Risk Factors for Delayed Antimicrobial Treatment in Febrile Children with Urinary Tract Infections

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Objectives To identify factors associated with delayed antimicrobial treatment in febrile children with urinary tract infection (UTI).

Study design We reviewed data from 802 children with UTI enrolled in 2 previously conducted prospective studies (Randomized Intervention for Children with Vesicoureteral Reflux and Careful Urinary Tract Infection Evaluation) and extracted data on possible predictors of delayed treatment including age, sex, history of UTI, ethnicity, race, primary caregiver's education level, insurance, and income. We used univariate and multivariable analyses to investigate the relationship between these predictors and treatment delay.

Results We included 660 febrile patients with a mean age of 17.0 months old. Older age and commercial insurance were associated with delayed treatment on univariate analysis. Compared with younger children, treatment was delayed by an average of 26.2 hours in children ≥12 months of age. This relationship remained significant on multivariable analysis. Treatment also was delayed by an average of 12.6 hours in patients with commercial insurance. Race, ethnicity, primary caregiver's education level, and income were not associated with delayed treatment.

Conclusions Older age was a consistent predictor of delayed antimicrobial treatment. Delays in the initiation of antimicrobial therapy for UTI has previously been associated with renal scarring. Educating parents with older children regarding the management of fever as well as providers regarding prompt evaluation and management may help to reduce renal scarring. *(J Pediatr 2019;205:126-9).*

U rinary tract infections (UTIs) are a frequently occurring bacterial infection in young children; 8.4% of girls and 1.7% of boys will have a UTI within the first 6 years of life.[1] The long-term goal of managing UTIs is to prevent permanent renal scarring. Delayed treatment of febrile UTIs is associated with greater rates of acquired renal scarring.[2] The primary objective of this study was to identify factors associated with delayed antimicrobial treatment in children with febrile UTIs.

Methods

To evaluate the question posed in this study, we used data from 2 prospective, longitudinal studies of children with UTI, Randomized Intervention for Children with Vesicoureteral Reflux (RIVUR) and Careful Urinary Tract Infection Evaluation (CUTIE), conducted in 2007-2011 and 2008-2011, respectively. The children in these studies were 2-72 months old and presented following their first or second UTI at primary and subspecialty care settings throughout the US. The methodology of these studies has been reported previously.[3,4] To summarize, children with vesicoureteral reflux were enrolled in the RIVUR trial (n = 607), whereas those without vesicoureteral reflux were enrolled in the parallel CUTIE study (n = 195). Not all sites participating in the RIVUR trial participated in the CUTIE study. Data-collection forms in both studies were identical with a few exceptions. Institutional review boards at all participating sites approved the RIVUR and CUTIE study protocols. From these datasets, we extracted the data on the following variables: age, sex, history of UTI, ethnicity, child's race, primary caregiver's education level, insurance, income, household size, and duration of fever before the initiation of antimicrobial therapy. Income was reported and analyzed as a categorical variable (<$13 500, $13 500-23 499, $23 500-33 499, $33 500-57 999, $58 000-99 999, $100 000-149 999, and >$150 000). We included race, ethnicity, caregiver's education level, and income because these factors were found to be associated with delayed treatment in studies in adults (with conditions other than UTI).[5-9] Insurance was included based unequal access to care could potentially be related to treatment delay.[10]

CUTIE	Careful Urinary Tract Infection Evaluation
RIVUR	Randomized Intervention for Children with Vesicoureteral Reflux
UTI	Urinary tract infection

At the time of enrollment in the CUTIE and RIVUR studies, parents were asked about the duration of their child's fever (in hours as a continuous variable) before the initiation of antimicrobial therapy for the UTI. We defined treatment delay as the number of hours between the onset of fever and the start of antimicrobial therapy. As this was our main outcome measure, we excluded children who were afebrile (reported temperature ≤38°C) or in whom duration of fever was missing.

We categorized each patient as "poor" or "not poor" based on the reported family income and household size using the average poverty threshold recommended by the Census Bureau during the study period (2007-2011).

We conducted univariate analyses to evaluate each variable's effect on treatment delay. T-test, one-way ANOVA, or linear regression was used depending on the type of variable. We then constructed a multivariable regression model with treatment delay as the dependent variable. Potential predictor variables are listed in Table I. STATA 14.0 (StataCorp LLC, College Station, Texas) was used for all analyses.
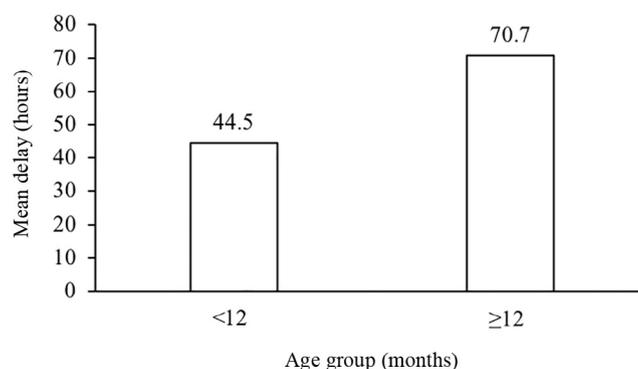

Figure. Relationship between age and time from onset of fever to treatment of febrile UTIs.

Results

Of the 802 children enrolled in the RIVUR and CUTIE studies, we excluded 113 children who were missing information about treatment delay and 29 children who were afebrile; 660

Table I. Demographic and clinical characteristics of 689 children with UTI

Characteristics	Number (%)
Age, mo	
<12	366 (55.5)
≥12	294 (44.5)
Sex	
Male	59 (8.9)
Female	601 (91.1)
History of UTI	
Yes	46 (7.9)
No	537 (92.1)
Ethnicity	
Hispanic	95 (14.5)
Not Hispanic	561 (85.5)
Race	
White	504 (77.8)
Black	52 (8.0)
Asian	17 (2.6)
Multiracial	48 (7.4)
Other	27 (4.2)
Primary caregiver's education	
Less than high school	14 (2.1)
Some high school	37 (5.7)
Completed high school	143 (21.8)
Some college	165 (25.2)
Completed college	191 (29.2)
Postgraduate	105 (16.0)
Income	
<$13 500	51 (9.0)
$13 500-23 499	60 (10.6)
$23 500-33 499	54 (9.6)
$33 500-57 999	106 (18.8)
$58 000-99 999	163 (28.9)
$100 000-149 999	83 (14.7)
≥$150 000	48 (8.5)
Insurance	
Commercial	427 (65.3)
Noncommercial	227 (34.7)
Tricare	10 (1.5)
Medicaid	213 (32.6)
Uninsured	3 (0.5)
Multi-insured	1 (0.2)

Table II. Factors associated with delayed treatment on univariate analysis

Characteristics	Delay, h Mean (SD)	P value
Age, mo		<.001
<12	44.5 (44.5)	
≥12	70.7 (53.2)	
Sex		.32
Male	50.0 (42.4)	
Female	56.8 (50.9)	
History of UTI		.46
Yes	61.8 (57.1)	
No	56.1 (50.2)	
Ethnicity		.56
Hispanic	53.6 (46.8)	
Not Hispanic	56.8 (50.9)	
Race		.81
White	56.9 (51.7)	
Black	50.2 (46.2)	
Asian	60.0 (41.9)	
Multiracial	58.8 (53.1)	
Other	49.0 (35.4)	
Primary caregiver's education		.97
Less than high school	55.7 (35.7)	
Some high school	48.9 (38.8)	
Completed high school	56.1 (45.7)	
Some college	57.5 (54.9)	
Completed college	57.1 (50.8)	
Postgraduate	56.5 (54.0)	
Income		.62
<$13 500	49.4 (37.5)	
$13 500-23 499	48.3 (35.8)	
$23 500-33 499	49.2 (44.5)	
$33 500-57 999	61.1 (54.0)	
$58 000-99 999	57.4 (51.3)	
$100 000-149 999	57.1 (58.1)	
≥$150 000	55.7 (58.6)	
Insurance		.002
Commercial	60.7 (54.7)	
Noncommercial	48.1 (40.0)	

Table III. Predictors associated with delayed treatment on multivariable linear regression

Predictors	Contrast	Coefficient (SD)	Beta	P value
Age	1-mo increase	0.7 (0.1)	0.24	<.001
Sex	Female vs male	0.6 (8.2)	0.00	.94
Race	Nonwhite vs white	5.1 (5.6)	0.04	.36
Ethnicity	Hispanic vs other	2.8 (6.7)	0.02	.68
History of UTI	No vs yes	6.1 (8.4)	0.03	.47
Primary caregiver's highest education level	High school or less vs other	10.4 (6.1)	0.09	.09
Income below Federal Poverty Level	No vs yes	5.5 (7.2)	0.5	.44
Commercial insurance	No vs yes	13.4 (6.5)	0.12	.04

children were included in the analysis. The mean age of the study population was 17.0 months. Other characteristics of the study population can be found in Table I. Compared with children who were excluded, those included were significantly younger (mean age 17.0 months for included children vs 36.0 months for excluded children) and significantly less likely to have a previous history of UTIs (7.9% vs 20.9%). All other demographic characteristics were comparable in included and excluded patients.

The mean time before the initiation of antimicrobial therapy was 56.2 hours. On univariate analysis, only age and insurance type were significantly associated with treatment delay on ($P < .001$ and $P = .002$ respectively). Older children were more likely to have delayed treatment; children <6, ≥6-11, ≥12-23, ≥24 months old had mean delay times of 30.3, 59.3, 68.5, and 72.6 hours, respectively. Treatment was delayed by an average of 26.2 hours in children ≥12 months of age compared with younger children (Figure). When we compared commercial with noncommercial insurance types, treatment was delayed by a mean of 12.6 hours in patients with commercial insurance (Table II).

In the multivariable model, older age and insurance status remained significantly associated with longer treatment delays even after we adjusted for sex, history of UTI, ethnicity, race, education, insurance, and income (Table III).

Discussion

We found that febrile children with UTI who were ≥12 months of age received antimicrobial therapy 26.2 hours later than children <12 months of age. This finding is consistent with a previous study[11] and might reflect increased parental concern and urgency toward febrile illnesses in younger children. This is concerning because recent studies have found that older children with febrile UTIs may have greater rates of renal scarring compared with younger children; a study conducted on a population derived from RIVUR and CUTIE studies[2] as well as a meta-analysis[12] of 9 cohort studies also found greater rates of renal scarring in older children. Consequently, it seems important to educate physicians, parents, and triage nurses about the importance of early evaluation of children with fever, even for children >12 months of age.

We also found that children with commercial insurance had longer delays than those without commercial insurance. This is contrary to studies in adult populations and in studies from pediatric emergency departments, which found that patients who were uninsured or receiving Medicaid had increased delays compared with those with private insurance.[7,13] Some reports suggest that, compared with patients without commercial insurance, patients with commercial insurance are less likely to seek care in an emergency department.[13-16] Delayed treatment in children with commercial insurance in our study could be explained if these patients were disproportionately evaluated in private clinics, where screening tests for UTI often are sent to an off-site laboratory (compared with an emergency department, where testing occurs on site 24 hours a day). It also is possible in the private sector that providers choose to follow patients before pursuing UTI, or parents and providers desire to avoid catheterization, especially of older children. In contrast, children without commercial insurance may have been more likely to have been evaluated in an emergency department, where testing is performed onsite.

A limitation of our study is that the location where the child was first evaluated and treated for UTI (ie, emergency department vs outpatient clinic or private office) was not gathered, which prevented us from examining whether it was associated with delayed treatment. Also, duration of fever was reported by parents and thus may not be accurate. Strengths of our study include the relatively large samples size, involvement of multiple centers, and availability of data on family income and other potential confounding factors.

Older age and delayed antimicrobial treatment of febrile UTIs are associated. It is important to advise parents to seek evaluation for prompt treatment of UTIs, especially in older children. These data also should encourage providers to pursue diagnosis and rapid treatment. ∎

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References

1. Hellstrom A, Hanson E, Hansson S, Hjalmas K, Jodal U. Association between urinary symptoms at 7 years old and previous urinary tract infection. Arch Dis Child 1991;66:232-4.
2. Shaikh N, Mattoo TK, Keren R, Ivanova A, Cui G, Moxey-Mims M, et al. Early antibiotic treatment for pediatric febrile urinary tract infection and renal scarring. JAMA Pediatr 2016;170:848-54.

3. Investigators RT, Hoberman A, Greenfield SP, Mattoo TK, Keren R, Mathews R, et al. Antimicrobial prophylaxis for children with vesicoureteral reflux. N Engl J Med 2014;370:2367-76.

4. Keren R, Shaikh N, Pohl H, Gravens-Mueller L, Ivanova A, Zaoutis L, et al. Risk factors for recurrent urinary tract infection and renal scarring. Pediatrics 2015;136:e13-21.

5. Dracup K, Moser DK. Beyond sociodemographics: factors influencing the decision to seek treatment for symptoms of acute myocardial infarction. Heart Lung 1997;26:253-62.

6. Lannin DR, Mathews HF, Mitchell J, Swanson MS, Swanson FH, Edwards MS. Influence of socioeconomic and cultural factors on racial differences in late-stage presentation of breast cancer. JAMA 1998;279:1801-7.

7. Weissman JS, Stern R, Fielding SL, Epstein AM. Delayed access to health care: risk factors, reasons, and consequences. Ann Intern Med 1991;114:325-31.

8. Mayberry RM, Mili F, Ofili E. Racial and ethnic differences in access to medical care. Med Care Res Rev 2000;57(suppl 1):108-45.

9. Moser DK, Kimble LP, Alberts MJ, Alonzo A, Croft JB, Dracup K, et al. Reducing delay in seeking treatment by patients with acute coronary syndrome and stroke: a scientific statement from the American Heart Association Council on cardiovascular nursing and stroke council. Circulation 2006;114:168-82.

10. Newacheck PW, Stoddard JJ, Hughes DC, Pearl M. Health insurance and access to primary care for children. N Engl J Med 1998;338:513-9.

11. Doganis D, Siafas K, Mavrikou M, Issaris G, Martirosova A, Perperidis G, et al. Does early treatment of urinary tract infection prevent renal damage? Pediatrics 2007;120:e922-8.

12. Shaikh N, Craig JC, Rovers MM, Da Dalt L, Gardikis S, Hoberman A, et al. Identification of children and adolescents at risk for renal scarring after a first urinary tract infection: a meta-analysis with individual patient data. JAMA Pediatr 2014;168:893-900.

13. Smink DS, Fishman SJ, Kleinman K, Finkelstein JA. Effects of race, insurance status, and hospital volume on perforated appendicitis in children. Pediatrics 2005;115:920-5.

14. Chande VT, Krug SE, Warm EF. Pediatric emergency department utilization habits: a consumer survey. Pediatr Emerg Care 1996;12:27-30.

15. Irvin CB, Fox JM, Smude B. Are there disparities in emergency care for uninsured, medicaid, and privately insured patients? Acad Emerg Med 2003;10:1271-7.

16. Phelps K, Taylor C, Kimmel S, Nagel R, Klein W, Puczynski S. Factors associated with emergency department utilization for nonurgent pediatric problems. Arch Fam Med 2000;9:1086-92.