Predictors of Long Length of Stay in Infants Hospitalized With Urinary Tract Infection

AUTHORS

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KEY WORDS

urinary tract infections, length of stay, diagnostic imaging, pediatrics

ABBREVIATIONS

AAP: American Academy of Pediatrics
CI: confidence interval
ED: emergency department
HSC: Hospital for Sick Children
ICD-10: International Classification of Diseases, 10th Revision
IV: intravenous
LOS: length of stay
OR: odds ratio
UTI: urinary tract infection
VCUG: voiding cystourethrogram

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abstract

OBJECTIVE: Urinary tract infection (UTI) is the most common serious bacterial infection in infants. To use resources optimally, factors contributing to costs through length of stay (LOS) must be identified. This study sought to identify clinical and health system factors associated with long LOS in infants with UTI.

METHODS: Using a case–control design, we included infants <6 months old hospitalized with UTI. Cases had LOS ≥96 hours; controls had LOS <96 hours. Clinical and health system variables were extracted from medical records. Cases and controls were compared by using comparative statistics and multiple logistic regression analysis.

RESULTS: Cases ($n = 71$) and controls ($n = 71$) did not differ by gender; cases were more likely to be younger (4.2 vs 7.1 weeks, $P = .04$), born preterm (13% vs 3%, $P = .03$), have known genitourinary disease (17% vs 4%, $P = .01$), an ultrasound (85% vs 68%, $P = .02$) or voiding cystourethrogram (VCUG) (61% vs 34%, $P = .001$) ordered, longer wait for VCUG (53 vs 27 hours, $P = .002$), consult requested (54% vs 10%, $P < .001$), and longer duration of intravenous (IV) antibiotics (125 vs 62 hours, $P < .001$). Multiple logistic regression demonstrated that cases were more likely to be premature (odds ratio [OR] 7.6), have known genitourinary disease (OR 7.3), and have VCUG ordered in the hospital (OR 4.5).

CONCLUSIONS: Infants who are older, are born full term, have no genitourinary disease, receive shorter courses of IV antibiotics, and do not have a VCUG ordered have shorter stays and may be eligible for a short-stay unit. Earlier transition to oral antibiotics and delayed ordering of a VCUG may decrease LOS.

Urinary tract infection (UTI) is the most common serious bacterial infection in young infants.[1] Approximately 7% of girls and 2% of boys will have a UTI by 6 years of age.[2] Although most UTIs can be managed effectively on an outpatient basis, infants are often hospitalized for treatment.[3] UTI accounts for ~8% of infant infectious disease hospitalizations and ~2% of all pediatric hospitalizations.[4,5] Although rates and duration of hospitalization for UTI have remained fairly constant over the past decade, hospital costs have risen by ~34% and continue to impose a significant financial burden on the health care system.[5]

To use health care resources optimally and reduce costs wherever possible, it is important to identify factors contributing to costs through hospitalization. Previous studies using a large administrative database have investigated selected factors contributing to length of stay (LOS) for UTI and found that children who were younger, were hospitalized at an institution without clinical practice guidelines, or received initial empiric antibiotic therapy to which the uropathogen was not susceptible had greater LOS.[6,7] We sought to identify additional clinical and health system factors associated with long LOS in infants hospitalized for UTI to facilitate evidence-based decision-making about admission to a short-stay unit and to identify processes that may be extending LOS and thus may be targets for future cost-saving measures.

METHODS

Design and Setting

This was a case–control study conducted at the Hospital for Sick Children (HSC) in Toronto, Ontario, Canada. This research was approved by the institutional research ethics board.

Study Population

Infants who met the following criteria were included: age <6 months; admitted to the Pediatric Medicine Inpatient Unit at HSC between April 2002 and June 2011; and diagnosis of UTI, indicated by one of the following International Classification of Diseases, 10th Revision (ICD-10) discharge diagnosis codes: N39.0 (UTI, site not specified), N10 (acute tubulo-interstitial nephritis including acute pyelonephritis), N12 (tubulo-interstitial nephritis, not specified as acute or chronic, including pyelonephritis NOS), N13.6 (pyonephrosis), N15.1 (renal and perinephric abscess), N28.8 (other specified disorders of kidney and ureter including pyelitis, pyeloureteritis, ureteritis), N30.0 (acute cystitis), N30.8 (other cystitis), N30.9 (cystitis, unspecified), or P39.3 (neonatal UTI). Diagnoses of UTI by ICD-10 code were confirmed by positive urine culture but not urinalysis.

Infants who met the following criteria were excluded: admission after call back to the hospital for positive blood or urine cultures, admission after a repeat visit to the emergency department (ED), admission ≤30 days from discharge from a previous hospitalization for UTI, transfer to HSC from another hospital, transfer to another hospital on discharge, positive blood (except for coagulase negative *Staphylococcus,* a common contaminant) or cerebrospinal fluid cultures, treatment as presumed meningitis, and no urine culture documented, or urine culture with no or insignificant growth or growth of mixed organisms. For infants with multiple hospitalizations, only 1 randomly selected hospitalization was included, unless hospitalizations were ≤30 days apart, in which case the first hospitalization was selected.

Outcome Variable

LOS from the time of admission to the Pediatric Medicine Inpatient Unit to time of discharge was collected from patient charts. Time of admission or discharge was defined as the time the order to admit the patient to or discharge the patient from the Pediatric Medicine Inpatient Unit was written by the Pediatric Medicine staff or housestaff. Cases were defined as infants with LOS ≥96 hours (long-stay group) and controls as infants with LOS <96 hours (short-stay group). Median hospital mean LOS across several children's hospitals in the United States reported in the literature is 3.2 days.[6] Another study investigating the relationship between length of intravenous (IV) antibiotic therapy and treatment failure considered long-duration IV therapy to be ≥4 days.[8] Results from these 2 studies led to our selection of 96 hours as a breakpoint for defining cases and controls. An equal number of controls was randomly selected by random number generator to achieve a 1:1 case-to-control ratio.

Explanatory Variables

The following clinical and health system variables were defined a priori, abstracted from each patient's health record using a standardized data collection form and analyzed as possible predictors of LOS: age, gestational age, birth weight, gender, past medical history including known genitourinary disease, maximum temperature in the ED, blood band count, blood leukocyte count, Canadian Triage Acuity Scale score, presence of lethargy, dehydration, vomiting or poor feeding on presentation, urinalysis results, urine culture results including sensitivities, nasopharyngeal swab results, order for, wait times and results of ultrasound and voiding cystourethrogram (VCUG), admission to the intensive care unit, requests for consults, and duration of IV antibiotic therapy.

Statistical Analysis

Continuous variables were analyzed by using *t* test and Mann–Whitney *U* test, and discrete variables using χ^2 and Fisher's exact tests, to compare the short-stay and long-stay groups with respect to each of the clinical and health system variables specified. Multiple logistic regression analysis was also performed by using clinically and statistically significant variables. The optimal model was selected initially by χ^2 score criterion and modified to include only clinically significant variables. A *P* value of ≤.05 was considered significant.

RESULTS

Study Population

A total of 522 infants <6 months of age were admitted to HSC for UTI between April 2002 and June 2011. Of these, 141

(27%) were hospitalized for ≥96 hours (cases), and 381 (73%) were in the hospital <96 hours (controls). Seventy cases were excluded; 6 were admitted after call back to the hospital for positive blood or urine cultures, 1 was admitted after a repeat visit to the ED, 7 were admitted ≤30 days from discharge from a previous hospitalization for UTI, 17 were transferred to HSC from another hospital, 11 were transferred to another hospital on discharge, 17 had positive blood cultures, 1 had presumed meningitis, 4 were admitted to another service with Pediatric Medicine consulting, 4 did not have a positive urine culture documented, and 2 cases were excluded for infants with multiple hospitalizations.

For the 71 remaining cases, 71 controls were ultimately selected, with random selection from the total cohort of controls occurring until the target number was achieved, taking into account exclusions. During selection, 40 controls were excluded: 1 was admitted after call back to the hospital for positive blood or urine cultures, 2 were admitted after a repeat visit to the ED, 2 were admitted ≤30 days from discharge from a previous hospitalization for UTI, 5 were transferred to HSC from another hospital, 11 were transferred to another hospital on discharge, 1 was both transferred to HSC from another hospital and transferred to another hospital on discharge, 3 had positive blood cultures, 7 did not have a culture-proven UTI, and 8 controls were excluded for infants with multiple hospitalizations. Only controls randomly selected from the larger control pool were examined for exclusion criteria.

The median LOS for the control group was 62.5 hours (range 37.9–95.6 hours), and the median LOS for the case group was 140.1 hours (range 96.6–1264.6 hours).

Clinical Predictors

Patient characteristics of cases and controls are shown in Table 1. Cases were significantly more likely than controls to be younger (4.2 vs 7.1 weeks, $P = .04$); be born prematurely, defined as birth at a gestational age of <37 completed weeks (13% vs 3%, $P = .03$); and have known genitourinary disease (17% vs 4%, $P = .01$). Cases and controls did not differ by gender or birth weight.

Clinical features and laboratory results on presentation are described in Table 2. On presentation, cases and controls did not differ significantly by presence of lethargy, dehydration, vomiting, maximum temperature or presence of fever in the ED, or Canadian Triage Acuity Scale score.

Features of the clinical course in the hospital are described in Table 3. Cases and controls did not differ by presence of leukocytes, bacteria, or erythrocytes found on urine microscopy, but cases were more likely than controls to have an organism other than *E. coli* found on urine culture (39% vs 11%, $P < .001$). There was no significant difference between the groups in rates of resistance to a single antibiotic or to both antibiotics with oral equivalents. Among infants for whom diagnostic imaging was performed in the hospital, cases were significantly more likely than controls to have an abnormal ultrasound result (80% vs 60%, $P = .03$), but no difference was seen in VCUG results. Cases and controls did not differ by rates of admission to intensive care.

Health System Predictors

Health system factors and resource use for cases and controls are described in Table 4. Cases were significantly more likely than controls to have an ultrasound (85% vs 68%, $P = .02$) or VCUG (61% vs 34%, $P = .001$) ordered in the hospital. Cases had a longer waiting time for their VCUG than controls (53.2 vs 27.2 hours, $P = .002$), but there was no difference in waiting time for ultrasound. Cases were more likely than controls to have a consult requested from urology (18% vs 3%, $P = .003$), nephrology (15% vs 3%, $P = .009$), or another service (39% vs 6%, $P < .001$). These other services consulted were anesthesia, cardiology, dermatology, endocrinology, gastroenterology, general surgery, genetics, hematology, infectious diseases, neonatal intensive care, neurology, neurosurgery, ophthalmology, otolaryngology, and pediatric intensive care. Cases were also more likely to receive IV antibiotic therapy for >48

TABLE 1 Patient Characteristics for Cases and Controls

Predictor	Control Central Tendency	Control, *n*	Case Central Tendency	Case, *n*	*P*
Age (wk), median [IQR]	7.1 [3.3–13.1]	71	4.2 [2.1–10.6]	71	.04
Neonate,[a] *n* (%)	22 (31)	71	32 (45)	71	.08
Gender (male), *n* (%)	49 (69)	71	56 (79)	71	.18
Gestational age (wk), median [IQR]	40 [38–40]	49	39 [37–40]	57	.05
Preterm,[b] *n* (%)	2 (3)	70	9 (13)	70	.03
Birth wt (g), mean ± SD	3473 ± 620	65	3333 ± 829	65	.28
Previous medical condition, *n* (%)	24 (34)	71	34 (48)	71	.09
Known genitourinary disease, *n* (%)	3 (4)	71	12 (17)	71	.01

IQR, interquartile range. SD, standard deviation.
[a] Neonate defined as admission to the hospital at <28 d of age.
[b] Preterm defined as birth at gestational age <37 wk.

TABLE 2 Clinical Features and Laboratory Results on Presentation to ED for Cases and Controls

Predictor	Control Central Tendency	Control, *n*	Case Central Tendency	Case, *n*	*P*
CTAS 1 or 2, *n* (%)	30 (42)	71	36 (52)	69	.24
Maximum temperature (°C), mean ± SD	38.5 ± 1.0	71	38.5 ± 1.2	71	.84
Febrile, *n* (%)	56 (79)	71	51 (72)	71	.33
Lethargy, *n* (%)	2 (3)	71	3 (4)	70	.68
Dehydration, *n* (%)	2 (3)	71	7 (10)	71	.17
Vomiting, *n* (%)	21 (30)	70	27 (40)	68	.23
Poor feeding, *n* (%)	36 (51)	71	46 (66)	70	.07
Blood work results					
Band count (10^9/L), median [IQR]	0.35 [0.0–1.1]	71	0.25 [0.03–0.9]	71	.87
White blood cell count (10^9/L), median [IQR]	17.8 [11.7–21.4]	71	15.0 [9.3–20.4]	71	.06
Urinalysis results					
Blood, *n* (%)	55 (77)	71	42 (65)	65	.10
Protein, *n* (%)	33 (47)	70	33 (51)	65	.67
Nitrites, *n* (%)	30 (42)	71	19 (29)	65	.11
Leukocytes, *n* (%)	63 (89)	71	46 (70)	66	.01

CTAS, Canadian Triage Acuity Scale; IQR, interquartile range. SD, standard deviation.

hours (97% vs 77%, $P < .001$) and had a significantly longer duration of IV antibiotic therapy overall (124.7 vs 61.5 hours, $P < .001$).

Multiple Logistic Regression Model

The final multiple logistic regression model contained 3 clinically meaningful variables: prematurity, history of genitourinary disease, and order for a VCUG as an inpatient (Table 5). Cases were more likely than controls to be premature (odds ratio [OR] 7.6; 95% confidence interval [CI], 1.4–40.0) and have known genitourinary disease (OR 7.3; 95% CI, 1.8–29.5). Cases were also more likely than controls to have a VCUG ordered in the hospital (OR 4.5; 95% CI, 2.1–9.7).

DISCUSSION

In this study, we found several clinical and health system factors associated with long LOS for infants <6 months of age admitted to the hospital with UTI. Clinical factors associated with a long hospital stay were younger age, prematurity, and known genitourinary disease. Poor feeding was not significantly associated with long hospital stay, contradicting our hypothesis that infants with long stays would be more likely to present with poor feeding. However, it is possible that our study was underpowered to detect this relationship and that a study with a larger sample size may prove an association. Health system factors associated with long stay were ordering an ultrasound or VCUG in the hospital, longer wait time for VCUG, consult requested, and longer duration of IV antibiotic therapy. In multiple regression analysis, factors associated with long stay included prematurity, known genitourinary disease, and order for a VCUG in the hospital.

Short-stay units are becoming increasingly common, but there are no evidence-based guidelines that recommend which patients with UTI are suitable for admission to a pediatric short-stay unit. Given that infants who are younger, were born prematurely, and have known genitourinary disease tend to have longer stays in the hospital, it is conceivable that children without these factors might be ideally suited to admission to the short-stay unit. Allocation of resources in such a targeted way may help safely reduce costs associated with hospitalizations for infants with UTIs. The results of this study may also provide anticipatory guidance for parents and health care providers alike in predicting a short or long stay based on clinical and health system factors.

Previous studies have investigated various factors associated with LOS in children with UTIs. Conway and Keren[6] conducted a retrospective

TABLE 3 Features of Clinical Course in the Hospital for Cases and Controls

Predictor	Controls, *n* (%)	Control, *n*	Cases, *n* (%)	Case, *n*	*P*
Urine cell count results					
Leukocytes in urine	54 (76)	71	48 (68)	71	.26
Bacteria in urine	51 (72)	71	50 (70)	71	.85
Erythrocytes in urine	36 (51)	71	29 (41)	71	.24
Organism other than *E. coli* on urine culture	8 (11)	71	28 (39)	71	<.001
Antibiotic resistance					
Ampicillin	32 (46)	69	31 (46)	67	.99
Gentamicin	3 (5)	65	2 (4)	57	1.00
Cephalosporins	12 (19)	64	15 (26)	57	.32
Ampicillin and cephalosporins	12 (18)	68	15 (22)	67	.49
Imaging results					
Abnormal ultrasound	29 (60)	48	48 (80)	60	.03
Abnormal VCUG	7 (29)	24	19 (44)	43	.23
NICU or PICU admission	0 (0)	71	3 (4)	71	.25

NICU, neonatal intensive care unit; PICU, pediatric intensive care unit.

TABLE 4 Health System Factors and Resource Utilization for Cases and Controls

Predictor	Control Central Tendency	Control, *n*	Case Central Tendency	Case, *n*	*P*
Order for imaging as an inpatient					
Ultrasound, *n* (%)	48 (68)	71	60 (85)	71	.02
VCUG, *n* (%)	24 (34)	71	43 (61)	71	.001
Wait time for imaging					
Ultrasound (h), median [IQR]	13.8 [4.0–33.5]	46	22.6 [4.5–48.4]	59	.30
VCUG (h), median [IQR]	27.2 [19.8–47.1]	24	53.2 [39.6–90.1]	43	.002
Request for consult					
Any service, *n* (%)	7 (10)	71	38 (54)	71	<.001
Urology, *n* (%)	2 (3)	71	13 (18)	71	.003
Nephrology, *n* (%)	2 (3)	71	11 (15)	71	.009
Another service, *n* (%)	4 (6)	71	28 (39)	71	<.001
Duration of IV antibiotic therapy (h), median [IQR]	61.5 [49.4–71.8]	70	124.7 [91.1–164.4]	70	<.001
IV antibiotic therapy >48 h, *n* (%)	54 (77)	70	68 (97)	70	<.001

IQR, interquartile range.

cohort study examining the association of several patient and hospital factors with LOS in 20 892 children from 1 month to 12 years of age admitted with a UTI. Data were obtained from the Pediatric Health Information System, a large administrative database containing data from multiple children's hospitals in the United States. This study found that patients with longer stays were more likely to be younger, male, black, and Hispanic. Hospitals without clinical practice guidelines also had longer hospital stays. Our study similarly found that infants with longer hospital stays were more likely to be younger, although patient gender was not significant in our analysis.

Jerardi et al[7] also performed a retrospective cohort study investigating the association between discordant antibiotic therapy (initial antibiotic therapy to which the uropathogen is not susceptible) and LOS and time to fever resolution in 216 children from 3 days to 18 years old admitted with UTI. This study also obtained data from the Pediatric Health Information System, supplemented by data from medical records. This study found that discordant antibiotic therapy, which occurred in ~10% of cases, was associated with longer stays in the hospital but was not associated with time to fever resolution. Discordant antibiotic therapy occurred more commonly in non–*E. coli* UTIs. Although our study did not specifically investigate the relationship between discordant antibiotic therapy and LOS, we did not find any significant difference in rates of resistance to the most commonly used empiric antibiotics among infants with short and long stays in the hospital. However, we did find that infants with long stays in the hospital were more likely to be infected with an organism other than *E. coli*.

Several studies have investigated the optimal treatment of febrile UTIs. Montini et al[9] randomly assigned children aged 1 month to <7 years with a febrile UTI to either oral antibiotics for 10 days or IV antibiotics for 3 days followed by oral antibiotics for 7 days. This study found no significant difference between the groups in terms of time to defervescence and renal scarring at 12 months. Bocquet et al[10] randomly assigned children aged 1 to 36 months with their first episode of febrile UTI to either oral antibiotics for 10 days or IV antibiotics for 4 days followed by oral antibiotics for 6 days. There was no difference between the 2 groups in terms of rates of renal scarring at 6 to 8 months. In a retrospective cohort study, Brady et al[8] found that there was no difference in rates of readmission to the hospital between infants <6 months old hospitalized for UTI who had been treated with IV antibiotics for ≤3 days and those treated ≥4 days. Bouissou et al[11] randomly assigned children aged 3 months to 16 years with their first episode of pyelonephritis to either 3 days of IV antibiotics followed by 5 days of oral antibiotics or 8 days of IV antibiotics. This study found that the rates of renal scarring at 6 to 9 months were not significantly different between the children who received 3 or 8 days of IV antibiotics. Hodson et al[12] performed a meta-analysis of 23 studies, which found no difference in clinical outcomes between children treated with oral antibiotics and IV antibiotics initially followed by oral antibiotics, or short-course and long-course IV antibiotics. Clinical practice guidelines from the American Academy of Pediatrics (AAP)[13] state that oral and IV antibiotics are equally effective for treatment

TABLE 5 Multiple Logistic Regression Analysis

Predictor	OR	95% CI	*P*
Preterm[a]	7.6	1.4–40.0	.02
Known genitourinary disease	7.3	1.8–29.5	.006
Order for VCUG as an inpatient	4.5	2.1–9.7	<.001

[a] Preterm defined as birth at gestational age <37 wk.

of febrile UTIs. The current study found that almost all infants admitted to our institution with UTI were treated with IV antibiotics, many with extensive duration. Infants with longer hospital stays are more likely to have longer duration of IV antibiotic therapy, which may reflect greater illness severity in these children both causing long stays and necessitating longer durations of IV therapy or long durations of IV therapy causing longer hospital stays. It is thus possible that initiating shorter-course IV or oral antibiotics, as suggested by previous studies, may decrease LOS.

Limitations of this study include the retrospective design and small sample size. Because the data collection was retrospective, certain data points were not always recorded in the medical chart, leading to some missing data. However, data regarding diagnostic imaging (ordering, timing, and results) were well documented. We were also unable to access medical records at other hospitals for infants who were both transferred into our hospital for care and transferred to another hospital on discharge, and therefore had to exclude these patients from our analysis, because overall LOS in the hospital was unknown. We chose to focus our research on infants admitted to the hospital so as to investigate factors associated with duration of inpatient stay, which contributes more to health care costs than outpatient treatment. However, in limiting our population to inpatients, we are unable to determine the proportion of UTIs managed on an outpatient basis in our institution and thus how this contributes to costs. Moreover, analyses of health resource use may have been subject to confounding by indication. Although infants with long stays clearly had more resource use, our study cannot determine whether these infants had a more complex or severe disease process, thus necessitating both longer hospital stays and more investigations and prolonged treatment, or if the additional resource use may have prolonged these infants' stays in the hospital. However, children with bacteremia and meningitis were excluded, and known genitourinary disease and ordering of a VCUG were independent risk factors. Although our study could not distinguish factors associated with unnecessarily long LOS from those associated with a necessarily long LOS, clinicians may consider these factors when assessing the needs of individual infants. In addition, given that our study was limited to a single center, results may not be generalizable to other institutions with different practices. Lastly, we chose a breakpoint of 4 days to define cases and controls based on previous publications. We acknowledge that other breakpoints may have also been appropriate and that our division between short and long stay may not apply to all institutions.

Strengths of this study include the many clinical and health system variables analyzed that were not examined in previous studies and our focus on the young infant age group.

The AAP guidelines provide recommendations about requisition of diagnostic imaging in infants with initial and recurrent UTIs.[13] The AAP recommends that renal and bladder ultrasound, but not VCUG, be routinely performed after a first febrile UTI. A VCUG should be performed if ultrasound findings are concerning or if the infant experiences a second febrile UTI, although a recent study of >2000 infants <60 months of age evaluating the sensitivity and specificity of ultrasound for abnormalities on VCUG suggests that ultrasound may not be a good screening test for vesicoureteral reflux.[14] Our study found that infants with longer stays in the hospital were more likely to have a VCUG ordered and longer wait time for their VCUG. Findings from our study, conducted before the AAP guidelines were published, suggest that delayed ordering of a VCUG until a second UTI or on an outpatient basis may substantially decrease the number of infants with longer hospital stays.

A recent initiative by Jerardi et al[15] evaluated the ability of several quality improvement interventions, including physician education and changes to order sets in the electronic medical record, to decrease ordering of VCUGs among children with an initial UTI and normal renal ultrasound in both an inpatient and outpatient setting. This quality improvement initiative demonstrated a decrease in inappropriate ordering of VCUGs from 92% to 0% within 1 month in the inpatient setting and from 100% to 40% within 4 months in the outpatient setting.

CONCLUSIONS

Infants who are older, were born at or after term, and do not have known genitourinary disease have shorter hospital stays and thus may be considered for admission to a short-stay unit in the hospital. Infants with long hospital stays have more health resource use, which may reflect greater disease severity or resource use prolonging hospital stays. These findings suggest that earlier transition to oral antibiotics and delayed ordering of a VCUG until a second UTI, as per AAP guidelines, or on an outpatient basis may substantially decrease the number of infants with longer hospital stays, although additional research is needed to delineate this relationship.

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