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Development of a urinary-specific antibiogram for gram-negative isolates: Impact of patient risk factors on susceptibility

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Background: Traditional antibiograms guide clinicians in selecting appropriate empiric antimicrobials, but they lack data on syndrome/disease-specific susceptibility, isolate location, polymicrobial infections, and patient risk factors. The aim of this study was to develop a urinary-specific antibiogram and to evaluate the impact of risk factors on antimicrobial susceptibility.

Methods: This retrospective descriptive study used culture and susceptibility data from January 1 to December 31, 2012. A urinary antibiogram specific for *Escherichia coli* (EC), *Proteus mirabilis* (PM), *Klebsiella pneumoniae* (KP), and *Pseudomonas aeruginosa* (PA) was developed. Urinary and standard antibiogram susceptibilities were compared. Urinary isolates were then stratified by risk factors—residence before admission, age, systemic antimicrobial use for ≤ 30 days, hospitalization for ≤ 30 days, and hospital unit—to determine the impact on antimicrobial susceptibility.

Results: There were 2,284 urinary isolate encounters. Overall antimicrobial susceptibility was increased, and the prevalence of extended-spectrum β -lactamase-producing isolates was significantly greater (KP, 14% vs 7% [$P = .001$]; EC, 13% vs 9% [$P < .001$]; PM, 18% vs 10% [$P = .004$]) in the urinary antibiogram vs the standard antibiogram. Health care facility residence had the greatest impact on susceptibility for all urinary isolates, especially on fluoroquinolone susceptibility for EC and PM.

Conclusions: Using a syndromic antibiogram and incorporating patient risk factors into susceptibility data may be more useful in guiding clinicians in selecting more appropriate empiric therapy.

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Antimicrobial resistance to gram-negative pathogens has increased considerably, impacting morbidity and mortality, and leading to more challenging therapeutic management.¹ Significant increases in *Klebsiella pneumoniae* (KP) resistance to third-generation cephalosporins, extended-spectrum β -lactamase (ESBL)-producing Enterobacteriaceae, and *Pseudomonas aeruginosa* (PA) resistance to fluoroquinolones are of particular concern and have been well documented by national antimicrobial surveillance programs.^{2–4} Gram-negative pathogens have been shown to affect hospital costs and length of stay. In one analysis, gram-negative resistant pathogens incurred a 29.3% higher total hospital cost and a 23.8% increase in length of stay compared with their susceptible counterparts.⁵ Increased antimicrobial resistance also can affect the utility of

currently available antimicrobials, which, combined with a lack of new antimicrobials in the pipeline, can make therapeutic management more difficult.

An antimicrobial regimen is often selected before culture data are available, but studies have shown that empiric treatment with broad-spectrum agents can increase harm to patients,^{6–10} hospital costs,⁴ and antimicrobial resistance.⁵ One study examined the impact of inappropriate first-dose antimicrobial selection and delayed antimicrobial administration on the mortality of septic patients with bacteremia and found an increased mortality rate with both factors.¹¹ In this study, inappropriate initial therapy selection had a significant impact on health care-associated and hospital-acquired infections for 42.6% of patients ($n = 29$), with the greatest inappropriate selection reported for genitourinary site infections (27.9%; $n = 20$).¹¹ Based on these findings, risk factors for drug-resistant organisms and local antimicrobial susceptibility patterns should be considered when selecting empiric regimens.

An antibiogram is a tool used by clinicians that provides institution-specific antimicrobial susceptibility data to help guide

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empiric antimicrobial therapy. Standard antibiograms have several limitations, however, including lack of syndrome or disease-specific advice, organism site distribution, information on polymicrobial infections or the usefulness of combination antimicrobial therapy, and information on patient risk factors that influence susceptibility.¹²

A recent study used a weighted-incidence syndromic combination antibiogram (WISCA) to identify causative organisms of 2 common infectious syndromes, urinary tract infection (UTI) and abdominal biliary infection, and compared susceptibility detected by the WISCA with that detected by a traditional antibiogram.¹² For UTIs, the WISCA-UTI demonstrated decreased susceptibility for fluoroquinolone (62%) and ceftriaxone (71%) compared with the traditional antibiogram (84% and 97%, respectively). This study also revealed that patient risk factors, including age >65 years, recent emergency room/inpatient visit, and fluoroquinolone exposure in the previous 30 days, affected susceptibility.

The aim of the present study was to determine whether detection of antimicrobial susceptibility differs between the standard antibiogram and the urinary-specific antibiogram for the 4 most common gram-negative urinary isolates: *Escherichia coli* (EC), *Proteus mirabilis* (PM), *Klebsiella pneumoniae* (KP), and *Pseudomonas aeruginosa* (PA).

METHODS

This study was conducted at Advocate Lutheran General Hospital/Advocate Children's Hospital (ALGH/ACH) in Park Ridge, IL. ALGH/ACH is a 638-bed teaching, research, and referral hospital with a level I trauma center, level III neonatal intensive care unit (NICU), and large nursing home patient population.

This was a retrospective, descriptive study. Antimicrobial culture and susceptibility data for the 4 most common gram-negative urinary isolates (EC, PM, KP, and PA) were collected from microbiology laboratory reports between January 1 and December 31, 2012. Urinary isolates from inpatient and outpatient settings were included, and isolates other than the 4 aforementioned gram-negative pathogens were excluded.

In an attempt to decrease inappropriate empiric antimicrobial selection for UTIs, a syndromic antibiogram was created to determine the impact of patient risk factors on antimicrobial susceptibility. The primary objective was to determine whether antimicrobial susceptibility differs between the standard antibiogram published annually by our microbiology laboratory and the urinary-specific antibiogram for the 4 most common gram-negative urinary isolates. Patient risk factors were incorporated to determine their impact on susceptibility, provide more specific UTI guidelines at our institution, and potentially reduce inappropriate empiric antimicrobial selection.

Urinary antibiogram

The urinary antibiogram was constructed in congruence with ALGH/ACH's standard antibiogram, in which all first urinary isolate encounters over a 1-year period were included, regardless of a final diagnosis (International Statistical Classification of Diseases and Related Health Problems, Ninth Revision [ICD-9] code) consistent with a UTI and colony-forming units (CFU)/mL threshold. The most resistant urine culture was selected for patients with multiple positive urine cultures for the same isolate during 1 admission, and intermediate antimicrobial susceptibility was considered resistant. Antimicrobial susceptibility was calculated as a percentage by dividing the number of susceptible cases by the total number of cases (susceptible plus nonsusceptible) for each urinary isolate. The urinary antibiogram was compared with the same 4 gram-negative

Table 1
Baseline characteristics of the study population

Characteristic	Urinary isolate			
	EC (n = 1,652)	PM (n = 195)	KP (n = 301)	PA (n = 136)
Age, years				
≤18	272 (16)	22 (11)	24 (8)	15 (11)
19–64	553 (33)	47 (24)	87 (29)	31 (23)
≥65	827 (50)	126 (65)	190 (63)	90 (66)
Previous residence				
HC facility	216 (13)	76 (39)	61 (20)	46 (34)
Community	1,383 (84)	114 (58)	238 (79)	87 (64)
Hospital unit				
ICU	50 (3)	1 (0.5)	14 (5)	12 (9)
Non-ICU	1,602 (97)	194 (99)	286 (95)	124 (91)
Antimicrobial use within ≤30 days				
Yes	253 (15)	45 (23)	78 (26)	52 (38)
No	1,399 (85)	150 (77)	223 (74)	84 (62)
Hospitalization within ≤30 days				
Yes	261 (16)	43 (22)	86 (29)	67 (49)
No	1,391 (84)	152 (78)	215 (71)	69 (51)

NOTE. Data are expressed as n (%). The urinary antibiogram comprises 2,284 EC, PM, KP, and PA isolates. Each urinary isolate was stratified by subject risk factors (ie, age, previous residence, hospital unit, antimicrobial use within ≤30 days, and hospitalization within ≤30 days).

isolates in the standard antibiogram that represented the overall susceptibility of isolates collected from all body sites.

Inclusion of subject risk factors in the urinary antibiogram

For each urinary isolate, subject risk factor data were obtained from the microbiology reports and through direct review of subjects' electronic medical record (EMR). The 5 subject risk factors assessed included age (ie, ≤18 years, 19–64 years, and ≥65 years), residence before admission, hospitalization within ≤30 days (admission ≥48 hours), antimicrobial use within ≤30 days (≥1 doses of antimicrobials), and hospital unit (ie, intensive care unit [ICU] versus non-ICU). Residence immediately before admission was classified as health care (HC) facility setting (ie, skilled nursing facility, long-term care facility, or nursing home) or community setting (eg, home, assisted-living facility) as documented in the EMR. The impact of antimicrobial susceptibility was analyzed when 1 and 2 subject factors (ie, age ≥65 years and health care facility) were present.

Data analysis

Descriptive statistics (n, %) were reported on all variables. The χ^2 or Fisher's exact test was used to compare the difference in susceptibility between the 2 antibiograms and the differences with regard to subject risk factors. In all analyses, a 2-tailed *P* value of <.05 was considered statistically significant. All statistical calculations were performed using SPSS version 20.0 (IBM, Armonk, NY). Sample sizes of antimicrobial susceptibility and risk factors varied for each urinary isolate; thus, variables were weighted to account for unequal sample sizes.

RESULTS

There were a total of 2,284 urinary isolate encounters between January 1 and December 31, 2012. Of these 2,284 urinary isolates, 1,509 (66%) had a documented ICD-9 code for a primary or secondary UTI diagnosis. Background characteristics of the study subjects are presented in Table 1.

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