Prevalence of Urinary Tract Infection in Childhood

A Meta-Analysis

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Background: Knowledge of baseline risk of urinary tract infection can help clinicians make informed diagnostic and therapeutic decisions. We conducted a meta-analysis to determine the pooled prevalence of urinary tract infection (UTI) in children by age, gender, race, and circumcision status.

Methods: MEDLINE and EMBASE databases were searched for articles about pediatric urinary tract infection. Search terms included urinary tract infection, cystitis, pyelonephritis, prevalence and incidence. We included articles in our review if they contained data on the prevalence of UTI in children 0–19 years of age presenting with symptoms of UTI. Of the 51 articles with data on UTI prevalence, 18 met all inclusion criteria. Two evaluators independently reviewed, rated, and abstracted data from each article.

Results: Among infants presenting with fever, the overall prevalence (and 95% confidence interval) of UTI was 7.0% (CI: 5.5–8.4). The pooled prevalence rates of febrile UTIs in females aged 0–3 months, 3–6 months, 6–12 months, and >12 months was 7.5%, 5.7%, 8.3%, and 2.1% respectively. Among febrile male infants less than 3 months of age, 2.4% (CI: 1.4–3.5) of circumcised males and 20.1% (CI: 16.8–23.4) of uncircumcised males had a UTI. For the 4 studies that reported UTI prevalence by race, UTI rates were higher among white infants 8.0% (CI: 5.1–11.0) than among black infants 4.7% (CI: 2.1–7.3). Among older children (<19 years) with urinary symptoms, the pooled prevalence of UTI (both febrile and afebrile) was 7.8% (CI: 6.6–8.9).

Conclusions: Prevalence rates of UTI varied by age, gender, race, and circumcision status. Uncircumcised male infants less than 3 months of age and females less than 12 months of age had the highest baseline prevalence of UTI. Prevalence estimates can help clinicians make informed decisions regarding diagnostic testing in children presenting with signs and symptoms of urinary tract infection.

Key Words: urinary tract infection, pediatrics, prevalence, meta-analysis

(*Pediatr Infect Dis J* 2008;27: 302–308)

Pediatric urinary tract infections (UTI) account for 0.7% of physician office visits and 5–14% of emergency department visits by children annually.[1] Accurate diagnosis of UTI has important clinical implications; most febrile infants with UTI show evidence of renal parenchymal involvement (pyelonephritis).[2] Nevertheless, the presenting signs and symptoms of UTI in childhood are often nonspecific and, among infants, definitive testing for UTI involves bladder catheterization. Accordingly, clinicians caring for young children are frequently faced with the decision of whether or not to obtain a urine sample for urinalysis and culture.

Knowledge of the prevalence of UTI among different subgroups of children can assist clinicians in selecting children who would benefit from further diagnostic testing. Using prevalence rates as an estimate of the prior probability of disease is the first step in evidence-based practice. In children with a very low pretest probability of disease, routine diagnostic testing is not necessary. In fact, in such children, an indiscriminate approach to diagnostic testing might lead to more harm than benefit. In contrast, in children with high pretest probability of disease, routine diagnostic testing would be appropriate. In a survey of 300 academic and community pediatricians regarding diagnostic testing in infants with unexplained fever, baseline risk was important in determining diagnostic decisions.[3] Specifically, only 10% of clinicians believed that a urine culture was indicated if the probability of UTI was <1%, whereas 80–90% would obtain a culture if the probability of disease was 3–5%, and all would do so if the probability exceeded 5%. Whether a certain child has a 2% or a 10% baseline probability of UTI makes a difference to the practicing clinician.

Prevalence was defined as the proportion of children with the target disorder among patients undergoing diagnostic testing.[4] This type of point prevalence, also known as pretest probability, provides clinicians with an estimate of the baseline risk of disease.

There are currently no pooled data available stratifying prevalence based on age, gender, race, or circumcision status, all of which can affect UTI risk. To address this we conducted a meta-analysis with the aim of providing clinicians with quantitative estimates of UTI prevalence for each subgroup.

Accepted for publication October 12, 2007.

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Dr. Morone was supported by the Roadmap Multidisciplinary Clinical Research Career Development Award Grant (1KL2RR02415401) from the National Institutes of Health.

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ISSN: 0891-3668/08/2704-0302

DOI: 10.1097/INF.0b013e31815e4122

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METHODS

As part of a larger meta-analysis on signs and symptoms of pediatric UTI, a large database was compiled. Two investigators searched MEDLINE and EMBASE for articles from January 1966 through October 2005. Search terms included the following: *UTI, cystitis, pyelonephritis, prevalence,* and *incidence*. This computerized search was supplemented with a manual review of references cited in the Technical Report on UTI from the American Academy of Pediatrics.[5] From this database, we reviewed full-text versions of articles that might contain data regarding prevalence of UTI. A second MEDLINE search was conducted 6 months later to ensure that all relevant articles were obtained. For the second search, the following terms were used: *incidence, prevalence, epidemiology, UTI, cystitis, and pyelonephritis*. We reviewed 652 titles. No additional articles were identified in the second search. We did not specifically search for unpublished studies. Articles meeting inclusion criteria were then independently reviewed, rated, and had data abstracted by 2 of the authors (NS, NEM). Both authors had previous experience with data abstraction and quality rating in meta-analysis.

Explicit a priori inclusion and exclusion criteria were applied. We included articles in our review if they: (1) presented data on the prevalence of UTI in children 0–19 years of age presenting with symptoms of UTI (including fever alone), (2) used urine cultures as the gold standard, and (3) defined a positive urine culture as $\geq 10^4$ for catheterized specimen, $>10^3$ for suprapubic specimen, and $\geq 10^5$ for clean catch or bag specimens. Articles were excluded if they: (1) were in languages other than English, (2) evaluated only a high risk subgroup (eg, malnourished, premature, genitourinary or neurologic abnormalities, nosocomial infections, sexually abused), (3) were performed in developing countries, (4) evaluated only a low risk subgroup (eg, asymptomatic well appearing children), (5) evaluated only children with other symptomatic illnesses (febrile seizures, infectious diarrhea, bronchiolitis), (6) contained fewer than 10 subjects, and (7) used bags to collect urine specimen in more than 25% of subjects with UTI without confirming results using more accurate methods such as suprapubic catheterization or bladder catheterization.

Four of the authors whose prevalence papers are included in this analysis (Zorc, Newman, Hoberman, and Shaw) provided us with additional data from their studies, which we included in our analyses.

Quality Rating. We used a published quality rating system for prevalence articles.[6] Two investigators (NS, NEM) assessed each study independently on a 5-point scale. We reviewed each article to determine whether: (1) study design was appropriate for obtaining prevalence estimates, (2) sample was representative of the general population of children presenting with a UTI, (3) UTI diagnostic criteria were acceptable (catheterized, suprapubic, or clean catch specimen with $>10^5$, $>10^3$, and $>10^5$ organisms, respectively), (4) urine culture was performed on a consecutive or random sample of subjects, and (5) the final diagnosis was known for >80% of eligible subjects. To avoid introducing bias, we included all articles meeting our inclusion criteria in the analysis, and used the quality rating to explore the effect of study quality on prevalence values.[7] Disagreements were resolved by consensus of the authors.

Statistical Analysis. Data were imported into STATA version 9.2 and a pooled estimate of UTI prevalence was calculated. To determine whether or not to use the fixed-or random-effects model, statistical heterogeneity between and within groups was measured using the Q statistic and assessed visually using the Galbraith plot of heterogeneity. If the Q test was not significant, the fixed effects methods were used. Otherwise pooled estimates and confidence intervals were calculated assuming a random-effects model with inverse-variance weighting using the DeSimonian and Laird method.[8]

Although we did not expect to see publication bias when assessing prevalence, this was assessed using the Begg rank correlation method and the Egger weighted regression method. We also looked at the cumulative effect of adding articles one at a time ordered by publication date on the pooled prevalence estimate. We also performed a similar analysis for quality ratings. To evaluate the weight of particular articles on the pooled estimate we performed influence analysis. This method recalculates the pooled prevalence estimate omitting 1 study at a time. Meta-regression was used to analyze the relationship between UTI prevalence and study quality, age, length of the study, setting (outpatient clinic versus ER), year of study, and whether the study was conducted in the United States or another country. All reported confidence intervals represent the 95% confidence intervals.

RESULTS

Description of Articles. From a total of >4000 articles found through our search strategy, we retrieved 330 for full text review. Fifty-one articles contained prevalence data and of these 18 articles evaluating 22,919 children met all criteria for inclusion. The setting for all articles was either the outpatient clinic, emergency department or both. There was no evidence of publication bias. We categorized the studies into 2 groups based on the population of children enrolled.

There were 14 articles which enrolled infants (0–24 months, Table 1); in these articles, enrollment was based on the presence of fever (of at least 38.0°C). We further subdivided this group into 4 smaller subgroups: infants ≤3 months, infants 3–6 months, infants 6–12 months, and infants 12–24 months of age.

There were 4 articles which enrolled children older than 2 years of age (Table 2). In these studies, enrollment was based on the presence of signs and symptoms referable to the urinary tract. Although some infants (with fever) were included in these studies, the majority of subjects were children >2 years of age (with urinary symptoms).

Prevalence of UTI Among Febrile Infants <2 Years of Age. Among the 14 studies of febrile infants <24 months of age, the pooled prevalence of UTI was 7.0% (CI: 5.5–8.4) (Fig. 1). The χ^2 test of homogeneity was highly significant ($P < 0.001$). Accordingly random effects estimates were used. The Begg and Egger tests showed no evidence of publication bias. The Galbraith plot, identified the populations studied by Newman et al,[9] Bachur and Harper,[10] and Shaw et al[11] as the most heterogeneous. However, influence analysis showed that no study, in-

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TABLE 1. Prevalence of Urinary Tract Infection Among Febrile Infants 0–24 Months of Age Stratified by Age

	Study Characteristics						Prevalence of Urinary Tract Infection (%)			
	Quality*	Setting	Country	Age	N†	Overall	Females	Males	Circumcised	Uncircumcised
Infants <3 Mo With Fever										
Krober et al,[23] 1985	1	Clinic	USA	<3 mo	182	11.0	7.2	14.1		
Crain and Gershel,[12] 1990‡	3	ED	USA	<2 mo	442	7.5	4.1	10.1	2.1	17.5
Bonadio et al,[24] 1993	1	ED	USA	<2 mo	233	2.9				
Bonadio et al,[25] 1993	1	ED	USA	<2 mo	1130	3.5				
Hoberman et al,[15] 1993	2	ED	USA	<3 mo	391	5.4	8.9	2.4		
Bonadio et al,[26] 1994	2	ED	USA	8–12 wk	321	5.3				
Shaw et al,[11] 1998	2	ED	USA	<3 mo	335	5.4	9.4	1.7		
Lin et al,[13] 2000	2	Clinic/ED	Taiwan	<2 mo	162	13.6	5.9	19.1		19.1
Kadish et al,[27] 2000	3	ED	USA	<1 mo	372	8.6				
Bachur and Harper,[10] 2001	4	ED	USA	≤3 mo	3768	7.1				
Herr et al,[28] 2001	1	ED	USA	<2 mo	434	5.7	9.0	2.7		
Dayan et al,[29] 2002	1	ED	USA	<2 mo	232	11.6	5.1	18.4		
Newman et al,[9] 2002‡	4	Clinic	USA	<3 mo	1608	10.4	13.0	7.4	2.6	20.8
Zorc et al,[14] 2005	2	ED	USA	<2 mo	1005	9.0	5.0	12.0	2.3	21.3
Pooled prevalence (CI)						7.2 (5.8–8.6)	7.5 (5.1–10.0)	8.7 (5.4–11.9)	2.4 (1.4–3.5)	20.1 (16.8–23.4)
Infants 3–6 mo With Fever										
Hoberman et al,[15] 1993	2	ED	USA	3–6 mo	171	2.9	3.7	2.2		
Shaw et al,[11] 1998	1	ED	USA	3–6 mo	390	5.6	7.5	4.2		
Bachur and Harper,[10] 2001	4	ED	USA	3–6 mo	1711	10.9				
Pooled prevalence (CI)						6.6 (1.7–11.5)	5.7 (2.3–9.4)	3.3 (1.3–5.3)		
Infants 6–12 mo With Fever										
Hoberman et al,[15] 1993	2	ED	USA	6–12 mo	390	6.2	10.9	2.7		
Shaw et al,[11] 1998	2	ED	USA	6–12 mo	1030	3.7	6.5	1.3	0.3	7.3
Bachur and Harper,[10] 2001	4	ED	USA	6–12 mo	3114	6.4				
Pooled prevalence (CI)						5.4 (3.4–7.4)	8.3 (3.9–12.7)	1.7 (0.5–2.9)		
Infants 12–24 mo With Fever										
Shaw et al,[11] 1998	2	ED	USA	12-24 mo	656		2.1			
Bachur and Harper,[10] 2001	4	ED	USA	12-24 mo	2928	4.5				
Pooled Prevalence of Febrile UTI in Infants 0–24 mo of Age										
Pooled prevalence (CI)						7.0 (5.5–8.4)	7.3 (5.0–9.6)	8.0 (5.5–10.4)		

*Quality rated from 1 to 5 using published criteria[5] with 1 being the best quality and 5 being the worst quality (see *Methods*).

†Three studies provided data stratified by age (Bachur, Shaw, Hoberman); for these studies, N represents number of children in the respective age group.

‡20–25% of positive urine cultures from bag specimen. For this analysis, children with growth of $\leq 10^5$ CFU/mL from bag specimen and a negative UA were considered not to have a UTI.

ED indicates Emergency Department; CI, 95% confidence interval.

TABLE 2. Prevalence of UTI in Children <19 Years With Urinary Symptoms and/or Fever

	Quality*	Setting	Country	Age	N	Prevalence
Heale et al,[30] 1973	2	Clinic/ED	Australia	<15 yr	789	9.1
Dickinson,[31] 1979	2	Clinic	UK	<15 yr	156	8.9
Shaw and McGowan,[32] 1997	3	ED	USA	<19 yr	1298	7.1
Struthers et al,[33] 2003	3	Clinic/ED	UK	<6 yr	110	6.4
Pooled prevalence (CI)						7.8 (6.6–8.9)

ED indicates Emergency Department; CI, 95% confidence interval.

cluding these 3, significantly impacted the pooled prevalence estimate. Although high study quality was associated with lower prevalence of UTI ($P = 0.001$), only small changes in the pooled prevalence rate was observed after eliminating the 2 bag studies (6.6, CI: 5.1–8.1) or the 2 level 4 studies 6.6% (5.1–8.1%). Meta-regression showed that study year, study length, location within the United States, and study setting did not impact prevalence rates significantly.

The effect of age and gender on prevalence of febrile UTI in infants is shown in Table 1. Fourteen articles contained data regarding the prevalence of UTI among febrile infants, 9 of which presented data according to gender. Among males, prevalence rates were highest during the first 3 months of life and declined thereafter. Among females, prevalence rates were highest during the first 12 months.

Prevalence of Febrile UTI According to Circumcision Status. Four articles contained information regarding UTI prevalence in circumcised and uncircumcised males in infants <3 months of age (Fig. 2).[9,11–14] The UTI prevalence rates for circumcised and uncircumcised males were 2.4% (CI: 1.4–3.5) and 20.1% (CI: 16.8–23.4), respectively. The prevalence of UTI among circumcised males was relatively similar across the articles. Elimination of the bag studies from this analysis did not significantly alter the results: prevalence of UTI among uncircumcised (2 studies) and circumcised infants (1 study) was 20.7% (CI: 16.7–20.8) and 2.3% (CI: 1.1–5.4), respectively.

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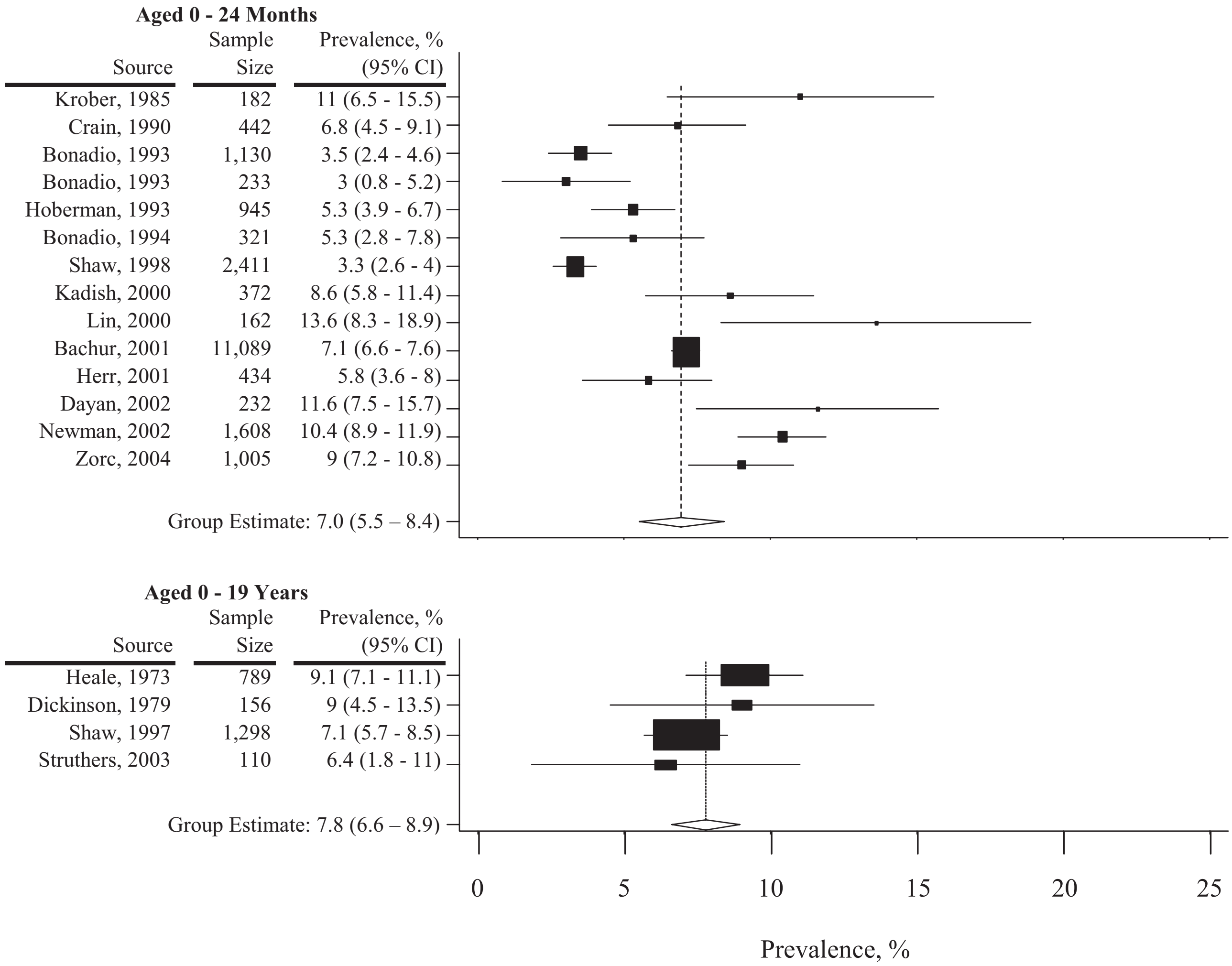

FIGURE 1. Urinary tract infection prevalence (rectangles), 95% confidence interval (lines), and pooled prevalence rate (diamonds) stratified by age.

One study provided data regarding prevalence of UTI among older infants by circumcision status. In that study the prevalence rates of UTI among circumcised and uncircumcised males 6–12 months of age were 0.3% and 7.3%, respectively. None of the studies included data regarding the prevalence of UTI in males >12 months of age.

Prevalence of Febrile UTI According to Race. Four articles provided data regarding race.[9,11,14,15] The prevalence of UTI among whites (8.0%; CI: 5.1–11.0) was significantly higher than the prevalence of UTI among African Americans (4.7%; CI: 2.1–7.3). However, there was heterogeneity among the articles. Three articles found significantly higher rates of UTI among whites than African Americans.[9,11,15] In the remaining study,[14] which used Hispanics as a race category, whites were less likely to have a UTI than nonwhites. Because Hispanic males are less likely to be circumcised,[16,17] the higher rate of UTI among nonwhites may be partially the result of the Hispanic male subgroup. Among female children, all 4 studies found higher rates of UTI among whites than African Americans.

Prevalence of UTI Among Older Children. Four studies presented data on the prevalence of UTI among children <19 years of age with signs or symptoms referable to the urinary tract (Table 2). The χ^2 test indicated that the studies were homogeneous ($P = 0.36$). The pooled prevalence of UTI (febrile and afebrile) was 7.8% (CI: 6.6–8.9).

DISCUSSION

This analysis found that the reported prevalence of UTI varies widely by age, gender and circumcision status. This confirms the importance of demographic and clinical characteristics when considering further diagnostic testing. The quantitative prevalence estimates presented in this article provide the clinician with a better sense of the relative importance of each of these factors. By incorporating information about the patient's age, race, gender and circumcision status, clinicians can make more informed decisions on a case-by-case basis.

We found slightly higher prevalence rates than a 1999 study of UTI prevalence conducted by the American Acad-

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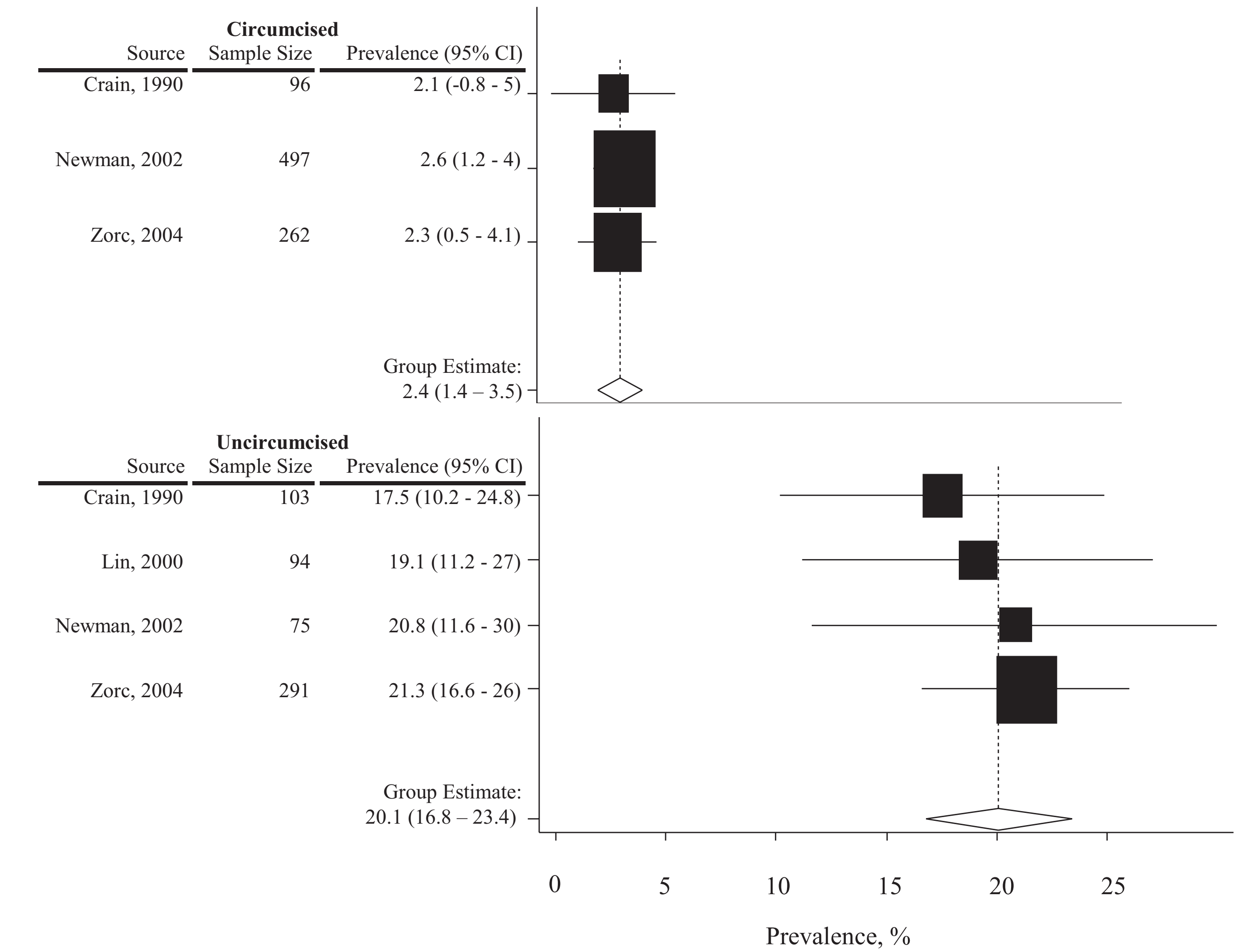

FIGURE 2. Urinary tract infection prevalence (rectangles), 95% confidence interval (lines), and pooled prevalence rate (diamonds) for circumcised and uncircumcised male infants younger than 3 months of age.

emy of Pediatrics (AAP) in which the pooled prevalence of UTI in 10 studies was 5%.[5] We used explicit a priori inclusion and exclusion criteria specifically related to prevalence studies, which led us to exclude several articles included in the AAP report. Furthermore, we were able to provide pooled estimates of prevalence by age, race and gender.

Female infants with fever had a relatively high prevalence rate of UTI, especially during the first year of life. Our results are consistent with data from large epidemiologic UTI studies,[18,19] which have shown a decreasing incidence of febrile UTI among females during the first 2 years of life. Accordingly, it would be reasonable to *consider* obtaining a urine specimen from febrile females younger than 1 year of age. Knowledge of the baseline probability of UTI, along with information on the unique clinical presentation, can help the clinician decide whether obtaining a urine specimen is indicated.

Among febrile males, circumcision status was important in determining risk for UTI. Uncircumcised male infants ≤3 months of age had the highest prevalence of UTI of any group, male or female, whereas circumcised males had one of the lowest rates. Among febrile male infants ≤3 months of age, 20.1% of uncircumcised males had a UTI. This finding suggests that clinicians need to carefully ascertain circumcision status in all male infants with unexplained fever. Among studies with circumcised male infants ≤3 months of age, the prevalence of UTI was 2.4%. Accordingly, approximately 42 such infants will need to undergo catheterization to detect a single UTI. Although the prevalence of UTI is relatively low in this subgroup, the risks of a misdiagnosed neonatal UTI (hematogeneous dissemination, sepsis, missed high grade vesicoureteral reflux) are high. Furthermore, in this age group more than any other, appropriate therapy depends on determination of the exact site and bacterial etiology of the infecting agent. Accordingly, catheterization of all febrile male infants <3 months of age should be considered.

Although we could not directly calculate the pooled prevalence of UTI in circumcised and uncircumcised males older than 1 year of age from the included articles, several important pieces of information are available. Among the studies compiled for this report, the overall prevalence of UTI

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among males decreased rapidly with age (Table 1). This is consistent with previous epidemiologic studies of UTI in which the highest rates of UTI were in the first month of life.[18,20] The decreasing prevalence of UTI with age has been documented in uncircumcised[18–21] and circumcised males.[10,11] In these epidemiologic studies, the rates of UTI decrease considerably after 6 or 12 months of age. Only one of the studies that included older male infants reported UTI prevalence by circumcision status; among circumcised male infants 6–12 months of age, the prevalence of UTI was 0.3% among uncircumcised males and 7.3% among circumcised males.[19] Accordingly, it would be reasonable to assume that the prevalence of UTI among circumcised males >12 months of age is <1%.

The available data suggest that race is associated with UTI prevalence. Although more data are needed to clarify the mechanism by which race affects baseline risk of UTI, based on the available data, white children can be considered at higher risk of developing UTI than African American children.

Among older children with signs and symptoms referable to the urinary tract, the prevalence of UTI was 7.8% (CI: 6.6–8.9). In contrast, among adult females presenting with genitourinary symptoms, approximately 50% are ultimately diagnosed with UTI.[22] The discrepancy between children and adults could be secondary to biologic differences such as sexual activity or bacterial flora. Alternatively, it could be related to the better ability of adults to recognize and communicate symptoms of UTI. Whatever the reasons, the difference in pretest probability dictates a different approach to diagnosis. Specifically, the relatively low prevalence of UTI in children calls for the use of more accurate tests to minimize false positive and false negative results. Furthermore, because of the relatively low prevalence of UTI in children, diagnosis of UTI based on signs or symptoms alone is unlikely to be accurate.

Our analysis had several limitations. First, the heterogeneity (among studies of infants ≤2 years) could be considered a limitation. Although pooled estimates and the confidence intervals include adjustments for the between study variances, clinical judgment is warranted to decide whether, in fact, there are studies that were "too different" to be included. We found little difference in study design or quality between studies having the greatest and least impact on heterogeneity. Second, because most of the articles about older children did not differentiate cystitis from pyelonephritis, the estimates provided include both. Finally, we could not directly calculate a prevalence rate for verbal children according to gender as no study that included older children reported this data.

This analysis, however, has several strengths. By using rigorous methodology (comprehensive search strategy and use of a priori inclusion/exclusion criteria), our results provide a more updated picture of UTI prevalence. The pooled estimates have relatively narrow confidence intervals and are consistent with previous epidemiologic studies. Pooled prevalence values provided in this study can be used as an estimate of baseline probability in an evidence-based approach. Neither cumulative incidence nor population prevalence, often reported in epidemiologic articles, can be used in this fashion. In pediatrics, signs and symptoms of disease are often nonspecific. Consequently, more prevalence meta-analyses are needed to provide clinicians with baseline estimates of risk for common diseases.

ACKNOWLEDGMENTS

Dr. Shaikh had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. The authors thank Drs. Gorelick, Newman, Zorc, Lin and Hoberman for providing us with additional data from their studies.

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