(TSAP) - Antimicrobial pre-treatment and blood culture positivity rates for S. Typhi, iNTS and other invasive bacterial pathogens

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Background

-Typhoid Fever (TF) is caused by *Salmonella enterica* serovar Typhi and is a vaccine preventable disease

-TF requires the identification of *Salmonella Typhi* (S. Typhi) bacteria through blood culture

-Patients commonly treat themselves with antibiotics prior to the establishment of a final diagnosis

-We investigated the effect of pre-usage of antibiotics* on blood culture results from invasive bloodstream infections caused by S. Typhi and non-typhoidal *Salmonella* spp(iNTS) compared to other invasive bacterial pathogens

*Defined as patient reporting using antibiotic to treat the current illness prior to visiting the healthcare facility recruiting for TSAP
Methods

- Study period
  : March 2010 to January 2014

- Location
  : 13 health facilities, 10 countries (Burkina Faso, Ethiopia, Ghana, Guinea-Bissau, Kenya, Madagascar, South Africa, Senegal, Sudan and Tanzania)

- Data preparation
  : Used all recruited patients during the study period which is different with published TSAP main paper*
  : 20,352 all recruitment patients
  : Standardized procedure (Lab, case definition, etc.)
  : Data collected on pre-usage of antibiotic

- Data capturing
  : 6 countries captured by Foxpro database developed by IVI
  : 4 countries database extract from existing database

- Analysis
  : Data on blood culture positivity and pre-usage of antibiotics analyzed by logistic regression with stratification measure (SAS, version 9.4)

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Blood culture results by country

- 4% of all patients enrolled had a positive blood culture
- *Salmonella* – among the main pathogens isolated (39.1%) by blood culture

<table>
<thead>
<tr>
<th>Country</th>
<th>Enrolled</th>
<th>Real pathogen* (% by Enrolled)</th>
<th>S. Typhi (% by real pathogen)</th>
<th>iNTS (% by real pathogen)</th>
<th>Other bacteremia (% by real pathogen)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burkina Faso</td>
<td>1,721</td>
<td>46 (2.7)</td>
<td>18 (39.1)</td>
<td>14 (30.4)</td>
<td>14 (30.4)</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>901</td>
<td>12 (1.3)</td>
<td>3 (25.0)</td>
<td>0</td>
<td>9 (75.0)</td>
</tr>
<tr>
<td>Ghana</td>
<td>5,699</td>
<td>359 (6.3)</td>
<td>65 (18.1)</td>
<td>88 (24.5)</td>
<td>206 (57.4)</td>
</tr>
<tr>
<td>Guinea Bissau</td>
<td>1,180</td>
<td>24 (2.0)</td>
<td>2 (8.3)</td>
<td>11 (45.8)</td>
<td>11 (45.8)</td>
</tr>
<tr>
<td>Kenya</td>
<td>2,457</td>
<td>167 (6.8)</td>
<td>69 (41.3)</td>
<td>9 (5.4)</td>
<td>89 (53.3)</td>
</tr>
<tr>
<td>Madagascar</td>
<td>3,579</td>
<td>41 (1.1)</td>
<td>10 (24.4)</td>
<td>1 (2.4)</td>
<td>30 (73.2)</td>
</tr>
<tr>
<td>South Africa</td>
<td>1,253</td>
<td>83 (6.6)</td>
<td>3 (3.6)</td>
<td>1 (1.2)</td>
<td>79 (95.2)</td>
</tr>
<tr>
<td>Senegal</td>
<td>1,709</td>
<td>41 (2.4)</td>
<td>8 (19.5)</td>
<td>6 (14.6)</td>
<td>27 (65.9)</td>
</tr>
<tr>
<td>Sudan</td>
<td>689</td>
<td>10 (1.5)</td>
<td>0</td>
<td>0</td>
<td>10 (100)</td>
</tr>
<tr>
<td>Tanzania</td>
<td>1,154</td>
<td>41 (3.6)</td>
<td>11 (26.8)</td>
<td>4 (9.8)</td>
<td>26 (63.4)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>20,352</strong></td>
<td><strong>825 (4.1)</strong></td>
<td><strong>189 (22.9)</strong></td>
<td><strong>134 (16.2)</strong></td>
<td><strong>502 (60.8)</strong></td>
</tr>
</tbody>
</table>

*Real pathogen: pathogens isolated by blood culture excluding contaminants*
Reported pre-usage of antibiotic in patients with bloodstream infections (Percentage of bacteremia(% by Enrolled))

- 10.7% of enrolled patients reported pre-usage of antibiotics

Graph of reported blood culture positive by pre-usage of antibiotics:

- 4.26% of patients reported pre-usage of antibiotics
- 4.03% did not report pre-usage of antibiotics

- 10.7% of enrolled patients reported pre-usage of antibiotics
Pre-usage of antibiotics in S. Typhi patients compared to patients with other bloodstream infections

✓ S. Typhi patients were two times more likely to report pre-usage of antibiotics when compared to patients with other bloodstream infections.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>S. Typhi (N=189)</th>
<th>Other bloodstream infections (N=636)</th>
<th>OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-usage of antibiotics</td>
<td>34/93 (36.6)</td>
<td>59/93 (63.4)</td>
<td>2.11 (1.29-3.34)</td>
<td>0.003</td>
</tr>
<tr>
<td>No pre-usage of antibiotics</td>
<td>155/732 (21.2)</td>
<td>577/732 (78.8)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

✓ Similar result was observed when S. Typhi patients were compared to all febrile patients:

OR(95%,p)=1.97 (1.33-2.91, 0.001)
Result: Pre-usage of antibiotics in iNTS patients compared to patients with other bloodstream infections

- There is no difference in reported pre-usage of antibiotics between iNTS and other bloodstream infections.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>iNTS (N=134)</th>
<th>Other bloodstream infections (N=691)</th>
<th>OR (95% CI)*</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-usage of antibiotics</td>
<td>12/93 (12.9)</td>
<td>81/93 (87.1)</td>
<td>0.96 (0.49-1.88)</td>
<td>0.904</td>
</tr>
<tr>
<td>No pre-usage of antibiotics</td>
<td>122/732 (16.7)</td>
<td>610/732 (83.3)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- This result was consistent when iNTS patients were compared to all febrile patients:
  \[ \text{OR(95\%,p)} = 1.16 (0.63-2.14, 0.630) \]
Limitations

- Self reporting of antibiotics usage
- Antibiotics taken not documented
- Number of days antibiotics taken before seeking care unknown
• Patients infected with S. Typhi were probably exhibiting more severe symptoms than other invasive salmonella.
  • Hence, these patients took antibiotics prior to visiting a healthcare facility.
• Given these clinical considerations, we cannot fully assess whether or to what degree antibiotic pre-usage affected blood culture findings.
• TSAP S. Typhi isolates were resistant to commonly used antibiotics may have reduced the impact of antibiotic usage on blood culture isolation.
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