Epidemiology and antimicrobial susceptibility of Gram-negative pathogens causing intra-abdominal infections (IAI) in pediatric patients in Europe – SMART 2010-2013

R. Badal1, I. Morrissey2, S. Lob1, D. Biedenbach1, M. Hackel1*, S. Bouchillon1

1International Health Management Associates, Inc., Schaumburg, Illinois, USA
2IHMA Europe Sàrl, Epalinges, Switzerland
Methods

• Hospitals each collected up to 100 non-selected, consecutive Gram-negative pathogens each year. Only one isolate per species per patient accepted.

• 1,099 isolates were collected from pediatric patients (0-17 years) with IAI in 52 hospitals in 18 European countries.

• Organisms were classified as either CA or HA if they were isolated <48h or ≥48h from admission, respectively.

• Isolates were identified to the species level and sent to a central laboratory for susceptibility testing and confirmation of identification.

• MICs were determined by the Clinical and Laboratory Standards Institute (CLSI) recommended broth microdilution testing method [1].

• MICs were interpreted using EUCAST guidelines [2].


Distribution of Species
Pediatric IAI, Europe 2010-2013

Hospital-associated (n=412)

- *Escherichia coli*
- *Klebsiella pneumoniae*
- *Pseudomonas aeruginosa*
- *Enterobacter cloacae*
- *Klebsiella oxytoca*
- *Serratia marcescens*
- *Enterobacter aerogenes*
- *Acinetobacter baumannii*
- *Proteus mirabilis*
- *Enterobacter asburiae*
- Others (18 species)

Community-associated (n=646)

- *Escherichia coli*
- *Pseudomonas aeruginosa*
- *Klebsiella pneumoniae*
- *Enterobacter cloacae*
- *Klebsiella oxytoca*
- Others (18 species)

* Significant difference between HA and CA (p<0.05, chi-square test).
Susceptibility
Pediatric IAI, Europe 2010-2013

E. coli

% Susceptible (95% CI)

AMK = amikacin
SAM = ampicillin-sulbactam
FEP = cefepime
CTX = cefotaxime
CAZ = ceftazidime
CRO = ceftriaxone
ETP = ertapenem
IPM = imipenem
TZP = piperacillin-tazobactam

* Significant difference between HA and CA (p<0.05, chi-square test).
Susceptibility
Pediatric IAI, Europe 2010-2013

P. aeruginosa

% Susceptible (95% CI)

AMK=amikacin
SAM=ampicillin-sulbactam
FEP=cefepime
CTX=cefotaxime
CAZ=ceftazidime,
CRO=ceftriaxone
ETP=ertapenem
IPM=imipenem
TZP=piperacillin-tazobactam
Susceptibility
Pediatric IAI, Europe 2010-2013

K. pneumoniae

% Susceptible (95% CI)

<table>
<thead>
<tr>
<th>AMK</th>
<th>SAM</th>
<th>FEP</th>
<th>CTX</th>
<th>CAZ</th>
<th>CRO</th>
<th>ETP</th>
<th>IPM</th>
<th>TZP</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (n=87)</td>
<td>HA (n=62)</td>
<td>CA (n=18)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- AMK = amikacin
- SAM = ampicillin-sulbactam
- FEP = cefepime
- CTX = cefotaxime
- CAZ = ceftazidime
- CRO = ceftriaxone
- ETP = ertapenem
- IPM = imipenem
- TZP = piperacillin-tazobactam

* Significant difference between HA and CA (p<0.05, chi-square test).
Susceptibility
Pediatric IAI, Europe 2010-2013

All Gram-negative combined\(^1\)

<table>
<thead>
<tr>
<th>Drug</th>
<th>All (n=1099)</th>
<th>HA (n=412)</th>
<th>CA (n=646)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMK</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CTX</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAZ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRO</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ETP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TZP</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AMK = amikacin
SAM = ampicillin-sulbactam
FEP = cefepime
CTX = cefotaxime
CAZ = ceftazidime
CRO = ceftriaxone
ETP = ertapenem
IPM = imipenem
TZP = piperacillin-tazobactam

\(^1\) Susceptibility of all Gram-negative isolates combined was calculated using breakpoints appropriate for each species. For species with no breakpoints for any given drug, 0% susceptible was assumed.
Conclusions

• The top five species found in HA and CA IAI were identical, but the proportions were different:
  • *E. coli* was about twice as common in CA as in HA IAI
  • *K. pneumoniae* and *E. cloacae* were 5-fold and 3-fold, respectively, more common in HA IAI.

• Susceptibility was reduced in HA compared to CA IAI. For all Gram-negative pathogens combined,
  • in CA IAI, all study drugs, except ampicillin-sulbactam, cefotaxime, and ceftriaxone inhibited >90% of isolates.
  • in HA IAI only imipenem showed a %S >90%; in addition, of the drugs presented, only amikacin and ertapenem had %S >80%.

• Decreased susceptibility in HA IAI was in part due to significantly higher ESBL+ rates.

• Differences in species prevalence, ESBL+ rates, and susceptibility between HA and CA pediatric IAI indicate a need for different therapeutic options for treatment of these infections.
Acknowledgments

The SMART program is funded by Merck Research Laboratories, Inc. The authors thank all the participants in the SMART program for their continuing contributions to its success.