1.56	34.5 ± 1.14	0.64 [a]
Age, w	5.0 [3.0; 7.0]	5.00 [3.00; 8.00]	0.4 [b]
CW, kg	4.36 [3.85; 4.70]	4.08 [3.70; 5.10]	0.97 [b]
CH, cm	54.49 ± 3.23	53.83 ± 3.42	0.60 [a]
CHC, cm	37.13 ± 1.82	37.45 ± 1.67	0.63 [a]
Fever duration, h	8.00 [2.00; 24.00]	9.00 [3.50; 24.00]	0.60 [b]
Fever peak, C°	38.50 [38.20; 38.90]	38.50 [38.20; 39.00]	0.66 [b]
CRP level, mg/L	1.20 [0.80; 5.00]	7.00 [1.50; 12.60]	0.0057 [b]
WBC, $x10^3$/µL	8.94 [6.63; 12.90]	9.98 [5.81; 10.83]	0.95 [b]
Neutrophils, $x10^3$/µL	31.50 [25.20; 42.80]	41.30 [30.60; 49.70]	0.036 [b]
Lymphocytes, $x10^3$/µL	45.24 ± 17.19	41.52 ± 14.85	0.35 [a]
Urine WBC, $x10^3$/µL	4.00 [1.50; 14.00]	26.00 [8.00; 116.00]	0.0020 [b]
LP WBC, $x10^3$/µL	6.00 [4.00; 14.00] (N=54)	4.50 [4.00; 12.20] (N=8)	0.57 [b]
LP neutrophils, %	0 [0; 27] (N=54)	16.50 [0.00; 33.75] (N=8)	0.75 [b]
LP proteins, mg/dl	54.50 [43.50; 72.75] (N=54)	44.70 [34.75; 51.75] (N=8)	0.076 [b]
LP glucose, mg/dl	57.30 ± 7.9 (N=54)	58.88 ± 12.37 (N=8)	0.74 [a]
Hospitalization duration, d	2.00 [2.00; 3.00]	2.00 [2.00; 3.00]	0.76 [b]
Antibiotic therapy duration, h	48.00 [48.00; 48.00] (N=71)	42.00 [24.00; 66.00] (N=14)	0.18 [b]
Rehospitalization within 30 days, %	8.3 (N=11)	29.4 (N=5)	0.007[c]

BH=Body height at birth; BW=Body weight at birth; BMI=Body mass index; HC=Head circumference; CW=Current weight; CH=Current height; CHC=Current head circumference; CRP= C-reactive protein; LP=Lumbar puncture; WBC=White blood cells; SD=Standard deviation; d=Days; h=Hours; w=Weeks

[a] Student's t-test, [b] Wilcoxon test, and [c] Pearson's chi-squared test were performed.

Table 3: Characteristics of patients and statistical analysis stratified by both age groups and the type of infection within the study population

	INFANTS ≤ 4 WEEKS			INFANTS AGED 1-3 MONTHS		
	VI (N=66)	BI (N=8)	p-value	VI (N=67)	BI (N=9)	p-value
Terms, weeks of pregnancy	39.00 [38.00; 40.00]	38.50 [38.00; 39.00]	0.14 [b]	39.00 [38.00; 40.00]	40.00 [39.00; 40.00]	0.06 [b]
BH, cm	50.09 ± 2.01	48.40 ± 0.54	0.0002 [a]	49.81 ± 2.54	49.29 ± 0.75	0.27 [a]
BW, kg	3.35 ± 0 .48	3.08 ± 0.26	0.04 [b]	3.25 ± 0.46	3.20 ± 0.54	0.82 [a]
BMI	14.41 ± 1.74	14.19 ± 1.37	0.79 [a]	14.70 ± 1.67	14.74 ± 1.33	0.96 [a]
HC, cm	35.00 [34.00; 36.00]	34.50 [34.00; 35.00]	0.36 [b]	34.34 [33.00; 36.00]	34.50 [34.00; 35.75]	0.72 [a]
Age, w	3.00 [3.62; 4.45]	3.00 [2.00; 4.00]	0.80 [b]	7.00 [5.50; 8.00]	8.00 [6.00; 10.00]	0.11 [b]
CW, kg	4.04 ± 0.56	3.53 ± 0.51	0.03 [a]	4.69 ± 0.744	5.07 ± 0.58	0.08 [b]
CH, cm	53.26 ± 2.79	49.75 ± 0.35	0.000009 [a]	55.89 ± 3.15	55.0 ± 2.9	0.49 [a]
CHC, cm	36.32 ± 1.34	35.67 ± 0.29	0.03 [a]	38.47 ± 1.73	38.52 ± 1.01	0.94 [a]
Fever duration, h	4.50 [2.25; 24.00]	14.00 [5.00; 21.00]	0.63 [b]	12.00 [2.00; 24.00]	7.50 [3.25; 36.00]	0.84 [b]
Fever peak, C°	38.40 [38.10; 38.70]	38.45 [38.35; 38.77]	0.28 [b]	38.60 [38.20; 39.00]	38.70 [38.00; 39.00]	0.77 [b]
CRP level, mg/L	1.00 [0.50; 4.67]	10.45 [6.35; 19.32]	0.004 [b]	1.60 [0.95; 5.00]	3.60 [1.00; 7.00]	0.36 [b]
WBC, x10^3/µL	8.67 [6.95; 12.92]	8.62 [4.75; 10.43]	0.28 [b]	9.26 [5.51; 11.88]	10.77 [7.32; 17.95]	0.25 [b]
Neutrophils, x10^3/µL	31.90 [24.93; 40.77]	47.75 [40.35; 66.12]	0.02 [b]	31.20 [25.50; 42.80]	37.00 [30.00; 41.30]	0.62 [a]
Lymphocytes, x10^3/µL	43.24 ± 17.92	34.21 ± 14.11	0.13 [a]	47.21 ± 16.33	48.01 ± 12.88	0.87 [a]
Urine WBC, x10^3/µL	3.00 [1.75; 11.00]	26.00 [6.50; 112.50]	0.03 [b]	7.00 [1.50; 14.50]	21.00 [12.00; 100.50]	0.03 [b]
LP WBC, x10^3/µL	6.00 [3.50; 21.00] (N=36)	4.00 [4.00; 12.00] (N=5)	0.63 [b]	5.00 [4.25; 7.50] (N=18)	5.0 [4.00; 13.50] (N=3)	0.58 [a]
LP neutrophils, %	1.00 [0.00; 44.00] (N=36)	0.00 [0.00; 30.50] (N=5)	0.81 [b]	0.00 [0.00; 17.00] (N=18)	33.00 [16.50; 33.50] (N=3)	0.37 [b]
LP proteins, mg/dl	58.00 [46.50; 84.25] (N=36)	49.00 [46.00; 60.00] (N=5)	0.42 [b]	45.50 [39.00; 67.25] (N=18)	25.00 [23.00; 31.50] (N=3)	0.03 [b]
LP glucose, mg/dl	55.91 ± 8.16 (N=36)	53.80 ± 8.04 (N=5)	0.60 [a]	59.65 ± 7.01 (N=18)	67.33 ± 15.31 (N=3)	0.48 [a]
Hospitalization duration, d	2.00 [2.00; 3.00]	3.00 [2.00; 3.50]	0.20 [b]	2.00 [1.00; 3.00]	2.00 [1.00; 2.00]	0.60 [b]
Antibiotic therapy duration, h	48.00 [48.00; 48.00] (N=49)	48.00 [36.00; 84.00] (N=8)	0.94 [b]	48.00 [48.00; 48.00] (N=22)	24.00 [24.00; 42.00] (N=6)	0.06 [b]

BH=Body height at birth; BW= Body weight at birth; BMI=Body Mass Index; HC=Head circumference; CW=Current weight; CH=Current height; CHC=Current head circumference; CRP= C-reactive protein; LP= Lumbar puncture; WBC=White blood cells; SD=Standard deviation; d=Days; h=Hours; w=Weeks

[a] Student's t-test and [b] Wilcoxon test were performed.

protein levels are typically higher in cases of suspected SBI than in cases of viral infection (24,25). However, in our study, when LP was performed on children between one and three months old, the protein level was surprisingly higher in VI than SBI. One possible explanation for this inconsistency could be attributed to the limited sample size of the SBI group.

This limited understanding of fever etiology also applies to the biological field. The C-reactive protein (CRP), an inflammatory marker measured during the initial biological work-up, is often normal or only slightly increased, which can lead to false reassurance. Although CRP levels were higher in cases of SBI in children under four weeks old, we also observed that fever duration was longer in this subgroup, suggesting a potential bias. The addition of a procalcitonin assay to the management protocol would have been appropriate. This biomarker has been shown to display more rapid kinetics than CRP levels, making it more suitable for clinicians (7,26). Additionally, it is worth noting that the procalcitonin assay is included in the 'Step-by-Step' algorithm developed by a European group of pediatric emergency physicians (14). The goal was to accurately identify febrile infants at low-risk of SBI, who could thus be discharged without any LP or empirical antibiotic therapy. The initial results are promising (7,26). However, during the COVID-19 pandemic, the step-by-step approach was effective in identifying SBI but misclassified most children as high-risk, leading to unnecessary care (27).

Other biological parameters are currently being investigated to help physicians better identify children at low risk of SBI. These include polymerase chain reaction (PCR)-tested viremia or using a host-protein (BV) score based on circulating immune protein levels (18,19). Therefore, a more comprehensive approach, including the use of procalcitonin, is required.

Strengths and weaknesses

To our knowledge, this study is the first of its kind to analyze the clinical course of children under 3 months old who were admitted to the ED and subsequently hospitalized for FWS at a tertiary Belgian hospital. We consider this to be a strength of the study. The retrospective single-center design employed in this study is subject to limitations inherent to this type of study design. One such limitation is that presumed VI or SBI etiologies were only retrospectively applied. Although our study's SBI rate aligns reasonably well with published data, its relevance may be limited. Therefore, it may be challenging to draw conclusions applicable to routine practice. Additionally, we focused solely on febrile infants under 3 months old who were assessed at ED admission and subsequently hospitalized, excluding those who were discharged. We did not assess procalcitonin levels, despite its proven sensitivity in detecting bacteremia and bacterial meningitis in young febrile infants (7,26). Additionally, we identified two significant weaknesses in the supplementary tests conducted: the use

of non-sterile urine collection, primarily through the bag method, and a significant omission of lumbar puncture in almost half of febrile children under 4 weeks of age, despite guideline recommendations. It is important to note that the diagnosis of urinary tract infection was based on the recorded concluding diagnosis in patients' medical records. However, since the urinary collection method was not mentioned and threshold values differ for each type of collection method, the number of urinary tract infections in this study may have been over or underestimated.

Conclusion

The management of febrile children under 3 months of age admitted to the ED and the need to hospitalize these children for further monitoring remain a subject of debate. The implementation of new guidelines in our institution, including procalcitonin dosage, would likely be beneficial to improve the selection of children at low-risk for SBI, thereby reducing unnecessary diagnostic tests, antibiotic treatments, and hospitalizations, eventually resulting in time and cost savings. Further studies are required to assess the specific impact of algorithms such as 'Step-by-Step' or the 'Pediatric Emergency Care Applied Research Network (PECARN) rule' after their implementation (28).

Conflicts of Interest

The authors have no conflicts of interest relevant to this article to disclose.

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