SHORT REPORT

Clinical and laboratory characteristics of non-*E coli* urinary tract infections

S Friedman, S Reif, A Assia, I Levy

Arch Dis Child 2006;91:845–846. doi: 10.1136/adc.2005.080721

Comparison of the clinical and laboratory characteristics of infants and children with urinary tract infection caused by *E coli* (n=107) or other pathogens (n=32) yielded a significantly higher association of non-*E coli* disease with urinary tract anomalies, younger age, and previous antibiotic treatment. Underlying urinary tract anomalies were noted in 18 patients, of whom 14 (77%) were infected by non-*E coli* pathogens. The most frequent anomaly was grade 3–4 vesicoureteral reflux (50%), followed by hydronephrosis (22.7%), ureteropelvic junction obstruction (9%), hypospadias (4.5%), pinpoint meatus (4.5%), and dysplastic kidney (4.5%).

Renal scarring is an important complication of urinary tract infections, which predisposes patients to hypertension and renal impairment.¹ Known risk factors for renal scarring are younger age, anatomical malformations, especially vesicoureteral reflux, delayed treatment, and a causative pathogen other than *Escherichia coli*.^{2–5} Honkinen *et al* found that non-*E coli* UTI is associated with more urinary tract abnormalities than *E coli* UTI.^{6,7} The aim of this study was to further characterise the clinical and laboratory features of non-*E coli* UTI compared to *E coli* UTI.

PATIENTS AND METHODS

The medical records and databases of the Department of Pediatrics and the Microbiology Laboratory of Dana Children's Hospital, Tel Aviv were reviewed for all infants and children (age 1 week to 16 years) hospitalised for UTI between January 2000 and 31 March 2004. The diagnosis of

UTI was based on the isolation of uropathogens in suprapubic aspiration, pure growth of >10³ colony forming units in a catheter sample, or isolation of 10⁵ pathogens in a midstream urine specimen.

The initial laboratory work-up of all patients with UTI included complete blood count (CBC), erythrocyte sedimentation rate (ESR), C reactive protein (CRP), blood urea nitrogen, serum creatinine, urinalysis, and blood and urine cultures. Empiric therapy for suspected UTI consists of intravenous ampicillin and gentamicin in neonates, and cefuroxime in older infants and children pending urine culture results. Renal and urinary tract ultrasound is performed in patients with a first episode of UTI.

The patients were divided into those with *E coli* and non-*E coli* UTI and compared for demographic data, clinical data (degree and duration of fever and chills, time to defervescence, and length of hospital stay), underlying urinary tract anomalies (by history and ultrasound), recurrent infection (by history and past medical records), use of antibiotics of more than 48 hours for any reason in the two weeks prior to the present episode, and laboratory data (urinalysis, ESR, WBC, and serum creatinine).

RESULTS

Of the 257 children initially diagnosed with UTI during the study period, 139 fulfilled the diagnostic criteria for UTI, 107 (76.9%) with *E coli* UTI and 32 (23.1%) with UTI caused by other pathogens: *Klebsiella pneumoniae*, n = 10 (31%); *Pseudomonas aeruginosa*, n = 7 (21%); *Enterobacter* spp., n = 5 (16%); *Citrobacter* spp., n = 3 (9%); *Serratia* spp., *Proteus mirabilis*, *Enterococcus* spp., n = 2 each (6%), and *Morganella morganii*, n = 1 (3%). Nineteen per cent of the *E coli* group and 21.8% of the non-*E coli* group were neonates. The clinical and laboratory characteristics of the groups are shown in table 1.

Table 1 Comparison of demographic clinical and laboratory characteristics of *E coli* and non-*E coli* UTI

Characteristics	<i>E coli</i> (n = 107)		Non- <i>E coli</i> (n = 32)		p value
Sex: male, n (%)	20	(18.7)	11	(34.4)	0.09
Age median	1.42		0.42		
Age (y), mean (SD)	2.59	(3.15)	1.85	(3.15)	0.008
Urinary tract malformations, n (%)	4	(5.6)	14	(43.8)	<0.0001
Recurrent infections, n (%)	17	(15.8)	13	(40.6)	0.002
Previous antibiotic treatment, n (%)	19	(17.8)	13	(40.6)	0.015
Hospitalisation duration (days), mean (SD)	5.58	(1.88)	7.22	(2.88)	0.004
Maximal temperature (°C), mean (SD)	39.6	(0.73)	39.0	(0.74)	<0.0001
Fever duration prior to hospitalisation (days), mean (SD)	2.63	(2.32)	1.93	(1.93)	0.09
Time to defervescence (days), mean (SD)	1.52	(1.44)	1.13	(1.1)	0.001
Positive blood culture, n (%)	3	(2.9)	1	(3.2)	0.34
Peripheral white blood cell count ($\times 10^3/\text{mm}^3$), mean (SD)	20.52	(7.61)	17.01	(6.11)	0.016
Erythrocyte sedimentation rate (mm/h), mean (SD)	61.29	(33.14)	32.19	(25.0)	<0.0001
Serum creatinine (mg/dl), mean (SD)	0.58	(0.16)	0.64	(0.25)	0.27

Table 2 Multivariate logistic regression for variables associated with non-*E coli* UTI

Variable	OR (95% CI)	p value
Age		
2–12 mth	0.066 (0.011–0.41)	0.004
>12 mth	0.041 (0.006–0.27)	0.001
Female sex	3.35 (0.64–17.5)	0.15
Urinary anomalies	8.16 (1.88–35.48)	0.005
Recurrent UTI	4.19 (0.89–19.6)	0.068
Previous antibiotic treatment	4.74 (1.12–19.94)	0.034
Maximal temperature >39°C	0.4 (0.12–1.32)	0.13
Peripheral white blood cell count	0.42 (0.113–1.56)	0.19

Underlying urinary tract anomalies were noted in 18 patients, of whom 14 (77%) were infected by non-*E coli* pathogens (*Pseudomonas aeruginosa*, 50%; *Klebsiella pneumoniae*, 35%; *Morganella morganii*, 7%; and *Enterobacter* spp., 7%). The difference in the prevalence of urinary tract anomalies between the non-*E coli* and *E coli* groups (43.8% and 5.6%, respectively) was statistically significant ($p < 0.0001$). Four of the 18 patients had more than one anomaly. The most frequent anomaly was grade 3–4 vesicoureteral reflux (50%), followed by hydronephrosis (22.7%), ureteropelvic junction obstruction (9%), hypospadias (4.5%), pinpoint meatus (4.5%), and dysplastic kidney (4.5%). Non-*E coli* UTI was also significantly associated with younger age, previous antibiotic therapy, recurrent UTIs, lower maximal temperature, shorter time to defervescence, prolonged hospital stay, and lower mean WBC and ESR ($p < 0.05$ for all variables), but not with urinalysis. On multivariate regression analysis, significant factors were younger age, underlying urinary tract anomalies, and previous antibiotic treatment (table 2).

DISCUSSION

In this study of infants and children with *E coli* and non-*E coli* UTI, we detected significant differences in the clinical and laboratory characteristics between the two groups. Patients with non-*E coli* UTI were younger, had milder clinical signs, longer hospitalisation, and higher rates of urinary tract anomalies. Our higher rate of urinary tract anomalies in patients with non-*E coli* UTI agrees with an earlier study showing that UTI caused by *Klebsiella* or *Enterococcus* was significantly associated with ureterovesical reflux compared to *E coli* UTI.⁶ The severity of the UTI is related to host susceptibility and bacterial virulence. Uropathogenic *E coli* belong to specific capsular and flagellar strains and have multiple virulence factors, such as alpha haemolysins, P fimbriae, aerobactins, Sat proteins, and necrotising factors, which enable them to colonise and invade the normally sterile urinary tract and bloodstream. By contrast, except for endotoxins, no constant virulence factors were found in *Klebsiella* or *Enterobacter*.^{8,9} Therefore, we assume that the higher rate of *E coli* UTI in the patients with a normal urinary tract in our study is associated with the higher virulence of *E coli* compared to non-*E coli* strains and that the abnormal urinary tract may have made it possible for the less virulent non-*E coli* bacteria to cause infection.⁹

Indeed, the more enhanced inflammatory response of fever, increased WBC, and increased ESR in the patients with

E coli UTI, in addition to their significantly longer time to defervescence, may also be associated with the high virulence of this pathogen compared to non-*E coli* strains. Nevertheless, hospitalisation was longer in the non-*E coli* UTI group, owing to their greater number of urinary tract anomalies which required prolonged antibiotic therapy being defined as complicated UTI, the absence of an approved oral treatment for certain pathogens such as *Pseudomonas aeruginosa*, or inappropriate initial antibiotic therapy. Antibiotic treatment prior to hospitalisation was also a risk factor for non-*E coli* UTI. This treatment may have selected for non-*E coli* bacteria and colonisation by more resistant organisms. This may also have accounted for the milder nature of the UTI episode in children with *E coli* compared to non-*E coli* infections.

There are limitations in this study. First, we included in the study a selected group of hospitalised patients who did not necessarily represent the whole population of patients with UTI. Second, due to the relative small number of children with non-*E coli* UTI, no further subdivision according to age or causative organism was performed.

In summary, non-*E coli* may have milder clinical and laboratory features than *E coli* UTI and a higher prevalence of urinary tract anomalies. Future larger prospective studies are needed to confirm these results, determine the possible causes of these differences, and integrate these observations into clinical guidelines.

Authors' affiliations

S Friedman, S Reif, A Assia, Department of Pediatrics, Dana Children's Hospital, Sourasky Medical Center, Tel Aviv, Israel

I Levy, Infectious Disease Unit, Schneider Children's Medical Center of Israel, Petah Tiqva, and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Competing interests: none declared

Correspondence to: Dr I Levy, Infectious Disease Unit, Schneider Children's Medical Center of Israel, Petah Tiqva 49202, Israel; itzhakl@clalit.org.il; lavyguy@bezeqint.net

Accepted 18 May 2006

Published Online First 22 May 2006

REFERENCES

- 1 Hellstrom A, Hanson E, Hansson S, et al. Association between urinary symptoms at 7 years old and previous urinary tract infection. *Arch Dis Child* 1991;**66**:232–4.
- 2 Decter Ross M. Vesicourethral reflux. *Pediatr Rev* 2001;**22**:205–9.
- 3 AAP. Practice parameter: The diagnosis, treatment, and evaluation of the initial urinary tract infection in febrile infants and young children. American Academy of Pediatrics. Committee on Quality Improvement. Subcommittee on Urinary Tract Infection. *Pediatrics* 1999;**203**:843–52.
- 4 Smelli JM, Poulton A, Prescod NP. Retrospective study of children with renal scarring associated with reflux and urinary infection. *BMJ* 1994;**308**:1193–6.
- 5 Rushon HG. Urinary tract infections in children: epidemiology, evaluation and management. *Pediatr Clin N Am* 1997;**44**:1133–69.
- 6 Honkinen O, Lehtonen OP, Ruuskanen O, et al. Cohort study of bacterial species causing urinary tract infection and urinary tract abnormalities in children. *BMJ* 1999;**318**:770–1.
- 7 Honkinen O, Jahnukainen T, Mertsola J, et al. Bacteremic urinary tract infection in children. *Pediatr Infect Dis J* 2000;**19**:630–4.
- 8 Eisenstein BI, Zaleznik DF. Enterobacteriaceae. In: Mandell JL, Bennett JE, Dolin R, eds. *Principle and practice of infectious diseases*, 5th edn. Philadelphia, PA: Churchill Livingstone, 2000:2294–310.
- 9 Johnson JR, Scheutz F, Ulleryd P, et al. Host-pathogen relationship among *Escherichia coli* isolates recovered from men with febrile urinary tract infection. *Clin Infect Dis* 2005;**40**:813–22.