Clinical Value of an Ambulatory-Based Antibiogram for Uropathogens in Children

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Unnecessarily broad-spectrum antibiotic prescribing for ambulatory pediatric urinary tract infections may result from clinicians not having antibiograms specific to this population. Comparing an existing hospital-based with a proposed ambulatory uropathogen antibiogram for children in Utah, *Escherichia coli* accounted for a larger percentage and was more susceptible to narrower-spectrum antibiotics, demonstrating the potential need for ambulatory pediatric antibiograms.

Key words. Antibiogram; Drug Resistance; Bacterial; Urinary Tract Infections; *Escherichia coli*

Urinary tract infections (UTIs) are among the most common bacterial infections in ambulatory pediatrics and require empiric antibiotic selection, pending the results of urine culture and sensitivity testing [1]. Empiric antibiotic selection for UTI is influenced by practice patterns, cost, guidelines, and, ideally, knowledge of regional resistance patterns. Empiric selection is challenging due to the emergence of antibiotic-resistant organisms in hospital and community settings. Emerging resistance, most often documented in antibiograms generated from hospitalized, as opposed to ambulatory patients, may drive providers to select unnecessarily broad-spectrum therapy in both settings [2].

Copp et al [3] have reported that broader-spectrum antibiotics (eg, third-generation cephalosporins) are prescribed one third of the time for ambulatory pediatric UTI. Broader-spectrum antibiotic use, when a narrower spectrum drug would suffice, has the potential to add cost and pressure for selecting antibiotic-resistant bacterial strains. Whereas pediatric UTI is a problem primarily managed in the outpatient setting, antibiotic selection is mostly based on data derived from inpatients. Hospital antibiograms may suggest different resistance rates than those that exist among ambulatory patients, thus leading providers to favor prescribing unnecessarily broad antibiotics. If this occurs, then presenting providers with data about regional antibiotic resistance patterns of uropathogens isolated from ambulatory pediatric could promote more judicious antibiotic use.

Although the spectrum and antimicrobial susceptibility of a variety of pediatric uropathogens have been well characterized in the literature [4-6], no studies have compared antibiogram data about uropathogens derived exclusively from ambulatory pediatric patients with traditional hospital-based antibiograms. The objective of this study was to compare the spectrum and antimicrobial susceptibility, using current antibiogram guidelines, of the most common uropathogens isolated in hospital and community clinic settings in Salt Lake County, Utah.

**MATERIALS AND METHODS**

**Setting**

This study was conducted at Intermountain Healthcare (IH), an integrated healthcare delivery organization that operates 23 hospitals and over 100 ambulatory primary care facilities throughout Utah and Idaho. Primary Children’s Medical Center (PCMC) is IH’s 289-bed children’s hospital that serves as both the community hospital for Salt Lake County, Utah, and as a tertiary referral center for 5 Intermountain West states (Utah, Idaho, Wyoming, Nevada, and Montana). PCMC has over 10 000 admissions and over 40 000 emergency
department visits annually. PCMC admissions account for the vast majority of pediatric hospitalizations in Salt Lake County and are the principal source of pediatric antibiograms.

Study Design and Population
We conducted a retrospective cross-sectional study. We identified positive urine cultures obtained from pediatric patients (<18 years of age) admitted to IH hospitals (n = 5, including PCMC) and seen at ambulatory clinics (n = 32) located in Salt Lake County, using the IH computerized microbiology database. Urinary isolates, for which an organism and its antimicrobial sensitivity profile were available and which were collected between January 1, 2008 and December 31, 2008, were included in our analyses. Cultures were considered positive if there was (1) growth of >10^3 colony-forming units (CFU)/mL of a single uropathogen and <10^2 CFU/mL urogenital or skin flora collected by catheterization or suprapubic aspiration; or (2) growth of >10^4 CFU/mL of a single uropathogen and <10^3 CFU/mL urogenital or skin flora collected by midstream clean catch.

Susceptibility Testing
IH laboratories follow Clinical and Laboratory Standards Institute (CLSI) guidelines for antimicrobial susceptibility testing, quality control and analysis, and presentation of cumulative results [7]. At PCMC, minimal inhibitory concentrations (MICs) are determined by disk diffusion for a maximum of 12 antibiotics selected by laboratory, pharmacy, and infectious disease personnel. Amoxicillin-clavulanate was not among the 12 selected for testing against inpatient urine isolates. At all other IH facilities, a standard MicroScan panel is used to determine MIC. CLSI MIC breakpoints are used to interpret susceptibility. For cefuroxime, where CLSI articulates 2 MIC breakpoints (oral vs parenteral), IH interpreted susceptibility based on the oral MIC breakpoint only.

Exclusion Criteria
Exclusions for spectrum analysis were as follows: we only included bacterial species with 5 or more bacterial isolates in the hospital-derived and ambulatory-derived groups. Exclusions for the antimicrobial susceptibility analysis were as follows: as per the CLSI guidelines, we (1) used only the first patient isolate, (2) excluded duplicate isolates, and (3) excluded species with less than 30 isolates from analysis [7]. Emergency department patients that were not admitted were excluded from both analyses.

Statistical Methods
We performed statistical comparisons of antimicrobial susceptibility using Fisher’s exact test. A two-tailed P value <.05 was considered statistically significant. After consulting with pediatric infectious disease physicians at PCMC, we set the threshold for clinical significance at ≥10% difference in antimicrobial susceptibility.

Human Subjects Protection
This study was approved by the Institutional Review Boards of IH and the University of Utah.

RESULTS
Prevalence and Spectrum
There were dramatic differences in the relative contribution of individual bacterial species to the overall number of isolates from hospital and ambulatory settings. A total of 243 bacterial isolates was obtained from urine collected from the hospitalized pediatric patients. *Escherichia coli* was the most common bacteria isolated (29.6%). Other bacteria isolated included the following: *Enterococcus* species (23.9%), *Enterobacter* species (9.9%), *Staphylococcus epidermidis* (9.5%), *Pseudomonas aeruginosa* (6.6%), *Klebsiella oxytoca* (5.4%), *Klebsiella pneumoniae* (4.9%), *Staphylococcus aureus* (4.5%), *Citrobacter* species (3.3%), and *Proteus mirabilis* (2.5%). A total of 696 bacterial isolates was obtained from urine collected in the ambulatory pediatric patients. *E. coli* was the most commonly isolated bacteria (85.5%). Other isolates included the following: *Enterococcus* species (3.6%), *S. epidermidis* (2.6%), *P. mirabilis* (2.3%), *K. pneumoniae* (1.9%), *Enterobacter* species (1.9%), *P. aeruginosa* (1.3%), and *Staphylococcus simulans* (1.0%).

Antimicrobial Susceptibility
*E. coli* was the only bacterial species with more than 30 isolates in both the hospital-derived and ambulatory-derived groups. Seventy-two hospital-derived and 595 ambulatory-derived urinary *E. coli* isolates were tested for antimicrobial susceptibility with 8 common antimicrobials (ampicillin, cephalexin, cefotaxime, ciprofloxacin, cefuroxime, nitrofurantoin, gentamicin, and trimethoprim-sulfamethoxazole). For all tested antimicrobials, susceptibility was higher in the ambulatory-derived urinary isolates compared with hospital-derived isolates (Table 1). The differences (ambulatory vs hospital) in antimicrobial susceptibility for ampicillin (54.6% vs 38.8%), cephalexin (54.8% vs 27.8%), and cefuroxime (98.3% vs 55.6%) were all clinically (ie, ≥10%) and statistically significant. No significant differences were demonstrated for the 5 other tested antibiotics. In comparing all hospital-derived vs ambulatory-derived urinary bacterial isolates tested for susceptibility to cefuroxime, we found that 51% (65 of 127) of the hospital isolates
Our study sought to determine whether anti-hospital-derived antibiograms for empiric antibiotic selection are prioritized. Community practitioners typically rely on available isolates. There is a paucity of uropathogen susceptibility data available for community physicians who treat pediatric patients. The susceptibility of Escherichia coli is the most commonly isolated uropathogen in both the hospital and the community, it is much more common in the community, accounting for >85% of bacterial isolates. When considering the likely etiology of UTI, a community pediatrician can be much more confident that an unknown uropathogen is E. coli compared with treatment among hospitalized patients. The susceptibility of E. coli to 3 of the 8 antibiotics commonly tested was significantly higher in the community. Although a previous study [3] indicated that third-generation cephalosporins are frequently prescribed for UTI in ambulatory pediatrics, these data suggest that in our community, cefuroxime can be relied upon for most patients.

This proof-of-concept study with pediatric UTI in our community demonstrates clinically important differences in best available bacterial culture results for pediatric UTI. Further research should seek to discover whether this discrepancy exists in other patient populations (ie, adults versus children), and in other geographic locales and with additional conditions (eg, skin and soft tissue infections). Developing antibiograms that are specific to certain conditions and clinical settings may improve empiric therapy decision making by increasing knowledge of local antibiotic resistance patterns [10]. Determining optimal dissemination mechanisms and rigorously assessing the degree to which these interventions improve antibiotic prescribing patterns should be prioritized.

This study has several limitations. Because of the small number of non–E. coli isolates collected from ambulatory patients, we were not able to evaluate less prevalent uropathogens for differences in susceptibility. The population of hospitalized patients and the resultant antibiogram data are heterogeneous, including those with and without underlying urologic abnormalities, and does not distinguish between community-onset and hospital-acquired infections. More granular information would come from detailed clinical studies that account for these patient factors. The extent to which our findings can be generalized to other communities is unknown.

CONCLUSIONS

Antibiograms derived from hospital-based laboratory data may provide inaccurate information about antibiotic resistance patterns for ambulatory pediatric patients. Ideally, clinicians will have access to computerized provider order entry, coupled with clinical decision support systems that take advantage of regional resistance data and the specific patient’s clinical condition and setting to provide targeted treatment recommendations. Until such systems are ubiquitous in practice, we should be striving to provide clinicians with community-level antibiograms tailored to specific populations and conditions.

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