Increased Risk of Pneumococcal Pneumonia Among HIV and Influenza Co-Infected Patients Hospitalized with Pneumonia in South Africa, 2009-2010

Presented by
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(on behalf of the SARI Investigators Team)

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Pneumonia and *Streptococcus pneumoniae*

- Leading cause of morbidity and mortality.

- 2008: ± 1.5 million children <5 years of age died from pneumonia.

- South Africa, 2008: pneumonia 2nd most common natural cause of death in children <15 years (12.4% of deaths).

- *Streptococcus pneumoniae* (pneumococcal) – common and often predominant, bacterial cause of pneumonia.

- 2000: ± 13.8 million cases of pneumococcal pneumonia occurred in children < 5 years of age.

Global burden of pneumococcal disease in children under 5

Source: GAVI Alliance, www.gavialliance.org, October 2011
Diagnosis of Pneumococcal Pneumonia

- Etiological-specific diagnosis of pneumococcal pneumonia is difficult.

- Gold standard: Blood culture from normally sterile sites.

- High specificity, but low sensitivity, slow, influenced by prior antibiotic therapy and need large volumes of blood.

- Alternatives: urinary antigen detection (Binax NOW) and sputum collection are influenced by nasopharyngeal carriage.

- Real-time PCR: sensitive, fast, not influenced by prior antibiotic therapy.

- Specificity determined by target – lytA (autolysin).

- lytA not detected in blood of healthy controls.

Aim

To use quantitative real-time PCR to:

- Determine the prevalence of pneumococcal DNA in patients with hospitalised pneumonia during the introduction of the Heptavalent Pneumococcal Conjugate Vaccine (PCV7) in South Africa.

- To identify risk factors for pneumococcal pneumonia.
Methods

• Severe Acute Respiratory Illness (SARI) surveillance programme: prospective hospital-based surveillance programme initiated in February 2009.

• Aims to describe the etiology and risk factors of community-acquired pneumonia in South Africa.
SARI surveillance sites

Chris Hani Bara
Temperate, urban

Agincourt
Sub-tropical, rural

Klerksdorp
Temperate peri-urban

Edendale
Sub-tropical, peri-urban
Severe Acute Respiratory Illness (SARI) Surveillance Programme

Patients with hospitalised pneumonia

- Clinical and epidemiological data
- Whole blood in EDTA-tube
- Naso/oropharyngeal swab/aspirate in viral transport medium

  Pneumococcal detection by quantitative real-time PCR (lytA)
  HIV testing by ELISA/PCR
  Real-time reverse transcription PCR detection of 10 respiratory viruses
  Influenza subtyping by real-time reverse transcription PCR

May 2009-December 2010
Results

- May 2009-December 2010: 6910 SARI cases enrolled.
- *S. pneumoniae* results were obtained from 74% (5130/6910).
- 46% (2345/5130) were males.
- 40% (2075/5130) were children ≤ 5 years.
- Of 92% (4702/5130) patients with known HIV status, 54% (2532/4702) were HIV positive:

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>HIV infection % (n/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2</td>
<td>15% (223/1453)</td>
</tr>
<tr>
<td>2-5</td>
<td>24% (81/334)</td>
</tr>
<tr>
<td>6-18</td>
<td>52% (79/151)</td>
</tr>
<tr>
<td>19-44</td>
<td>87% (1606/1850)</td>
</tr>
<tr>
<td>44+</td>
<td>59% (543/914)</td>
</tr>
</tbody>
</table>
Results

• Of 5096/5130 (99%) cases with influenza results, 478 (9%) were positive for influenza.

• Influenza subtype could be obtained from 467 (98%) positive samples.
Results

Percentage of hospitalized pneumonia cases PCR-positive for pneumococcal \textit{lytA} by age group, South Africa, 2009-2010

Overall prevalence 7\% (372/5130)
Results

• Blood cultures were performed at the discretion of the respective hospital as part of in-patient care.

• Blood cultures were performed on 897 cases.

• 2% (19) were positive for pneumococcus on blood culture.

• 10% (94) were positive for pneumococcus on PCR.

PCR five-fold higher detection rate than blood culture
Influenza virus and *S. pneumoniae* Detection Rate (%), SARI Surveillance, South Africa – May 2009 through December 2010
Factors associated with pneumococcal infection (*lytA* positive) amongst patients with hospitalized pneumonia, South Africa, 2009-2010

<table>
<thead>
<tr>
<th>Variable</th>
<th>SARI cases n (%)</th>
<th>lytA positive cases n (%)</th>
<th>lytA negative cases n (%)</th>
<th>Odds Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV infection</td>
<td>N=4614*</td>
<td>N=341*</td>
<td>N=4273*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza co-infection</td>
<td>2487 (54)</td>
<td>248 (73)</td>
<td>2239 (52)</td>
<td>1.9 (1.5-2.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time from symptom onset &gt;2 days</td>
<td>3302 (72)</td>
<td>290 (85)</td>
<td>3012 (70)</td>
<td>1.9 (1.4-2.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospital stay &gt;5 days</td>
<td>2160 (47)</td>
<td>204 (60)</td>
<td>1956 (46)</td>
<td>1.3 (1.1-1.7)</td>
<td>0.015</td>
</tr>
<tr>
<td>Death</td>
<td>255 (6)</td>
<td>35 (10)</td>
<td>220 (5)</td>
<td>1.7 (1.1-2.5)</td>
<td>0.008</td>
</tr>
<tr>
<td>Received antibiotics in previous 24 hrs</td>
<td>229 (5)</td>
<td>10 (3)</td>
<td>219 (5)</td>
<td>0.5 (0.3-0.9)</td>
<td>0.035</td>
</tr>
</tbody>
</table>
Conclusions

• 7% pneumococcal pneumonia detected amongst severe pneumonia cases.

• Although still lower than the true burden of pneumococcal pneumonia is thought to be, real-time PCR detected five-fold more cases than detected by blood culture.

• Real-time PCR as a diagnostic tool: fast, not dependent on viability of the pathogen.

• HIV infection or influenza co-infection are significant risk factors for pneumococcal disease.

• Of all hospitalized pneumonia patients in this study, those with pneumococcal pneumonia had a higher risk of dying compared to all other causes of pneumonia.
SARI Acknowledgments 2011

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