Pediatr Nephrol (2016) 31:239–245
DOI 10.1007/s00467-015-3199-y

ORIGINAL ARTICLE

Urinary tract infection in infants: the significance of low bacterial count

Svante Swerkersson [1,6] · Ulf Jodal [1] · Christina Åhrén [2,3] · Rune Sixt [4] · Eira Stokland [5] · Sverker Hansson [1]

Received: 3 May 2015 / Revised: 18 August 2015 / Accepted: 19 August 2015 / Published online: 10 September 2015

Abstract
Background In national guidelines for urinary tract infection (UTI) in children, different cut-off levels for defining bacteriuria are used. In this study, the relationship between bacterial count in infant UTI and inflammatory parameters, frequency of vesicoureteral reflux (VUR), kidney damage, and recurrent UTI was analyzed.
Methods We conducted a population-based retrospective study of 430 infants age <1 year with symptomatic UTI diagnosed by suprapubic aspiration. Clinical and laboratory parameters, findings on voiding cystourethrography and ^{99m}technetium dimercapto-succinic acid scintigraphy, and frequency of recurrence were related to bacterial count at the index UTI.
Results Eighty-three (19 %) infants had bacterial counts <100,000 colony-forming units (CFU)/ml and 347 (81 %) had ≥100,000 CFU/ml. There was similar frequency of VUR (19 % in both groups), kidney damage (17 and 23 %, p=0.33) and recurrent UTI (6 and 12 %, p=0.17) in the low and high bacterial group. Non-*E. coli* species were more prevalent (19 versus 6 %, p=0.0006) and mean C-reactive protein was lower (50 vs. 79 mg/l, p <0.0001) in the low bacteria group.
Conclusions UTI with low bacterial count is common and of importance since it may be associated with VUR and renal damage. Non-*E. coli* species and low inflammatory response were more prevalent in UTI with low bacterial count.

Keywords Urinary tract infection · Bacterial count · Vesicoureteral reflux · Kidney damage · Children · Infants

✉ Svante Swerkersson
svante.swerkersson@gu.se

1 Department of Pediatrics, The Queen Silvia Children's Hospital, Sahlgrenska University Hospital, Gothenburg, Sweden

2 Department of Clinical Bacteriology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

3 STRAMA, The Swedish Strategic Programme against Antibiotic Resistance, Region of Västra Götaland Göteborg, Sweden

4 Pediatric Clinical Physiology, The Queen Silvia Children's Hospital, Sahlgrenska University Hospital, Gothenburg, Sweden

5 Pediatric Radiology, The Queen Silvia Children's Hospital, Sahlgrenska University Hospital, Gothenburg, Sweden

6 Pediatric Uronephrologic Center, The Queen Silvia Children's Hospital, Sahlgrenska University Hospital, 416 85 Göteborg, Sweden

Introduction

Urinary tract infection (UTI) is one of the most common bacterial infections in small children, affecting 2 % of those below 2 years of age [1]. The symptoms are nonspecific and the diagnosis is based on growth of bacteria in the urine. A crucial point is to distinguish true bacteriuria from contamination. The number of bacteria regarded as "significant growth" goes back to studies by Kass of adults from the 1950s where a bacterial count ≥100,000 colony-forming units (CFU)/ml was established as criterion of UTI [2]. However, later studies showed that women with symptoms of UTI often had lower numbers of bacteria and a lower cut-off level was recommended [3].

Urine collection through suprapubic aspiration (SPA) of the bladder was introduced by Pryles et al. in 1959 and this method has become the "gold standard" for detecting UTI in infants [4]. They proposed that SPA is a means of resolving the problem of low bacterial counts by avoiding contamination during sampling of urine. Nevertheless, other methods of urine collection are frequently used, such as bag, clean catch, and catheter [5, 6]. These methods are associated with varying degrees of contamination and thus different cut-off levels for significant growth are set according to sampling method.

Most children with UTI have bacterial counts of 100, 000 CFU/ml or more irrespective of collection methods [7–10]. However, 14–20 % of children with UTI diagnosed by SPA, catheter or clean catch, had a lower bacterial count [7–10]. These infections are easily missed if using sampling methods with a high cut-off level [11]. In contrast, sampling techniques that give a high rate of contamination carry a risk of false-positive urine culture.

Considering that UTIs with low bacterial counts have been associated with similar frequencies of vesicoureteral reflux (VUR) and acute uptake defects on ^{99m}technetium dimercapto-succinic acid (DMSA) scintigraphy as UTI with high bacterial counts, it is remarkable that so few studies have focused on the importance of low bacterial counts in children [8, 9]. As a consequence, recently published national guidelines use different cut-off levels for significant bacteriuria. The NICE guidelines underline that the value of the colony count "has clinical limitations", while other guidelines exclude UTI when there is a low bacterial count [12–18] (Table 1).

The primary aim of this study was to analyze the differences between patients with low and high bacterial counts regarding VUR and kidney damage in a cohort of infants with first-time UTI. Secondary aims were to analyze the significance of bacterial count concerning recurrent UTI, bacterial findings, and inflammatory parameters.

Methods

Patients

This population-based retrospective study comprises children with symptomatic UTI consecutively diagnosed at the emergency room of the Queen Silvia Children's Hospital, Göteborg, over the 10 years from 1994 through 2003. This is the only pediatric hospital in the region and the vast majority of infants with symptomatic UTI are managed primarily at the emergency room of the hospital and then followed at the UTI clinic.

The inclusion criteria were: (a) age below 12 months, (b) first-time UTI, (c) suprapubic aspiration with bacterial growth of any number of a single species, (d) symptoms related to UTI, i.e., fever, poor weight gain, vomiting, or irritability. Infants with asymptomatic bacteriuria were excluded, as were children with urinary tract obstruction, other urogenital malformation, neurogenic bladder, or other severe neurological disease. Excluded were also infants where culture showed mixed growth.

Clinical and laboratory parameters

The clinical data registered included temperature and duration of fever before start of antibacterial therapy. Recurrent febrile UTI within 24 months of index UTI was looked for. Febrile recurrence was defined as temperature ≥38.5 °C and bacteriuria with growth of a single species of at least 100,000 CFU/ml in midstream or bag samples, 10,000 CFU/ml in catheter sample, or any bacterial growth in urine obtained by suprapubic aspiration.

C-reactive protein (CRP) and temperature were analyzed repeatedly during the acute phase and the highest value was used. Urine nitrite was analyzed by dipstick and urine leukocyte count by leukocyte esterase reaction (ECUR-4, Boehringer-Mannheim). Pyuria was defined as more than 10 cells/mm^3 according to the scale for the esterase test. Urine for culture was obtained by suprapubic aspiration and analyzed according to standard procedures. The included infants were grouped by bacterial count; the low bacteria group with less than 100,000 CFU/ml and the high bacteria group with 100, 000 CFU/ml or more.

Radiologic and scintigraphic examinations

During the study period, all children with their first UTI were followed by the same protocol including ultrasonography, voiding cystourethrography (VCUG) and dimercaptosuccinic acid (DMSA) scintigraphy. To ascertain uniform assessment, the radiologic examinations were revaluated by the same pediatric radiologist (ES) and DMSA scintigraphy by the same nuclear medicine specialist (RS), both blinded for other clinical data. VCUG was performed in 407 infants. VUR was graded according to the International Reflux Study in Children [19]. The highest VUR grade was used to classify each case.

DMSA scintigraphy was done according to European guidelines [20]. Kidneys with a split function of 45 % or more and without uptake defect were classified as normal, split function of 45 % or more and reduced uptake in one or more areas as minor, split function of 40–44 % as moderate, and split function below 40 % as pronounced defect. In cases with bilateral defects or renal duplication, an arbitrary classification was done to the same categories. DMSA scintigraphy may be performed early after UTI to diagnose acute parenchymal involvement or late to detect permanent renal damage. The acute uptake defects may either resolve during the following months or persist as permanent renal damage [21]. To avoid the inclusion of infants with transient defects, the end point in this study was an abnormal late DMSA scintigraphy 6 months or more after a UTI. Infants with a normal early DMSA scintigraphy without recurrent UTI were considered to have normal kidneys as the end point in line with a previous study [22].

Table 1 Recommended cut-off levels for bacterial count related to sampling method in published urinary tract infection (UTI) guidelines for children

Guideline [reference]	SPA CFU/ml	Catheter CFU/ml	Clean catch CFU/ml
ESPU 2015 [15]	Any growth	$\geq 10^3$–5×10^4	$\geq 10^4$–10^5
Canada 2014 [18]	Any growth	$\geq 5\times10^4$	$\geq 10^5$
AAP 2011 [13]	$\geq 5\times10^4$	$\geq 5\times10^4$	Not defined
Italy 2011 [14]	Not defined	$>10^4$	$>10^5$
Nice 2007 [12]	Not defined	Not defined	Not defined
France 2007 [16]	$\geq 10^3$	$\geq 10^3$	$\geq 10^5$
Germany 2007 [17]	Any growth	10^3–$>10^4$	10^4–$>10^5$

Statistics

The distribution of continuous variables is given as mean, SD, median, minimum, and maximum and of categorical variables as number and percentages. For comparison between two groups, Mann–Whitney *U* test was used for continuous variables, Fisher's exact test for dichotomous values, and Mantel–Haenszel Chi-square test for ordered categorical variables. In order to select independent associated factors to low bacterial count, all significant univariable variables were entered into a multivariable stepwise logistic analysis. All significance tests were two-sided and conducted at the 5 % significance level. All statistical analyses were performed using SAS® software version 9.2, SAS Institute, Cary, NC, USA.

Results

Included were 430 children, 275 boys and 155 girls. The mean age at diagnosis was 3.4 months (range, 5 days to 12 months) for boys and 6.1 months (range, 9 days to 12 months) for girls. The included infants were divided into two groups according to the bacterial count at the index UTI (<100,000 and ≥100, 000 CFU/ml, respectively). Altogether, 83 (19 %) infants had a low bacterial count (<100,000 CFU/ml); 6<1000 CFU/ml, 16 1000 to <10,000 CFU/ml, 52 10,000 to <50,000 CFU/ml, and 9 50,000 to <100,000 CFU/ml. The remaining 347 infants had a bacterial count ≥100,000 CFU/ml. There was no age or gender difference between the two groups at the index UTI; 54 (20 %) of the boys and 29 (19 %) of the girls had a low bacterial count. Univariable comparison between the two groups is shown in Table 2.

The predominating bacterial species was *E. coli*, found in 393 (91 %) of the specimens, *Klebsiella* in 21 (5 %), *Enterobacter* in five, enterococci in five, *Proteus* in four, and one each of *Haemophilus influenzae* and coagulase-negative staphylococci. *E. coli* was significantly more prevalent in UTI with high bacterial count ($p < 0.0001$) as was pyuria (Table 2).

The mean of the highest recorded temperature was 38.6 °C (range, 37.0–40.7 °C) in the low, and 39.1 °C (range, 36.6–41.3 °C) in the high bacteria group (p=0.0025). There was no difference between the groups concerning the duration of fever before start of antimicrobial therapy. Temperature <37.5 °C was found in 56, 37.5 to 38.4 °C in 47, and ≥38.5 °C in 323 infants.

CRP was significantly lower in the low bacteria group, mean concentration 50 mg/l (range, 5–260 mg/l) compared to 79 mg/l (range, 5–320 mg/l) in the high bacteria group ($p < 0.0001$). Similarly, CRP less than 20 mg/l was significantly more prevalent in the low bacteria group, 42 (52 %) vs. 76 (22 %) ($p < 0.0001$). Twenty-two infants, 19 boys and three girls, had temperature <37.5 °C and *CRP* <10. Of those, ten infants had urine cultured because of poor weight gain.

The presence and grade of VUR did not significantly differ between the groups. VUR occurred in 78 infants; 14 (19 %) in the low and 64 (19 %) in the high bacteria group. Corresponding figures for VUR grade III to V were seven (9 %) and 37 (11 %), respectively (p=0.84).

Altogether, 385 infants performed a DMSA scintigraphy. Of those, 342 infants were included in the analysis of renal damage, with a median follow-up time of 13.5 months (range, 6.0–65.7 months), and 43 were excluded (Fig. 1). Abnormal late DMSA scan was found in 74 (22 %) of the infants; the defects were minor in 44 (13 %), moderate in 14 (4 %), and pronounced in 16 (5 %). Scintigraphic defects were slightly more prevalent in the high bacteria group, 62 (23 %) vs. 12 (17 %), but this difference was not significant (p=0.33). Also, the categories of renal damage were similar in the two groups (Table 2). Of the infants not included in the analysis of renal damage (45 not investigated with DMSA scintigraphy and 43 children excluded), 13 (15 %) had a low bacterial count.

Recurrent UTI within 24 months of the index infection occurred in five (6 %, 95 % confidence interval 2–14 %) infants with low and in 41 (12 %, 95 % confidence interval 9–16 %) with high bacterial counts. This difference was not significant (p=0.17).

In a multivariable stepwise logistic model, the impact of the parameters age, gender, *E. coli*/non-*E. coli* species, temperature, CRP, and pyuria on the presence of low bacterial count was analyzed. *CRP* <20 mg/l, pyuria, and non-*E. coli* were independent factors associated with low colony count UTIs (Table 3).

Table 2 Clinical data according to bacterial count (mean (SD)/ median for continuous and number (%) for categorical variables)

	<100,000 CFU/ml (*n*=83)	≥ 100,000 CFU/ml (*n*=347)	*p* value
Gender, boys	54 (65.1 %)	221 (63.7 %)	0.90
Age, months	4.4 (3.1) 4.1	4.4 (3.2) 3.8	0.83
Fever			
Duration[a], days	2.7 (2.6) 2.0	2.5 (1.9) 2.0	0.76
Highest temperature °C	38.6 (1.1) 38.7	39.1 (1.0) 39.2	0.0025
CRP			
Highest, mg/l	50 (61) 17	79 (67) 65	<0.0001
<20 mg/l	42 (51.9 %)	76 (21.9 %)	
Pyuria	62 (77.5 %)	314 (92.1 %)	0.0005
Bacterial species			
E. coli	67 (80.7 %)	326 (94.0 %)	0.0006
Klebsiella sp.	6 (7.2)	15 (4.3)	
Enterobacter sp.	4 (4.8)	1 (0.3)	
Proteus sp.	2 (2.4)	2 (0.6)	
Haemophilus influenzae	0	1 (0.3)	
Enterococci	4 (4.8)	1 (0.3)	
Coagulase-negative staphylococci	0	1 (0.3)	
VUR			
No VUR	60 (81.1 %)	269 (80.8 %)	1.00
VUR grade I to II	7 (9.5 %)	27 (8.1 %)	
VUR grade III to V	7 (9.5 %)	37 (11.1 %)	
Not done	9	14	
DMSA scan abnormality[b]	12 (17.1 %)	62 (22.8 %)	0.33
Mild	5 (7.1 %)	39 (14.3 %)	
Moderate	3 (4.3 %)	11 (4.0 %)	
Pronounced	4 (5.7 %)	12 (4.4 %)	
Recurrent UTI	5 (6.0 %)	41 (11.8 %)	0.17

CRP C-reactive protein, *VUR* vesicoureteral reflux, *DMSA* dimercaptosuccinic acid, *UTI* urinary tract infection

[a] Duration of fever before start of antibacterial treatment

[b] Thirteen in low group and 75 from high group were not included according to method section

Discussion

The diagnosis of UTI in children is based on a positive urine culture from an adequately obtained urine sample. The different methods of urine collection are associated with varying risk of contamination. To minimize the risk of contamination but still not overlooking true UTI, cut-off levels are used to define significant bacterial growth. In this study of 430 infants under 12 months of age with first-time symptomatic UTI, diagnosed by SPA, the characteristics and significance of a low bacterial count was analyzed. Bacterial numbers below 100,000 CFU/ml were found in 19 % of the urine specimens, which is in concordance with other pediatric studies [7–10].

Few studies have focused on the impact of UTI with low bacterial counts. In a Finnish study, 199 infants with symptomatic infection were examined by simultaneous SPA and clean-catch samples. Of the infants with positive culture from SPA, 38 (19 %) had growth of <100,000 CFU/ml in the clean catch sample and would consequently have been missed with a higher cut-off level [10]. In another study of 366 infants below 1 year of age, all with SPA, the rate of VUR was similar in infants with UTI of low and high bacterial count, 26/69 (38 %) and 83/279 (30 %), respectively [8]. Kanellopoulos et al. suggested that UTI with low bacterial count is a separate entity with special characteristics, as they observed low bacterial count more frequently in non-*E. coli* infections and in children under 2 years of age [9]. Of 541 children studied using different sampling methods, the proportion of specimens with bacterial count ≤50,000 CFU/ml increased by age, reaching a maximum at 12–24 months, then decreasing to a low level. UTI with a low bacterial count was not found to be of low-risk concerning the rate of VUR or acute DMSA scan abnormalities. Scintigraphy within 2 weeks of UTI was abnormal in 10/33 (30 %) in the low bacterial group and 104/246 (42 %) in the high bacterial group (p=0.26). A study from a Canadian neonatal intensive care unit showed that among 48

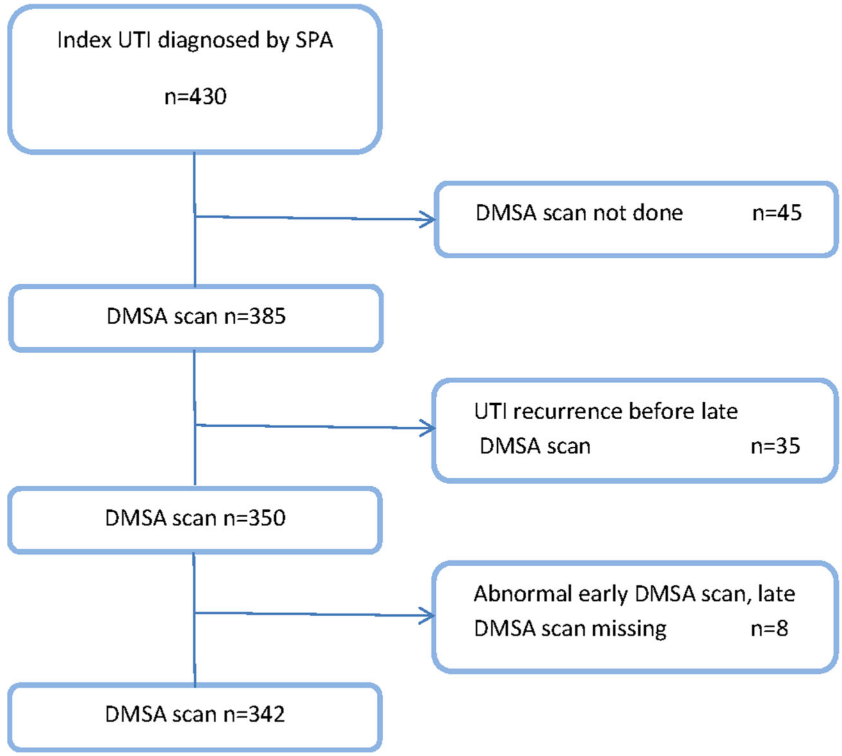

Fig. 1 Flow chart of 430 infants with first time UTI of which 342 had a dimercaptosuccinic acid (DMSA) scintigraphy performed at least 6 months after UTI. *SPA* suprapubic aspiration, *UTI* urinary tract infection

infants with positive urine culture and bacterial count of 1000 to 10,000 CFU/ml, five had positive blood culture with the same organism [23].

We found no relation between bacterial count and gender or age. To notice is that the infants included were all under 1 year of age with a higher proportion of boys. The young age

Table 3 Univariable logistic and multivariable stepwise logistic regression analysis of probable associated factors for low bacterial count

	Univariable analysis		Multivariable analysis*	
	Odds ratio (95 % CI)	*p* value	Odds ratio (95 % CI)	*p* value
Gender				
Boys (reference)	1.0	–	–	–
Girls	0.94	(0.57–1.56)	0.82	–
Age				
<4 months (reference)	1.0	–	–	–
≥4 months	1.18	(0.73–1.90)	0.51	–
Temperature				
≥38.5C° (reference)	1.0	–	–	–
<38.5C°	2.41	(1.43–4.05)	0.0009	
CRP				
≥20 mg/l (reference)	1.0	–	–	–
<20 mg/l	3.84(2.32–6.36)	<0.0001	3.06 (1.78–5.25)	<0.0001
Pyuria				
Yes (reference)	1.0	–	–	–
No	3.34(1.75–6.50)	0.0003	2.49 (1.22–5.08)	0.008
Bacterial species				
E. coli (reference)	1.0	–	–	–
Non-*E. coli*	3.71(1.84–7.48)	0.0003	2.50 (1.13–5.52)	0.021

CRP C-reactive protein

*area under the ROC curve was 0.68 with all 3 variables in the multivariable model included explains this gender distribution. In concordance with other studies, there was no difference in the frequency of VUR between the low and high bacteria group, 19 % in both. Also, when analyzing DMSA scan abnormalities at 6 months or more after UTI, the frequency of permanent renal damage was similar, 17 % with low and 23 % with high bacterial count (p=0.3). Acquired damage cannot with certainty be separated from congenital damage but either may impact the long-term prognosis.

In multivariable logistic analysis non-*E. coli* infection, CRP above 20 mg/l and presence of pyuria were associated with a high bacterial count. Pyuria was prevalent in both groups but occurred significantly more often in the high bacteria group (92 %) than in children with low bacteria count (78 %, $p < 0.001$). Also, the median level of CRP was significantly higher in the high (65 mg/l) as compared to the low bacteria group (17 mg/l). *E. coli* were, however, more prevalent in the former group, which may have influenced these results as described previously [24]. We did not anticipate this outcome and it is in contrast to the study by Kanellopoulos et al., who did not find any significant difference between the groups concerning sedimentation rate, CRP, or leucocyte count [9]. As all children in our study had urine sampling by SPA, contamination is an unlikely cause of the low bacterial numbers. The lower frequency of positive urine nitrite and pyuria in the low bacteria group may indicate a shorter bladder incubation time, but could also be explained by slower bacterial growth. Even if all children had symptoms consistent with UTI, it is possible that some children with asymptomatic bacteriuria may have been included, explaining a lower CRP.

The relationship between UTI with low bacterial count and the risk of recurrences has not previously been studied. Recurrent UTI was twice as frequent in infants with a high bacterial count, 12 % versus 6 %, but the samples were small and the difference was not significant (p=0.2).

The questions of sampling methods and cut-off levels for bacterial growth are crucial in the management of UTI in children. The ideal urine sampling method should be easy to use, also in primary care, acceptable to children and parents, and deliver reliable results from urinalyses and urine culture. The optimal cut-off level should be able to discriminate between true bacteriuria and contamination. Even if good-quality comparative studies between different samplings methods are scarce, there are some studies comparing suprapubic aspiration and clean catch showing good agreement in results of urine culture [25]. For catheter samples, the risk of contamination might be less than in clean-catch samples, but there are no studies of infants with UTI comparing catheter and SPA [26, 27]. In contrast, bag samples are associated with a high risk of contamination [27, 28].

During recent years, several guidelines regarding management of children with UTI have been published [12–18]. In these guidelines the question about appropriate urine sampling methods and cut-off levels of bacterial growth are addressed. The recommendations of sampling methods are diverse, where some prefer catheter or SPA as first choice [13, 15], others clean catch urine [12, 14, 16], while some leave the question open [17, 18]. Similarly, the cut-off levels recommended for different sampling methods vary; for SPA from any growth to 50,000 CFU/ml, catheter from 10,000 to 50,000 CFU/ml, and clean-catch urine from 10,000 to >100,000 CFU/ml.

The study by Hoberman et al. of bacteriuria in catheter specimens from young children with fever is the origin of the cut-off levels chosen in some guidelines [7]. This study included 2181 children below 2 years of age with fever. In isolates with growth of a single organism, bacterial counts of 10,000 to <100,000 CFU/ml were found in 18 of 110 (16 %). Mixed organisms or Gram-positive cocci were found in 15/23 (65 %) of the isolates with bacterial count 10,000 to <50,000 CFU/ml compared to 7/109 (6 %) with bacterial count ≥50,000 CFU/ml. The authors propose that, for urine samples obtained by catheter sample, the best definition of UTI is both leukocytes ≥10/mm^3 and a CFU count ≥50,000/ml, but they also declare that in patients with bacterial counts between 10,000 and 50,000 CFU/ml and persistent symptoms the management should be individualized. Our study shows that applying a cut-off level of 50,000 CFU/ml carries a risk of ignoring a significant portion of infants with UTI and that these infants have similar risk of VUR and renal damage as those with a high bacterial count.

In conclusion, this study shows that UTI with low bacterial count is common and of importance since it may be associated with both VUR and permanent renal damage. Furthermore, it indicates that UTI with low bacterial count is associated with non-*E. coli* UTI and low inflammatory response. The results show that infants with UTI may have a lower number of bacteria than indicated by several guidelines, and this must be kept in mind when evaluating infants with suspected UTI.

Conflict of interest The authors declare no conflicts of interest.

Ethical approval The study was approved by the Regional Ethical Review Board in Gothenburg (278-08).

References

1. Jakobsson B, Esbjorner E, Hansson S (1999) Minimum incidence and diagnostic rate of first urinary tract infection. Pediatrics 104: 222–226
2. Kass EH (1956) Asymptomatic bacteriuria of the urinary tract. Trans Assoc Am Phys 69:56–63
3. Stamm WE, Counts GW, Running KR, Fihn S, Turck M, Holmes KK (1982) Diagnosis of coliform infection in acutely dysuric women. N Engl J Med 307:463–468

4. Pryles CV, Atkin MD, Morse TS, Welch KJ (1959) Comparative bacteriologic study of urine obtained from children by percutaneous suprapubic aspiration of the bladder and by catheter. Pediatrics 24: 983–991
5. Coutinho K, Stensland K, Akhavan A, Jayadevan R, Stock JA (2014) Pediatrician noncompliance with the American Academy of Pediatrics guidelines for the workup of UTI in infants. Clin Pediatr 53:1139–1148
6. Hansson S, Bollgren I, Esbjörner E, Jakobson B, Mårild S (1999) Urinary tract infections in children below 2 years of age: a quality assurance project in Sweden. The Swedish Pediatric Nephrology Association. Acta Paediatr 88:270–274
7. Hoberman A, Wald ER, Reynolds EA, Penchansky L, Charron M (1994) Pyuria and bacteriuria in urine specimens obtained by catheter from young children with fever. J Pediatr 124:513–519
8. Hansson S, Brandstrom P, Jodal U, Larsson P (1998) Low bacterial counts in infants with urinary tract infection. J Pediatr 132:180–182
9. Kanellopoulos TA, Vassilakos PJ, Kantzis M, Ellina A, Kolonitsiou F, Papanastasiou DA (2005) Low bacterial count urinary tract infections in infants and young children. Eur J Pediatr 164:355–361
10. Koskimies O (1995) Diagnostic accuracy of urinary tract infection and subsequent development of renal scars. J Pediatr 126:157–159
11. Etoubleau C, Reveret M, Brouet D, Badier I, Brosset P, Fourcade L, Bahans C, Garnier F, Blanc P, Guigonis V (2009) Moving from bag to catheter for urine collection in non-toilet-trained children suspected of having urinary tract infection: a paired comparison of urine cultures. J Pediatr 154:803–806
12. National Institute for Health and Clinical Excellence (Nice) Guideline (2007) Urinary tract infection in children: diagnosis, treatment and long-term management. Issue date: August, 2007. Available at: http://www.nice.org.uk/guidance/cg54, last accessed April 22, 2015
13. Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management (2011) Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. Pediatrics 128:595–610
14. Ammenti A, Cataldi L, Chimenz R, Fanos V, La Manna A, Marra G, Materassi M, Pecile P, Pennesi M, Pisanello L, Sica F, Toffolo A, Montini G, Italian Society of Pediatric Nephrology (2012) Febrile urinary tract infections in young children: recommendations for the diagnosis, treatment and follow-up. Acta Paediatr 101:451–457
15. Stein R, Dogan HS, Hoebeke P, Kočvara R, Nijman RJ, Radmayr C, Tekgül S (2015) Urinary Tract Infections in Children: EAU/ESPU Guidelines. Eur Urol 67:546–558
16. AFSSAPS. Diagnostic et antibiothérapie des infections urinaires bactériennes communautaires du nourrisson et de l'enfant (2007) Available at: http://www.infectiologie.com/site/medias/_documents/consensus/afssaps-inf-urinaires-enfant-reco.pdf, last accessed April 22, 2015
17. Beetz R, Bachmann H, Gatermann S, Keller H, Kuwertz-Bröking E, Misselwitz J, Naber KG, Rascher W, Scholz H, Thüroff JW, Vahlensieck W, Westenfelder M (2007) Harnwegsinfektionen im Säuglings- und Kindesalter. Urol A 46:112–123
18. Robinson JL, Finlay JC, Lang ME, Bortolussi R, Canadian Paediatric Society, Infectious Diseases and Immunization Committee, Community Paediatrics Committee (2014) Urinary tract infections in infants and children: Diagnosis and management. Paediatr Child Health 19:315–325
19. Lebowitz RL, Olbing H, Parkkulainen KV, Smellie JM, Tamminen-Moebius TE (1985) International system of radiographic grading of vesicoureteric reflux. International Reflux Study in Children. Pediatr Radiol 15:105–109
20. Piepz A, Blaufox MD, Gordon I, Granerus G, Majd M, O'Reilly P, Rosenberg AR, Rossleigh MA, Sixt R (1999) Consensus on renal cortical scintigraphy in children with urinary tract infection. Semin Nucl Med 29:160–174
21. Jakobsson B, Berg U, Svensson L (1994) Renal scarring after acute pyelonephritis. Arch Dis Child 70:111–115
22. Hoberman A, Charron M, Hickey RW, Baskin M, Kearney DH, Wald ER (2003) Imaging studies after a first febrile urinary tract infection in young children. N Engl J Med 348:195–202
23. Clarke D, Gowrishankar M, Etches P, Lee B, Robinson J (2010) Management and outcome of positive urine cultures in a neonatal intensive care unit. J Infect Public 3:152–158
24. Swerkersson S, Jodal U, Sixt R, Stokland E, Hansson S (2007) Relationship among vesicoureteral reflux, urinary tract infection and renal damage in children. J Urol 178:647–651
25. Whiting P, Westwood M, Bojke L, Palmer S, Richardson G, Cooper J, Watt I, Glanville J, Sculpher M, Kleijnen J (2006) Clinical effectiveness and cost-effectiveness of tests for the diagnosis and investigation of urinary tract infection in children: a systematic review and economic model. Health Technol Assess 10:1–154
26. Tosif S, Baker A, Oakley E, Donath S, Babl FE (2012) Contamination rates of different urine collection methods for the diagnosis of urinary tract infections in young children: an observational cohort study. J Paediatr Child Health 48:659–664
27. Long E, Vince J (2007) Evidence behind the WHO guidelines: Hospital Care for Children: what are appropriate methods of urine collection in UTI? J Trop Pediatr 53:221–224
28. Al-Orifi F, McGillivray D, Tange S, Kramer MS (2000) Urine culture from bag specimens in young children: are the risks too high? J Pediatr 137:221–226