Prevalence and Regional Variation in ESBLs and CRE Enterobacteriaceae (ENT) Among Hospitalized Adult Patients on a Urine Culture: A Multicenter Evaluation

Thomas Lodise1; Vikas Gupta2; Kalvin Yu3; Kalpana Gupta4; Maureen Early5; Gang Ye6; Jennifer Schranz7; Steven Gelone8

1Albany College of Pharmacy and Health Sciences, Albany, NY; 2Becton, Dickinson and Company, Franklin Lakes, NJ, USA; 3Nabria Therapeutics US, Inc., King of Prussia, PA, USA; 4Division of Infectious Diseases, Veterans Affairs Boston Healthcare System and Boston University School of Medicine, West Roxbury, Massachusetts

BACKGROUND
• The US CDC has identified extended spectrum beta-lactamases (ESBL) Enterobacteriaceae (ENT) and carbapenem resistant ENT (CRE) as significant public health threats.
• The World Health Organization has categorized CRE and ESBL-producing ENT as threats needing critical priority for drug development.
• Carbapenem-resistant ENT (CRE) is a major threat to the treatment of infections.
• Inadequate antibiotic use is one of the main contributors to increasing risks of drug resistant pathogens.
• Scant data are available on the incidence and prevalence of ESBL ENT and CRE from clinical urine samples across a large representative sample of US hospitals.
• This study sought to quantify the prevalence and incidence of ESBL-producing ENT and CRE in the urine of adult hospitalized patients.

METHODS
• Isolates from all hospitalized adult patients with a urine culture (first urine isolate of a species per 30-day period) from 37 hospitals in 2018 were evaluated (BD Insite Infection Database, Becton, Dickinson & Company).
• ESBL ENT, E. coli, K. pneumoniae, K. oxytoca, K. pneumonia, and P. mirabilis (PM) isolates confirmed as ESBL positive by laboratory panels OR with intermediate susceptibility or resistance to ceftriaxone, cefotaxime, cefazolin, or cefepime.
• Carbapenem-resistant ENT (CRE), E. coli, K. pneumoniae, K. oxytoca, P. mirabilis, E. aerogenes, E. cloacae, S. marcescens, C. freundii, and M. morganii isolates with intermediate susceptibility or resistance to imipenem (excluded for HHS geographic region were assessed using the generalized linear models (GLM) –
• Urine isolates were classified as:
  • Community-onset (CO) < 3 days of a post-inpatient admission and no previous admission within 14 days.
  • Hospital-onset (HO) > 3 days post-inpatient admission or inpatient admission within 14 days of current admission.
  • Facility status:
    • Bed days < 100, 100-300, and ≥ 300.
    • Teaching status: teaching and non-teaching.
  • Urban or rural.

Statistical Analysis
• Prevalence (percent of non-susceptible [NS] isolates per organism tested) and rates per 1000 admissions were evaluated and by hospital location (CO, HO).
• The variations in prevalence and rate by U.S. Department of Health and Human Services (HHS) geographic region were assessed using the generalized linear models (GLM) adjusting hospital characteristics (377 hospitals). The zip code territory area figures are displayed for 330 facilities.

RESULTS
• In 2018, there were 195,476 non-duplicate ENT urine isolates across 4,623,760 admissions; 63.6% were EC, 19.3% were KPO, and 6.5% were PM.
• Overall, 12.8% (95% confidence interval [CI] 11.6-12.4) were ESBL, and 0.7% (95% CI 0.7-0.9) were CRE.
• The rates per 1000 admissions were 5.3 (95% CI 5.1-5.5) and 0.39 (95% CI 0.3-0.4) for ESBL, and CRE, respectively (Table 1).
• Among CO, 11.1% (95% CI 10.8-11.5) were ESBL and 0.67% (95% CI 0.6-0.8) were CRE.
• Among HO, 5.1% (95% CI 4.8-5.5) were ESBL and 0.7% (95% CI 0.6-0.9) were CRE.
• The rates per 1000 admissions were 1.3 (95% CI 1.2-1.5) and 0.5 (95% CI 0.4-0.7) for ESBL, and CRE, respectively.

Table 1. Distribution of Urine ESBL and CRE Isolates by Geographic Location and Hospital Characteristics.

<table>
<thead>
<tr>
<th>Hospital Characteristics</th>
<th>ENT Isolates</th>
<th>CRE Isolates</th>
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<tbody>
<tr>
<td>Geographical Region</td>
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<tr>
<td>Region 1 (Southwest)</td>
<td>140,509 (72.2%)</td>
<td>35 (0.2%)</td>
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<tr>
<td>Region 2 (Northeast)</td>
<td>8,047 (4.1%)</td>
<td>8 (0.1%)</td>
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<tr>
<td>Region 3 (Southeast)</td>
<td>4,629 (2.3%)</td>
<td>3 (0.0%)</td>
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<tr>
<td>Region 4 (Midwest)</td>
<td>5,493 (2.8%)</td>
<td>5 (0.1%)</td>
</tr>
<tr>
<td>Region 5 (West)</td>
<td>1,180 (0.6%)</td>
<td>4 (0.0%)</td>
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<tr>
<td>To 100 100-300 160 (42.4) 1,551,966 .67 (.6-.8)</td>
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<tr>
<td>Teaching 111 (29.4) 2,161,350 .87 (.7-1.0)</td>
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<tr>
<td>Urban/Rural 14 (3.7) 165,753 .17 (.0-.3)</td>
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<td>Region 6 (Central England &amp; Midwest) 32 (8.5) 271,285 .27 (.1-.5)</td>
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<td>Region 7 (Northwest)      84 (22.3) 344,061 .53 (.3-.7)</td>
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<tr>
<td>Region 8 (Southwest)      71 (18.8) 834,923 .53 (.4-.7)</td>
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CONCLUSIONS
• This large national database study demonstrates that more than 1 out of every 10 urine cultures with growth of ENT that are obtained from patients admitted from the community will have an ESBL pathogen; the proportion is even higher among hospital onset urine cultures.
• This rate doubles (>20%) when combining certain regions with site of onset (Southwest and hospital onset).
• CRE remains low, but also varies greatly by geographic region; with <1% along the west coast, and >1% among HO isolates regardless of geographic.
• Assessing risk factors for resistance such as geographic region and site of onset is a key critical step to optimizing empiric therapy decisions.

REFERENCES