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Original Contribution

Comparison of UTI antibiograms stratified by ED patient disposition☆,☆☆

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ABSTRACT

Objective: Institutional antibiograms guide Emergency Department (ED) clinicians' empiric antibiotic selection. For this study, we created and compared antibiograms of ED patients stratified by disposition (admitted or discharged).

Methods: We conducted a cross-sectional study at two hospitals for 2014, comparing antibiograms limited to *Escherichia coli* urinary tract infections. Study-Specific Antibiograms, created for the study, excluded polymicrobial samples and multiple cultures from the same patient. Study-Specific Antibiograms were arranged by patient disposition: admitted (IP-Only) vs discharged from the ED (ED-Only). Antibiogram data were presented as average antibiotic sensitivities with 95% confidence intervals and demographic data as medians with interquartile ranges. Sensitivities between Study-Specific Antibiograms were compared by Fisher's Exact Test, alpha = 0.05, 2 tails.

Results: For Hospital A, 13 antibiotics were compared between Study-Specific ED-Only (n = 313) vs IP-Only (n = 244). We found that sensitivities to all four antibiotics appropriate for empiric outpatient therapy by Infectious Disease Society of America guidelines were significantly ($p < 0.0001$) higher in the ED-Only compared to IP-Only groups: ciprofloxacin 80% (76–90%) vs 60% (53–69%), levofloxacin 81% (77–91%) vs 63% (57–72%), nitrofurantoin 75% (70–84%) vs 51% (44–58%), and trimethoprim/sulfamethoxazole 73% (68–82%) vs 58% (52–67%). For Hospital B, 14 antibiotics were compared between Study-Specific ED-Only (n = 256) and IP-Only (n = 168). Two out of the five appropriate empiric outpatient antibiotics had significantly ($p < 0.0001$) higher sensitivities for ED-Only compared to IP-Only: ciprofloxacin 87% (83–91%) vs 71% (64–78%) and levofloxacin 86% (82–91%) vs 71% (65–78%).

Conclusions: We found higher antibiotic sensitivities in ED-Only than the IP-Only Study-Specific Antibiograms. Our Study-Specific Antibiograms offer an alternative guide for antibiotic selection in the ED.

1. Introduction

Antibiotic resistance is a natural function of bacterial adaptation and has likely existed well before the routine use of antibiotics [1]. In the current era, however, the indiscriminate use of broad-spectrum antibiotics promotes bacterial resistance, prolongs hospitals stays, increases healthcare costs [2], and exposes patients to unnecessary adverse effects. The Centers for Disease Control (CDC) recommends four core strategies to address antibiotic resistance: 1) prevent the spread of infection and outbreaks, 2) track antibiotic resistance, 3) improve antibiotic stewardship, and 4) develop new drugs and diagnostic tests [3]. Of these four, the paramount strategy is antibiotic stewardship: the prudent use of antibiotics by prescribers [4].

The emergency department (ED) is at the forefront of the struggle for appropriate antibiotic use. As stated by May et al., [4], "the ED is at the interface between the hospital and the community." Among the large number of bacterial infections diagnosed and treated in the ED, urinary tract infections (UTIs) are among the most common [5]. Clinicians generally prescribe antibiotics in the ED before urine culture results are results available. This demands ED clinicians are equipped with the best information to guide empiric therapy, particularly accurate antibiograms that reflect the communities' resistance patterns. The 2011 Infectious Disease Society of America (IDSA) guidelines [6] for uncomplicated UTIs recommend consulting institutional

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antibiograms to predict local microbial resistance patterns. Because antibiograms are the cornerstone of empiric antibiotic selection, we seek to understand their development, strengths, limitations, and areas for improvement.

In this study we analyze two institutions' antibiograms and then offer our alternative. We developed Study-Specific Antibiograms stratified by ED patient disposition, IP-Only (admitted to the hospital) vs ED-Only (discharged from the ED), for a single pathogen from one tissue source (*E. coli* derived from urine specimens). We compared antibiotic sensitivities between Study-Specific IP-Only vs ED-Only Antibiograms.

We tested the null hypothesis that there would be no statistically significant differences between our Study-Specific IP-Only vs ED-Only Antibiograms for urinary *E. coli* antibiotic sensitivities.

2. Methods

2.1. Study design & setting

This was a cross-sectional study using data collected from de-identified electronic medical records (EMR) of eligible patients. A single Institutional Review Board of the State University of New York Downstate approved exemption status for both sites for this study prior to the collection and review of any data.

This study was carried out at Hospital A, a community hospital, which has 165,000 ED visits per year and >620 beds. Hospital B is an academic tertiary care center with approximately 70,000 ED visits per year and a 376-bed capacity.

2.2. Selection of participants

We selected UTIs because they are the most commonly diagnosed infection in the ED [7]. We focused on *E. coli* because it is the most commonly isolated organism from urine [8], accounting for 74% to 89% of isolates according to Zatorski et al. [9] and Hines et al. [10], respectively. Accordingly, empiric antimicrobial therapy is typically directed towards *E. coli*. We used the same inclusion criteria at each institution for each Study-Specific Antibiogram: a threshold colony forming unit per mL (CFU/mL) of $>10^5$ CFU/mL for clean catch urine samples.

We selected the antibiotics available from our institutions' antibiograms that the IDSA [6] recommend as first-line (nitrofurantoin and TMP/SMX) and second line (the fluoroquinolones) outpatient therapy. The Hospital A Antibiogram reports the susceptibility of *E. coli* to 19 antibiotics; five of which are not included in the Hospital B Antibiogram: cefotaxime, ceftazidime, ertapenem, imipenem/cilastatin, and levofloxacin. The Hospital B Antibiogram displays the *E. coli* susceptibility to 16 antibiotics, including two (moxifloxacin and nitrofurantoin) which the Hospital A Antibiogram does not publish.

The patient population of greatest interest to us was patients who are discharged from the ED. Emergency department clinicians prescribe empiric antibiotics without routinely reviewing culture results, and thus antibiograms are of the utmost importance in helping guide appropriate treatment.

2.3. Methods and measurements

2.3.1. Institutional antibiogram production and publication

Each institution publishes its own antibiograms using the same methodology for collecting samples for culture and testing of antibiotic sensitivities. The notable differences between the hospitals' institutional antibiograms include where the cultures were obtained (ED, ward patients, intensive care units, outpatient clinics), age of the patients (adults, pediatrics, or both), which antibiotics were displayed in the antibiograms, and timeframe. At Hospital A, antibiograms are produced semi-annually by the Department of Microbiology while at Hospital B, they are published annually by the Department of Pharmacology. Because Hospital A develops its antibiogram semi-annually and A Hospital B does so annually. Both institutions automatically exclude multiple samples from the same patient by Microscan automation. The Hospital A Antibiogram contains culture information from all departments (i.e., all inpatient units, all outpatient clinics, and the ED) and all ages (neonatal, pediatric, adult).

The Hospital B Antibiogram excludes isolates obtained in clinics or the ED and the data set is organized by hospital floor. Adult and pediatric patient data, however, are separated. The Hospital B Antibiogram reports isolates derived from MICU distinctly in one antibiogram. In another Hospital B Antibiogram, all the other adult hospital units are combined (e.g. cardiothoracic intensive care unit, coronary care unit, as well as medical, surgical, transplant, and hematology-oncology services). The Hospital B pediatric patient isolates are organized similarly.

As is typical for institutional antibiograms, neither Hospital A nor Hospital B separate isolates by tissue source (e.g. urine, blood, CSF, soft tissue, pleural fluid, etc.). Also like most other institutions, both Hospital A and Hospital B Antibiograms are point estimates of the data without providing further insight into the precision of the estimates (i.e. confidence intervals). The Hospital A Antibiogram also reports typical drug dosages, frequencies, cost, and information about prescribing restriction.

2.3.2. Study-specific antibiogram development

Our methodology to create Study-Specific Antibiograms at each hospital was based on the same goals but adapted to the distinct EMR systems. Our study combined two published antibiograms at Hospital A to create a comparable timeframe, January–December 2014. Because Hospital A develops its antibiogram semi-annually and A Hospital B does so annually, our study combined two published antibiograms at Hospital A to create a comparable timeframe, January–December 2014. At Hospital A, inclusion of isolates into the raw dataset was based on computer-generated selection of EMR. The program Toad, was used to run Oracle 11 managed Structured Query Language (SQL) in order to pull EMR data from a Clinical Data Warehouse produced by QuadraMed© (QuadraMed Corporation, Reston, VA). Specific conditions were put into the system in order to collect data solely on eligible isolates. Inclusion criteria consisted of the following: positive urine culture of *E. coli* with $>10^5$ CFU/mL for clean catch urine samples (negative urine cultures were excluded), a sampling timeframe of January–December 2014, and a discharge diagnosis of ICD-9-CM 590.0 (pyelonephritis), ICD-9-CM 595.0 (cystitis), or ICD-9-CM 599.0 (UTI, unspecified). Patients with only an emergent care event who did not undergo a subsequent hospitalization were readily differentiated for this study. This is how ED-Only visits were obtained.

At Hospital B the data collectors, LG, SL, MR, were already adept in the two EMR systems employed by the hospital (T-system© [Frankfurt, Germany] and Healthbridge). The MicroScan system used by the Hospital B Department of Microbiology was queried for all *E. coli* isolates that met criteria for sensitivity analysis between January 1, 2013 and December 31, 2014. This dataset included all specimens collected from the emergency department or clinics. Each data collector was given a trial of ten data points for training purposes prior to the formal collection of data. Prior data collection, each collector was trained on the inclusion and exclusion criteria and data extraction. Samples were excluded if from patients under eighteen years old, out-patient clinics, source tissue other than urine, and samples with more than one isolate. We recorded isolates that were sensitive as "Sensitive." We recorded isolates that were intermediate or resistant to an antibiotic as "Not Sensitive." A set of 10 patients was used to establish inter-rater reliability according to Cohen's kappa [11].

The antibiograms produced by the hospitals will be referred to as "Institutional," and those we created for study purposes will be referred to as "Study-Specific." The development of a Study-Specific Antibiogram offered a comparative dataset to test the null hypothesis. At Hospital A we developed three Study-Specific Antibiograms. The first is "Hospital-Wide," which refers to isolates derived from patients anywhere in