Antibiotic Resistance Patterns of Outpatient Pediatric Urinary Tract Infections

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Abbreviations and Acronyms

TMP/SMX = trimethoprim-sulfamethoxazole

TSN = The Surveillance Network

U.S. = United States

UTI = urinary tract infection

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Purpose: We characterize the current national patterns of antibiotic resistance of outpatient pediatric urinary tract infection.

Materials and Methods: We examined outpatient urinary isolates from patients younger than 18 years in 2009 using The Surveillance Network®, a database with antibiotic susceptibility results and patient demographic data from 195 United States hospitals. We determined the prevalence and antibiotic resistance patterns for the 6 most common uropathogens, ie Escherichia coli, Proteus mirabilis, Klebsiella, Enterobacter, Pseudomonas aeruginosa and Enterococcus. We compared differences in uropathogen prevalence between males and females using chi-square analysis.

Results: We identified 25,418 outpatient urinary isolates. E. coli was the most common uropathogen overall but the prevalence of E. coli was higher among females (83%) than males (50%, $p < 0.001$). Other common species among males were Enterococcus (17%), P. mirabilis (11%) and Klebsiella (10%). However, these uropathogens each accounted for 5% or less of female isolates ($p < 0.001$). Resistance among E. coli was highest for trimethoprim-sulfamethoxazole (24%) but lower for nitrofurantoin (less than 1%) and cephalothin (15%). Compared to 2002 Surveillance Network data, E. coli resistance rates increased for trimethoprim-sulfamethoxazole (from 23% to 31% in males and from 20% to 23% in females) and ciprofloxacin (from 1% to 10% and from 0.6% to 4%, respectively).

Conclusions: E. coli remains the most common pediatric uropathogen. Although widely used, trimethoprim-sulfamethoxazole is a poor empirical choice for pediatric urinary tract infections in many areas due to high resistance rates. First-generation cephalosporins and nitrofurantoin are appropriate narrow-spectrum alternatives given their low resistance rates. Local antibiograms should be used to assist with empirical urinary tract infection treatment.

Key Words: anti-bacterial agents; drug resistance, bacterial; pediatrics; urinary tract infections; uropathogenic Escherichia coli

Urinary tract infection is a common medical condition in children. The cumulative incidence in the first 6 years of life is 7% in girls and 2% in boys.[1] Collectively urinary tract infection accounts for 1.5 million to 1.75 million doctor visits annually.[2] Understanding antibiotic resistance patterns helps guide effective empirical antibiotic selection and decrease treatment failure. Ineffective empirical antibiotic therapy may contribute not only to increased morbidity, but also to increased costs due to prolonged antibiotic treatment, recurrent office or emergency room visits and hospital admissions.[3]

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There are limited data regarding the antibiotic resistance patterns of pediatric urinary tract infections in the outpatient setting. A previous study indicates that the most commonly used antibiotics for pediatric UTIs are TMP/SMX and broad-spectrum agents, especially third-generation cephalosporins.[2] There is not a clear explanation for these prescribing patterns, but it has been suggested that the increasing levels of antimicrobial resistance in the last decade have impacted antibiotic choice for a wide range of pathogens.[4] We describe the current national resistance patterns for the 6 most common uropathogens, ie Escherichia coli, Proteus mirabilis, Klebsiella, Enterobacter, Pseudomonas aeruginosa and Enterococcus.

METHODS

Study Design

We performed a retrospective observational study examining urinary isolates from patients younger than 18 years collected in the outpatient setting from clinical laboratories in the United States in 2009.

Data Sources

We analyzed data from The Surveillance Network, an electronic surveillance database that collects strain specific, qualitative and quantitative antimicrobial test results and patient demographic data from clinical laboratories across 195 U.S. hospitals across all 9 Census Bureau regions, ie Pacific, Mountain, West North Central, East North Central, New England, Mid Atlantic, South Atlantic, East South Central and West South Central. Data include antimicrobial agents tested, target organisms, infection site, institution type and test methodology. Patient demographic information including age, gender and site of infection are also available, although variables such as race and socioeconomic status are not available.

Each participating laboratory performs its own susceptibility testing. Positive culture data along with corresponding de-identified demographic data are sent to TSN for incorporation into the master data set. All participating laboratories use standard U.S. Food and Drug Administration testing methods with results interpreted according to the National Committee for Clinical Laboratory Standards, which specifies standardized methods for susceptibility testing including information about drug selection, interpretation and quality control with clear guidelines for minimum inhibitory concentrations.[5] If multiple isolates are collected from the same individual within a 5-day period, only the first isolate is used to determine susceptibility pattern.

We limited our data analysis to urine cultures obtained in the outpatient setting, defined as visits that took place at clinics or emergency departments. Isolates that grew more than 1 organism were considered contaminated and excluded. We also excluded urine samples obtained from outpatient skilled nursing and rehabilitation facilities. Finally, to prevent overestimation of resistance patterns, we imposed a strict definition of resistance and included only organisms that were truly resistant. Organisms with intermediate susceptibility were not included as "resistant" because numerous antibiotics concentrate in the urine and, therefore, can successfully eradicate certain bacteria in the urinary tract despite intermediate susceptibility.

Measurements

We analyzed antibiotic resistance patterns for the 6 most common pediatric uropathogens in the data set, ie E. coli, P. mirabilis, Klebsiella, Enterobacter, P. aeruginosa and Enterococcus. We report aggregate data for each organism and each of the 15 antibiotics (TMP/SMX, ampicillin, amoxicillin-clavulanate, nitrofurantoin, cephalothin, cefuroxime, ceftriaxone, cefazolin, ceftazidime, gentamicin, ciprofloxacin, piperacillin-tazobactam, imipenem, aztreonam and vancomycin). Broad-spectrum antibiotics were defined as amoxicillin-clavulanate, quinolones, macrolides, and second and third-generation cephalosporins.[2] Oral treatment options with a first-generation cephalosporin for outpatient UTI should be based on cephalothin susceptibility patterns since cephalothin is more predictive of cephalexin susceptibilities compared to cefazolin.[6,7] Further stratifications included patient demographic information (age, gender and geographic region). Age was evaluated as a categorical variable, with categories of younger than 2, 2 to 5, 6 to 12 and 13 to 17 years, because the prevalence of UTI varies by age in a nonlinear fashion.[8]

Statistical Analysis

Summary statistics were performed using frequencies and proportions for categorical data. Chi-square analysis was used to compare differences in uropathogen prevalence between males and females. All analyses were 2-sided, and $p \leq 0.05$ was considered statistically significant.

RESULTS

There were a total of 25,418 outpatient urinary isolates in 2009 from the 195 hospitals contributing data to TSN (table 1). The majority of these isolates (86%) were from females. Age distribution of isolates differed by gender. The smallest percentage of isolates in females was from children younger than 2 years (13%), while isolates were similarly distributed among the remaining age groups (28% in patients 2 to 5, 29% in patients 6 to 12 and 30% in patients 13 to 17 years). Conversely the majority of isolates in males were from children younger than 2 years (37%), and isolates from the remaining age groups were more variable (18%, 29% and 16%, respectively). Additionally, all 9 U.S. Census Bureau regions are represented, although not evenly so, with most isolates from the Pacific (greater than 20%) and South Atlantic (greater than 20%) regions, and few samples (less than 5%) from the Mountain, New England and East South Central regions.

E. coli was the most common uropathogen, accounting for 79% of urinary isolates overall. The prevalence of E. coli was significantly greater among females (83%) than males (50%, $p < 0.001$). All other species were more common in males than in females