Salmonella Typhi and Paratyphi in Bangladesh and Their Antimicrobial Resistance – SEAP Data

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SEAP Progress Milestones - Bangladesh

- **October 2016**: Hospital 1 IPD
- **November 2016**: Hospital 1 OPD
- **December 2016**: Hospital 2 IPD
- **January 2017**: Hospital 2 OPD
- **February 2017**
- **March 2017**

- **Lab Network**: 01/10/2016
- **05/11/2016**
- **05/11/2016**
- **14/02/2017**
Location of Study Sites
Enrollment of Cases

**DSH**
- Referred to study physician (N=607)
- Eligible N =429 (71%)
- Culture done N =378 (89%)
  - Positive N =101 (26%)
  - Negative N =277 (74%)
- Non Eligible N =178 (29%)
- Not done N =51 (11%)

**SSF**
- Referred to study physician (N=159)
- Eligible N =121 (76%)
- Culture done N =100 (83%)
  - Positive N =30 (30%)
  - Negative N =70 (70%)
- Non Eligible N =38 (24%)
- Not done N =21 (17%)

**Hospital Lab**
- N =30

**Lab Network**
- N =185

Total = 345
265 of 333 (80%) cases from catchment area

HCUS survey will tell what % of population seeking care at study hospitals
Typhi & Paratyphi Among Hospital/Community Patients (N=313)

Typhi/Paratyphi Ratio

<table>
<thead>
<tr>
<th>In Patient</th>
<th>Out Patient</th>
</tr>
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<tbody>
<tr>
<td>Typhi</td>
<td>Paratyphi</td>
</tr>
<tr>
<td>5 : 1</td>
<td>4 : 1</td>
</tr>
</tbody>
</table>

In patient (N=69)

- Typhi: 84%
- Paratyphi: 16%

Out patient (N=244)

- Typhi: 78%
- Paratyphi: 22%
Trend of Typhi and Paratyphi during SEAP period, Oct – Dec ‘16

<table>
<thead>
<tr>
<th>Typhi/Paratyphi Ratio</th>
<th>Overall (SEAP)</th>
<th>Average (2004 – 2014)</th>
<th>6:1 (Range 4:1 to 9:1)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4 : 1</td>
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</table>
Antimicrobial Resistance
“Multidrug Resistance” (MDR)

MDR among Typhi (N= 264) & Paratyphi (N=69) (N = 333)

Trend of MDR in Typhi '05 to '13

<table>
<thead>
<tr>
<th>Year</th>
<th>% MDR</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>63</td>
</tr>
<tr>
<td>2006</td>
<td>56</td>
</tr>
<tr>
<td>2007</td>
<td>38</td>
</tr>
<tr>
<td>2008</td>
<td>34</td>
</tr>
<tr>
<td>2009</td>
<td>41</td>
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<tr>
<td>2010</td>
<td>18</td>
</tr>
<tr>
<td>2011</td>
<td>22</td>
</tr>
<tr>
<td>2012</td>
<td>18</td>
</tr>
<tr>
<td>2013</td>
<td>16</td>
</tr>
</tbody>
</table>

Figure: Proportion of Typhi and Paratyphi isolates with Multidrug Resistance (MDR) compared to Non-MDR isolates from 2005 to 2013.
“Multidrug Resistance” and Haplotype 58

• Haplotype 58
  • Linked with Multidrug resistance (Ampicillin, Cotrimoxazole and Chloramphenicol)
  • Expanding among *Salmonella Typhi* globally
  • Impact of H58 beyond MDR
    • Reduced susceptibility to Fluoroquinolone
Fluroquinolone Susceptibility and Haplotype 58

- **Haplotype 58**
  - Expanding among *Salmonella Typhi* globally
  - Linked with Multidrug resistance (Ampicillin, Cotrimoxazole and Chloramphenicol)
  - Impact of H58 beyond MDR
    - Reduced susceptibility to Fluroquinolone
H58 Lineages – SEAP isolates

H58 (N=102)

Node, 8, 8%

H58/la, 94, 92%

Murgia et al 2016; Holt et al 2011
Susceptibility to Ciprofloxacin and Ceftriaxone – Typhi and Paratyphi

MIC-50 & MIC-90 of Ciprofloxacin and Ceftriaxone

Typhi vs Paratyphi (N=333)

Gyrase and Topoisomerase mutations

Typhi vs Paratyphi (N=333)

95% of gyrA mutation at location 83; 1% with double (83 & 87) mutations leading to high MICs
Conclusions

• Preliminary data showed (December to March)
  • High burden of Typhoid and Paratyphoid
  • Typhi : Paratyphi 4 : 1
    • Remains consistent for last several years
  • Roll down of MDR (20%)
    • Spread of H58 – potential of reemergence of MDR
  • High rate of non-susceptibility to Ciprofloxacin
    • H58 and mutations in Gyrase and Toposimerase have the roles in this resistance
• Continuous surveillance is needed to monitor the trend AMR
• Finally, prevention of typhoid and paratyphoid should be taken as a priority
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COALITION AGAINST TYPHOID

Child Health Research Foundation
Prevent Infections, Save Lives