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RESEARCH ARTICLE

Diagnosis of urinary tract infection in infants under 3 months with fever without a source: reliability of urinalysis and urine culture

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Abstract

Background: *Urinary tract infection (UTI) is infants' most common serious bacterial infection. This study aimed to investigate the reliability of urianalysis (UA) to predict UTI, to specify the colony forming units (CFU)/ml threshold for diagnosis, and to identify variables that help suspect bacteremia in infants under 3 months with UTI.* **Methods:** *We reviewed clinical records of children under 3 months hospitalized for a fever without source and recorded age, sex, days of fever pre-consultation, temperature and severity at admission, discharge diagnoses, laboratory tests, and treatments. According to the discharge diagnosis, we divided them into UTIs (-) and (+) with or without bacteremia.* **Results:** *A total of 467 infants were admitted: 334 with UTI and 133 without UTI. In UTIs (+), the pyuria had a sensitivity of 95.8% and bacteria (+) 88.3%; specificity was high, especially for nitrites (96.2%) and bacteria (+) (92.5%). Positive predictive value (PPV) for nitrites was 95.9%, for bacteria 96.7%, and oyuria 92.5%. Escherichia coli was present in 83.8% of urine and 87% of blood cultures. UTIs with bacteremia had inflammatory urinalysis, urine culture > 100,000 CFU/ml, and higher percentage of C reactive protein (CRP) > 50 mg (p= 0.002); 94.6% of the urine culture had > 50,000 CFU.* **Conclusions:** *The pyuria and bacteria (+) in urine obtained by catheterization predict UTI. The cut-off point for diagnosis was ≥ 50,000 CFU/ml. No variables to suspect bacteremia were identified in this study.*

Keywords: *Urinary tract infection in infants. Fever. Severe bacterial infection. Febrile infants.*

Diagnóstico de infección del tracto urinario en lactantes menores de 3 meses con fiebre sin foco identificado: fiabilidad del análisis de orina y urocultivo

Resumen

Introducción: *La infección del tracto urinario (ITU) es una infección bacteriana grave frecuente en lactantes. El objetivo de este trabajo fue investigar la fiabilidad del análisis de orina (AO) para predecirla, precisar el umbral de unidades formadoras de colonias (UFC)/ml para el diagnóstico y buscar variables que ayuden a sospechar de bacteriemia en lactantes menores de 3 meses con ITU.* **Métodos:** *Se revisaron fichas clínicas de lactantes menores de 3 meses hospitalizados por fiebre sin foco evidente, registrando edad, sexo, días de fiebre preconsulta, temperatura y gravedad al ingreso, diagnósticos de egreso, exámenes de laboratorio y tratamientos. Según diagnóstico de egreso, se separaron en ITU (-) y (+), con o sin bacteriemia.*

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Resultados: *Ingresaron 467 lactantes: 334 con ITU y 133 sin ITU. En ITU (+), la sensibilidad de la piuria fue de 95.8% y bacterias (+) 88.3%; la especificidad fue alta para nitritos (96.2%) y bacterias (+) (92.5%). El valor predictivo positivo (VPP) fue de 95.9% para nitritos, 96.7% para bacterias y 92.5% para piuria. Escherichia coli se encontró en el 83.8% de los urocultivos (UC) (+) y en el 87% de los hemocultivos (+). Las ITU con bacteriemia presentaron elementos inflamatorios, UC con ≥ 100,000 UFC/ml y mayor porcentaje de proteína C reactiva (PCR) > 50 mg/l (p= 0.002); el 94.6% de los UC (+) tuvo ≥ 50,000 UFC/ml.* **Conclusiones:** *La piuria y bacterias (+) en el AO son excelentes para pronosticar ITU en orina obtenida con sonda vesical y el punto de corte para el diagnóstico debe ser ≥ 50,000 UFC/ml. No encontramos señales que ayudaran a sospechar ITU con bacteriemia.*

Palabras clave: *Infección urinaria en lactantes. Fiebre. Infección bacteriana grave. Lactantes febriles.*

Introduction

Urinary tract infection (UTI) is common in childhood; its prevalence in infants under 3 months presenting with fever without a source (FWS) is 5-20%[1-4], with a predominance in males, especially in uncircumcised children[2,4-5].

National studies showed a prevalence of UTI of 16.4% in 550 infants under 3 months hospitalized for FWS and 18.4% in 468 newborns (NB) < 29 days. In both groups, as in other publications, UTI was the most common severe bacterial infection (SBI) (~70%)[1,2,4].

For infants under 3 months presenting to the Emergency Department (ED) with FWS, it is imperative to request a complete urinalysis (UA) and urine culture (UC)[6,7] because initiation of antibiotic treatment in cases of UTI within the first 48 to 72 hours of fever can significantly reduce the risk of renal scarring, hypertension, and chronic renal failure.

Although the diagnosis of this infection is confirmed with significant bacteriuria in the UC, UA is available within a few hours. If UA contains inflammatory elements (UAI) such as nitrites, pyuria, or bacteria, the probability of infection is high[6-17].

There is controversy in the available literature regarding the usefulness of UA for predicting UTI, with reported sensitivities of 48-99% and specificities of 88-98%[1,18-21]. In addition, there is no consensus on the threshold of colony forming units (CFU)/ml required to confirm the diagnosis in urine obtained by bladder catheterization (BCC). For the American Academy of Pediatrics (AAP) (2011 and 2016) and others[8-11,13,15] it is > 50,000 CFU/ml, but in other publications > 10,000 CFU/ml is accepted[8,22-24], accompanied by UAI. If UA is normal (UAN) and UC (+), contamination or asymptomatic bacteriuria should be suspected, and only in exceptional cases of incipient UTI[9,10].

Although UC (+) of urine obtained from a collection bag (B) is unreliable due to frequent contamination[9-11,24-27], some recommend this method for the initial screening of UTI in infants who, because of their good general condition and mild severity, do not require immediate antibiotic treatment[9,10,26]. If the UA of this sample shows inflammatory elements, the UA and UC are repeated in urine obtained by BCC or BP (bladder puncture). This strategy significantly reduces the need for these invasive methods, from 63% to less than 30% in one published study[26].

Because of the controversies on the usefulness of UA to predict UTI[2] and the CFU/ml threshold to confirm the diagnosis of UTI, we decided to conduct this analysis in a group of infants under 3 months discharged with this diagnosis from the Pediatric Service of the Hospital Clínico Roberto del Río and, secondarily, to look for general and laboratory variables that could predict the presence of bacteremia at an early stage.

Methods

For mainly descriptive purposes, a cohort of infants under 3 months consecutively admitted to the Pediatrics Service of the Hospital Clínico Roberto del Río with a diagnosis of FWS (ICD 10 R50) between 2/1/2010 and 2/28/2020 was randomly selected after approval by the Institutional Ethics Committee.

Patients were identified from the daily report of pediatric hospitalizations. The inclusion criteria were age under 3 months, fever without source > 38°C of ≤ 4 days of evolution, no history of UTI, hospitalizations, bladder catheterization, chronic diseases or antibiotic treatment in the last 10 days, and complete blood count (CBC), UA-UC in samples obtained with BCC or collector and blood culture (BC). Other tests such as C-reactive protein (CRP), ultrasound and renal scintigraphy, indirect viral immunofluorescence (IF), stool culture, and cerebrospinal fluid (CSF) were not required. The analysis was retrospective and descriptive, without a prior hypothesis. According to the discharge diagnosis, two groups were formed: UTI (+) and UTI (-).

Table 1. Infants under 3 months hospitalized for FWS, general characteristics and urinalysis

Variables n° (%)	Without UTI (n = 133)	With UTI (n = 334)	Value p*
Age (days), median (IQR)	25 (11-44)	40 (21-65)	< 0.001
Age group			
< 29 days	79 (59.4%)	129 (38.6%)	0.001
29-59 days	36 (27.1%)	102 (30.5%)	
60-89 days	18 (13.5%)	103 (30.8%)	
Sex			
Female	64 (48.1%)	78 (23.4%)	< 0.001
Male	69 (59.9%)	256 (76.7%)	
Severity at admission			
Mild	109 (94.8%)	288 (86.2%)	0.029
Moderate	6 (5.2%)	46 (13.2%)	
Temperature at admission			
< 38ºC	16 (13.8%)	29 (9.0%)	0.011
38-38.9ºC	94 (81.0%)	243 (75.5%)	
39-39.9ºC	5 (4.3%)	46 (14.3%)	
≥ 40ºC	1 (0.9%)	4 (1.2%)	
Days of hospitalization			
< 3	35 (26.3%)	11 (3.3%)	0.001
3 to 5	87 (65.4%)	153 (45.8%)	
6 to 8	8 (6.0%)	116 (34.7%)	
> 8	3 (2.3%)	54 (16.2%)	
Urine sample			
Collector	45 (33.83%)	0	0.001
Catheter	58 (43.61%)	88 (26.4%)	
Collector/catheter	30 (22.6%)	246 (73.7%)	
Nitrites			
(+)	5 (3.8%)	117 (35.0%)	0.001
(-)	128 (96.2%)	217 (65.0%)	
Bacteria			
(-)	123 (92.5%)	39 (11.7%)	0.001
(+)	7 (5.3%)	109 (30.2%)	
(++)	3 (2.30%)	101 (32.6%)	
(+++)	0	85 (25.4%)	
Leukocytes			
< 10	107 (80.5%)	13 (3.9%)	0.001
10 a 49	20 (15.0%)	26 (7.8%)	
50 a 99	3 (2.3%)	17 (5.1%)	
100 a 150	1 (0.8%)	21 (6.3%)	
151 a 200	1 (0.8%)	12 (3.6%)	
201 a 300	1 (0.8%)	22 (6.6%)	
≥ 300	0	223 (66.8%)	

p* Fisher's exact test for categorical variables. Wilcoxon-Mann-Whitney test for quantitative variables.
FWS: fever without source; IQR: interquartile range; UTI: urinary tract infection.

Table 2. Laboratory studies and cultures of infants under 3 months hospitalized for FWS

Variables n (%)	Without UTI (n = 133)	With UTI (n = 334)	PPV (95%CI)
Colony count (-)	133 (100%)	0 (0.0%)	NA
10,000	-	4 (1.2%)	
10,001 a 49,000	-	14 (4.2%)	
50,000 a 99,999	-	23 (6.9%)	
>100,000	-	293 (87.7%)	
Urine culture (-)	133 (100%)		
Urine culture (+)	0	334 (100%)	NA
Escherichia coli	-	280 (84.0%)	
Klebsiella pneumoniae	-	18 (5.4%)	
Klebsiella oxytoca	-	9 (2.7%)	
Enterococcus faecalis.	-	12 (3.6%)	
Enterobacter cloacae	-	11 (3.3%)	
Proteus mirabilis	-	4 (1.2%)	
Blood culture: (+)	0	54 (16.2%)	NA
Escherichia coli	-	47 (87.0%)	
Enterococcus faecalis.	-	3 (5.6%)	
Klebsiella pneumoniae	-	2 (3.7%)	
Klebsiella oxytoca	-	1 (1.9%)	
Enterobacter cloacae	-	1 (1.9%)	
CRP in blood (mg/l)			
<50	113 (92.60%)	173 (53.2%)	94.4 (90-97)
≥ 50	9 (7.40%)	152 (46.8%)	
Leukocytes in blood (mm^3)			
< 18,000	119 (93.00%)	233 (69.8%)	91.8 (85-96)
> 18,500	9 (7.00%)	101 (30.2%)	
Neutrophils in blood (mm^3)			
< 9,500	118 (92.20%)	223 (66.7%)	91.7 (86-95)
> 9,500	10 (7.80%)	111 (33.2%)	
Kidney US			
Normal	0	185 (56.2%)	
Altered	0	144 (43.8%)	NA

95%CI: confidence interval; CRP: C-reactive protein; FWS: fever without source; NA: not applicable; PPV: positive predictive value (+); US: ultrasound; UTI: urinary tract infect.

Table 3. Variables of 334 infants under 3 months hospitalized for FWS and discharged with a diagnosis of UTI. Comparative analysis between cases of UTI with blood culture (+) and (-)

Variables n (%)*	Blood culture		Value	PPV
	(-)	(+)	p†	(95%CI)
Nitrites				
(+)	93 (33.2)	24 (44.4)	0.121	NA
(-)	187 (66.8)	30 (55.6)		
Bacteria				
(-)	33 (11.8)	6 (11.1)	0.213	NA
(+)	89 (31.8)	12 (22.2)		
(++)	84 (30.0)	25 (46.3)		
(+++)	74 (26.4)	11 (20.5)		
Leukocytes				
< 10	11 (3.9)	2 (3.7)	0.644	NA
10 to 49	25 (8.9)	1 (1.9)		
50 to 99	14 (5.0)	3 (5.6)		
100 to 150	17 (6.1)	4 (7.4)		
151 to 200	11 (3.9)	1 (1.9)		
201 to 300	19 (6.8)	3 (5.6)		
> 300	183 (65.4)	40 (74.1)		
Nº of colonies				
10,000	4 (1.4)	0	0.021	NA
10,001 to 49,999	14 (5.0)	0		
50,000 to 99,999	23 (8.2)	0		
≥ 100,000	239 (85.4)	54 (100.0)		
Urine culture (+)	280	54	0.974	NA
Escherichia coli	233 (83.2)	47 (87.0)		
Klebsiella pneumoniae	16 (5.7)	2 (3.7)		
Klebsiella oxytoca	8 (2.9)	1 (1.9)		
Enterococcus faecalis.	9 (3.2)	3 (5.6)		
Enterobacter cloacae	10 (3.6)	1 (1.9)		
Proteus mirabilis	4 (1.4)	0 (0.0)		
CRP/blood				
< 50	156 (56.9)	17 (33.3)	0.002	22.4
≥ 50	118 (43.1)	34 (66.7)		(18.5-26.8)
Leukocytes/blood				
< 18,000	197 (70.4)	36 (66.7)	0.628	17.8
≥ 18,000	83 (29.6)	18 (33.3)		(12.5-24.8)
Neutrophils/blood				
< 9,500	187 (66.8)	36 (66.7)	1	16.2
≥ 9,500	93 (33.2)	18 (33.3)		(11.5-22.6)
Kidney US				
Normal	160 (58.2)	25 (46.3)	0.133	20.14
Abnormal	115 (41.8)	29 (53.7)		(15.9-25.1)

*Percentage of each category.
†Fisher's exact test.
95%CI: confidence interval; CRP: C-reactive protein; FWS: fever without source; NA: not applicable; PPV: positive predictive value; US: ultrasound; UTI: urinary tract infection.

We divided the children with UTI into those with BC (+) and BC (-) to compare them and identify general and laboratory variables that could help predict the presence of bacteremia early. The clinical records of the patients were reviewed, recording age, sex, days of fever before consultation, temperature, severity (estimated according to level of consciousness, environmental awareness, hydration, and type of breathing) on

Table 4. Correlation between urinary inflammatory variables and urine culture colony counts in infants under 3 months with UTI

			Colony counts			
Variables*	0 (n = 133)	10,000 (n = 4)	10,001-49,000 (n = 14)	50,000-99,000 (n = 23)	> 100,000 (n = 293)	p value†
Nitrites						< 0.001
-	96.20%	75%	100%	69.60%	63.00%	
+	3.80%	25%	0%	30.40%	37.00%	
Bacteria						< 0.001
-	92.50%	25%	42.90%	26.10%	9.20%	
+	5.30%	75%	42.90%	34.80%	28.50%	
++	2.30%	(-)	7.10%	17.40%	35.60%	
+++	(-)	(-)	7.10%	21.70%	26.80%	
Leukocytes						0.001
< 10	80.50%	0.00%	21.40%	4.30%	3.10%	
≥ 10	19.50%	100%	78.60%	95.70%	96.90%	

*Percentages of each category.
†Fisher's exact test.
UTI: urinary infection.

Table 5. Usefulness of some urinalysis and blood test variables to predict the diagnosis of UTI in infants under 3 months hospitalized for FWS

Variables*	Sensitivity	Specificity	PPV (+)	NVP (-)
Urine				
Nitrites (+)	35.03	96.24	95.9	37.1
95%CI	29.9 2-40.41	91.44-98.77	90.73-98.25	35.13-39.12
Bacteria (+)	88.32	92.48	96.72	75.93
95%CI	84.38-91.57	86.61-96.34	94.2-98.2	70.05-80.96
Leukocytes ≥ 10	96.1	80.5	92.6	89.2
95%CI	93.4-98.0	72.68-86.82	89.7-94.56	82.7--93.4
Blood				
CRP > 50mg/l	46.7	92.6	94.4	39.5
95%CI	41.2-52.4	86.5-96.6	89.9-97.0	36.8-42.3
Leukocytes ≥ 18,000	30.2	93	91.8	33.8
95%CI	25.4-35.5	87.1-96.7	85.4-95.6	31.9-35.7
Neutrophils ≥ 9,500	33.2	92.2	91.7	34.6
95%CI	28.2-38.6	86.1-96.2	85.7-95.4	32.6-36.7

*Percentage of each category.
95%CI: confidence interval; CRP: C-reactive protein; FWS: fever without source; NVP: negative predicitive value; PPV: positive predictive value; UTI: urinary tract infection.

admission to the ED and hospital, laboratory tests, procedures used to obtain urine, treatments indicated, and days of hospitalization. The information obtained was recorded in a specially designed database in an Excel spreadsheet.

For microscopic examination, we used non-centrifuged urine and leukocyte count in a Neubauer chamber, while the rest of the elements were measured with a reagent strip. We considered UAI when in the UA the following were identified: > 10 leukocytes/mm^3 (pyuria), or positive nitrites (+/+++), or positive bacteria (+/+++), and UAN when these elements were absent. We considered UC (+) when there was growth of > 10,000 CFU/ml of a uropathogenic microorganism and UC (-) when there was no bacterial growth, the count was below the pre-determined threshold, or when contaminants such as skin or genitourinary flora as coagulase-negative *Staphylococcus*, *Lactobacillus*, and *Corynebacterium* were isolated. We considered UC to be contaminated when two or more pathogens were isolated.

Table 6. Usefulness of blood tests to predict bacteremia in 344 infants under 3 months discharged from the hospital with a diagnosis of UTI

Variables	Sensitivity	Specificity	PPV	NVP
CRP > 50 mg/l	66.67	56.9	22.4	90.2
95%CI	52.1-79.2	50.8-62.9	18.5-26.8	86.0-93.3
Leukocytes > 18,000/mm^3	33.3	70.4	17.8	84.5
95%CI	21.1-47.5	64.6-75.6	12.5-24.8	81.7-87.0
Neutrophils > 9,500/mm^3	33.3	66.8	16.2	83.9
95%CI	21.1-47.5	60.9-72.3	11.4-22.6	80.9-86.5

95%CI: confidence interval; CRP: C-reactive protein; NPV: negative predictive value; PPV: positive predictive value; UTI: urinary infection.

The gold standard to confirm the diagnosis of UTI is UC (+) in urine obtained with BCC or any colony count with BP. UTI with bacteremia was identified with BC (+) to the same microorganism isolated in the UC, while it was considered without bacteremia when the BC was (-). For the statistical analysis, we used median (range) and Wilcoxon-Mann-Whitney test for quantitative variables; n (%) and Fisher's exact test for categorical variables or χ^2. Univariate and multivariate logistic regression was used to search for laboratory variables predictive of bacteremia.

Results

One thousand two hundred fifty infants with FWS under three months met the inclusion criteria. The sample included the 334 infants discharged with a diagnosis of UTI and 133 infants randomly selected without UTI as controls. From the group of infants with UTI, 54/334 (16.2%) had bacteremia and 129/334 (38.6%) were less than 29 days old; of these, 5.4% were between 4 and 6 days old.

Table 1 shows the general characteristics of infants with UTI and controls, all with UA and UC. In comparison, infants in the UTI group were found to be significantly ($p < 0.001$) older than controls, and there was a higher proportion of males. Also, more infants with UTI of moderate severity, temperature > 39°C, and frequency of nitrites (+), pyuria, or bacteria (+) were detected in the UA. In the control group, 3.8% had nitrite (+), 7.5% had bacteria (+), and 19.5% had pyuria, but this frequency decreased to 4.5% as the leukocyte threshold increased to > 50/mm^3. All children with UAI in specimens collected with the collector required another UA and UC in urine collected with BCC.

Table 2 shows the comparison of laboratory variables such as US, CRP, leukocytes, and neutrophils in febrile patients with and without UTI; the differences between groups are significant ($p < 0.001$). In the group with UTI, we observed a higher percentage of CRP > 50 mg/l: 152/161, positive predictive value (PPV): 94.4% (confidence interval [CI] 95%:90-97), negative predictive value (NPV): 39.5 (95%CI 36.8-42.3); leukocytes > 18,000 mm^3 in 101/110, PPV 91.8% (CI95% 85.4-95.6), NPV 33.8 (CI95% 31.9-35.7) and neutrophils > 9500 mm^3 in 111/121, PPV 91.7% (CI95%: 85.7-95.4), NPV 34.6 (CI95% 32.6-36.7). In addition, 94.6% of UC (+) had > 50,000 CFU/ml and 1.2% had 10,000 CFU/ml; *Escherichia coli* was isolated in 83.8% of UC (+) and 87.04% of BC (+).

Table 3 shows laboratory results in infants with and without bacteremia. In the latter, the frequency of blood CRP > 50 mg/l is higher ($p < 0.002$). When evaluating the proportion of infants with blood variables (+) who had bacteremia, we found that 34/152 had CRP > 50 mg/l, PPV 22.4% (95%CI 18.52-26.75), NPV 90.2 (95%CI 86-93.2); 18/101 with leukocytes > 18,000/mm^3, PPV 17.8 (95%CI 12.5-24.8), NPV 84.6 (95%CI 81.7-87) and 18/111 with neutrophils > 9500/mm^3, PPV 16.2 (95%CI 11.36-22.62), NPV 83.9 (95%CI 80.9-86.5). In 87.03% of UTIs with bacteremia, *E. coli* was the etiologic agent, and 100% of these were associated with UAI; in UTIs without bacteremia, *E. coli* was isolated in 83.2% of UC (+) and 96.7% of these were associated with UAI. Other etiologic agents were observed in 16.2% of UC, and 11.2% were associated with UAI. Bacteremia was present in 17% of UTIs in infants under 29 days and in 15.5% of UTIs in older infants.

Table 4 shows that the percentage of UAI (nitrites (+) or pyocytes or bacteria (+) in infants with UTI) increases

significantly ($p < 0.001$) in direct relation to the increase of CFU/ml in UC.

Considering positive those discharged with a diagnosis of UTI, we can see the diagnostic usefulness of some UA and blood variables (Table 5). The sensitivity of 95.81% (95%CI 93.07-97.69) for pyuria and 88.32% (95%CI 84.38-91.57) for bacteria (+) stand out; the specificity for the three variables is > 80%, with nitrites standing out with 96.24% (95%CI: 91.4-98.8) and bacteria (+): 92.48% (95%CI 86.6% -96.3%); PPV > 90% and NPV is low for nitrites, but improves > 70% for bacteria and leukocytes. In blood, all three variables have a PPV > 90%.

In Table 6, the multivariate logistic regression was adjusted by including in the model only those variables with $p < 0.25$ in the univariate analysis (Hosmer-Lemeshow criterion) for predicting BC (+). Therefore, we conclude that only the variable CRP > 50 mg/l has a significant effect on the variable blood culture (+).

Discussion

Although the signs and symptoms of UTI in infants under 3 months are not specific, UAI is an excellent tool for predicting the diagnosis and even justifying early initiation of antibiotics, which, as is well known, can significantly reduce the risk of renal scarring, hypertension, and chronic renal failure[5,9,10,14].

Our results, in agreement with other publications[6-16], show the high percentage of UAI in infants with UTI: sensitivity for pyuria was 95.8% (95%CI 93.7-97.7) and 88.3% for bacteria (+) (95%CI 84.4-91. 6); the specificity for the three inflammatory variables studied was also high, especially for nitrites 96.2% (95%CI 91.4-98.8) and bacteria (+) 92.5 (95%CI 86.6-96.3), showing that the percentage of UAN in children without UTI is also high. Similarly, the PPV > 90% confirms the good ability of UAI to predict UTI in infants younger than three months with FWS. The absence of nitrite does not satisfactorily predict the absence of infection, in contrast to bacteria (+) and pyuria, which have NPVs of 75.9% (95%CI 70.5-81) and 89.2% (95%CI 82.8-93.4), respectively.

In contrast to other publications[8,15], we found that 100% of UTIs with bacteremia were associated with UAI. In those without bacteremia, although somewhat less, UAI was also detected in 97.8% of those caused by *E. coli* and 93.6% of those caused by other microorganisms, consistent with what has been described in the literature[8,12].

Our results confirm that in infants with FWS, UA is a valuable tool in routine clinical practice for pediatricians to suspect the diagnosis of UTI and initiate the appropriate treatment empirically. At the same time, it is important to consider that UA and UC should always be requested simultaneously[12,18].

The low sensitivity and specificity of UA described in some publications could be due to the method used for urine collection, false positives, the etiologic agent, or the lower threshold of CFU/ml required to confirm the diagnosis[8,18-21]; the latter is consistent with what was observed in this study, where the frequency of UAI was significantly higher as the number of CFU/ml in the UC increased ($p < 0.001$).

As in other reports[19,22,23], our threshold of CFU/ml to confirm the diagnosis of UTI was 10,000; however, only 1.2% of UC (+) reached this value. Eighty-seven percent of all UTIs and 100% of UTIs with bacteremia had > 100,000 CFU/ml. When considering all UTIs, 94.6% had > 50,000 CFU/ml, which allows us to conclude that in samples obtained with BCC, the confirmatory threshold for UTI in infants under 3 months with FWS is > 50,000 CFU/ml, in agreement with the AAP and other authors[8-11,13,15,24]. However, counts of 10,000 to 49,900 CFU/ml are equally confirmatory in infants with FWS and UTI, but if the UA is normal, the test should be repeated.

The multivariate logistic regression analysis did not identify variables that could help predict the presence of UTI with bacteremia, consistent with the observations of other authors[28-31]. The frequency of BC (+) in patients younger than 29 days (17%) was not significantly different ($p > 0.05$) from those of older age (15.6%).

Despite the limitations inherent in retrospective studies and the lack of renal scintigraphy, we have satisfactorily met our objectives. In additon, our results may be useful in daily clinical practice and for future prospective studies.

In conclusion, we verified that UA is a valuable predictor of UTI in infants < 3 months with FWS, with good sensitivity, specificity, and PPV. *E. coli* is the main etiologic agent, present in 83.8% of UC (+) and in 87% of BC (+). In urine samples obtained with BCC, 94.6% of BC (+) have > 50,000 CFU/ml and 87.7% > 100,000 CFU/ml. Of the variables studied, CRP > 50 mg/l is the only one significantly associated with BC (+) ($p < 0.02$). However, it is not an acceptable indicator for an early prediction of bacteremia.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. This study involved a retrospective review of medical records, for which approval was obtained from a formally constituted review board (Institutional Review Board or Institutional Ethics Committee).

Conflicts of interest

The authors declare no conflicts of interest.

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