Risk Factors for Mortality in Patients with Urinary and Sterile Site Cultures Positive for Carbapenem-resistant Enterobacteriaceae (CRE) in Atlanta, 2011-2014

Mary Elizabeth Sexton, MD,1,2 Christopher Bower, MPH,2-3 Jesse T. Jacob, MD,1,2
1Division of Infectious Diseases, Emory University School of Medicine, 2Georgia Emerging Infections Program, and 3Emory Antibiotic Resistance Center, Atlanta, GA; 4Atlanta Veterans Affairs Medical Center and 5Atlanta Research and Education Foundation, Decatur, GA

Background
• CRE is emerging as a major problem in the United States
• Prior studies have estimated that the risk of mortality in severe CRE infections ranges from ~30-50%
• Pooled data from 7 EIP sites in 2012-2013 identified a 9% overall mortality rate (including patients with only urine cultures positive, but a 27.5% mortality rate in patients with a positive sterile site culture
• There is limited data on which patients with CRE have the highest risk of mortality, although patient comorbidities appear to contribute in multiple studies
• Identification of risk factors for mortality may have implications for early initiation of empiric therapy and targeting of prevention interventions

Methods
• Georgia Emerging Infections Program (EIP) conducts surveillance for CRE cases in the 8-county Atlanta metropolitan area
• CRE defined as nonsusceptible to imipenem, meropenem and doripenem, and resistant to all tested 3rd generation cephalosporins
• Incident case = isolation of CRE from urine or a normally sterile site with no prior cultures positive for the same organism in the last 30 days
• Data collected on in-hospital mortality (admitted patients) or 30-day mortality (long-term care or dialysis centers)
• Mortality rates compared for patients with a single positive urine or blood culture, those with an apparent urinary source followed by invasive infection within 30 days (progression), and those with multiple positive cultures for the same organism >30 days apart (recurrence)
• Prevalence of demographic and risk factors compared between patients with fatal and non-fatal outcomes, with chi-square analysis for categorical variables and t-tests for continuous variables
• Risk factors assessed with univariable and multivariable logistic regression to evaluate predictors of mortality in the setting of a positive CRE culture

Outcomes in 454 patients with at least one positive culture for CRE in Atlanta, 2011-2014

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>N</th>
<th>Percent (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>384/454 (84.6%) had an initial urinary infection</td>
<td>303/384 survived, no recurrence (78.9%)</td>
<td>44/573 had at least one invasive culture positive during a recurrence</td>
</tr>
<tr>
<td>70/454 (15.4%) had an initial invasive infection</td>
<td>10/70 with apparent urinary source and progression to invasive infection (14.3%)</td>
<td></td>
</tr>
<tr>
<td>60/70 with initial invasive culture positive (85.7%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Univariable and Multivariable Logistic Regression Analysis of Risk Factors For Mortality in Patients with a Positive CRE Culture

<table>
<thead>
<tr>
<th>Variable</th>
<th>Crude Odds Ratio*</th>
<th>95% Confidence Interval</th>
<th>Adjusted Odds Ratio*</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU stay</td>
<td>7.68</td>
<td>3.40 - 15.33</td>
<td>7.80</td>
<td>3.75 - 8.24</td>
</tr>
<tr>
<td>Central venous catheter present</td>
<td>6.70</td>
<td>3.33 - 13.48</td>
<td>2.89</td>
<td>1.26 - 6.61</td>
</tr>
<tr>
<td>Perioperative indwelling device present</td>
<td>4.75</td>
<td>2.77 - 8.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Invasive infection</td>
<td>4.44</td>
<td>2.22 - 8.00</td>
<td>2.25</td>
<td>1.03 - 4.91</td>
</tr>
<tr>
<td>Hospitalized for 24 days</td>
<td>3.76</td>
<td>1.92 - 7.36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In an ICU in the year prior</td>
<td>3.20</td>
<td>1.31 - 7.54</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary catheter present</td>
<td>1.75</td>
<td>0.90 - 3.39</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunocompromised</td>
<td>1.58</td>
<td>0.79 - 3.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In a LTCF in the year prior</td>
<td>0.67</td>
<td>0.34 - 1.29</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Results (continued)
• Overall mortality rate was 11.7% (33/454), and higher in invasive (22.9%) than urinary infections (6.3%), p<0.0001
• Most deaths (40/53) occurred with initial infection
• More patients died with progression to invasive infection (30%) or recurrent infection (33%), compared to an initial invasive infection (21.7%), although this was not statistically significant (p=0.63)
• Multivariable analysis, death was associated with markers of severe illness (ICU stay, presence of a central venous catheter) and invasive infections

Discussion
• Mortality was significant, but lower than in prior studies
• Early initiation of empiric therapy in high-risk patients may prevent progression to invasive infection and mortality, particularly in the setting of recurrence
• These data emphasize the importance of removal of unnecessary central lines, which may reduce mortality
• Other potential risk factors for progression and recurrent infection, such as antibiotic use and changes in the microbiome, warrant further evaluation for possible interventions to decrease mortality

References

Funding
MIES was supported by the National Center for Advancing Translational Sciences of the National Institutes of Health under Award Number U54TR000404. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Contact Information
Dr. Mary Beth Sexton, msexton@emory.edu
Emory University School of Medicine, Division of Infectious Diseases
49 Jesse Hill Jr. Drive, Atlanta, GA 30303
Phone: 404-251-8703