Characterization of Invasive Salmonellosis in Hospitalized Children with Acute Febrile Illness—Uganda, 2016–2017

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March 26–28, 2019
Uganda Acute Febrile Illness (AFI) Project
Objectives

- Establish leading causes of non-malarial acute febrile illness among hospitalized children in Uganda
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- Provide guidance for further expansion of relevant diagnostic capacity
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- Provide guidance for further expansion of relevant diagnostic capacity
- Obtain antimicrobial resistance patterns to guide proper use of antimicrobial therapies
Uganda AFI surveillance sites


**Recommended testing for children admitted with fever**

- **Positive**
  - *P. falciparum*

- **Negative**
  - **Fever < 5 days**
    - *B. burgdorferi*
  - **Fever ≥ 5 days**
    - *E. coli*
    - *Cryptosporidium*
    - *Giardia lamblia*
    - *Malaria testing*

*Further serologic testing: arboviruses, *Rickettsia, Borrelia, Brucella***
Uganda AFI project
(July 1, 2016 – Nov 16, 2017)

22,553
hospitalized children
(≤14 years)
Uganda AFI project (July 1, 2016 – Nov 16, 2017)

22,553 hospitalized children (≤14 years)

4,257 blood cultures (19%)
22,553 hospitalized children (≤14 years) in Uganda AFI project (July 1, 2016 – Nov 16, 2017)

4,257 blood cultures (19%)

- 3,894 no growth (91%)
- 220 contaminated (5%)
- 143 pathogens (3%)
Pathogens identified by blood culture
Uganda AFI Project: Jul 2016 – Nov 2017
n=143

Percentage of total pathogens (%)

- Salmonella enterica
- Staphylococcus aureus
- Citrobacter spp.
- Escherichia coli
- Klebsiella pneumoniae
- Enterococcus spp.
- Streptococcus pneumoniae
- Haemophilus influenzae
- Neisseria meningitidis
- Other
Pathogens identified by blood culture
Uganda AFI Project: Jul 2016 – Nov 2017
n=143
## Descriptive characteristics

**Uganda AFI project: Jul 2016 – Nov 2017**

<table>
<thead>
<tr>
<th></th>
<th>Children with <em>Salmonella</em> bacteremia (n=57)</th>
<th>Children without <em>Salmonella</em> bacteremia (n=22,496)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (range)</td>
<td>3 years (0–12)</td>
<td>2 years (0–14)</td>
<td>0.026</td>
</tr>
<tr>
<td>Male (%)</td>
<td>40 (70%)</td>
<td>12,627 (57%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Death (%)</td>
<td>3 (6%)</td>
<td>843 (4%)</td>
<td>0.537</td>
</tr>
</tbody>
</table>
Median length of hospital stay
Uganda AFI Project: Jul 2016 – Nov 2017

- Children without *Salmonella* bacteremia: 3 days
- Children with *Salmonella* bacteremia: 6 days

P = <0.001
Salmonella serotypes
Uganda AFI Project: Jul 2016 – Nov 2017
n=49

- Enteritidis: 43%
- Typhimurium: 27%
- I 4,[5],12:i-: 2%
- Typhi: 29%
Percentage of nontyphoidal and typhoidal serotypes
Uganda AFI Project: Jul 2016 – Nov 2017
n=49

Percentage of total isolates tested (%)

- Nontyphoidal: 71%
- Typhoidal: 29%
Uganda AFI surveillance sites
Percentage of *Salmonella* bacteremia per number of blood cultures drawn, by site
Uganda AFI Project: Jul 2016 – Nov 2017
n=57

<table>
<thead>
<tr>
<th>Site</th>
<th>Percentage of <em>Salmonella</em> bacteremia (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arua</td>
<td>4</td>
</tr>
<tr>
<td>Mubende</td>
<td>1</td>
</tr>
<tr>
<td>Apac</td>
<td>1</td>
</tr>
<tr>
<td>Jinja</td>
<td>0</td>
</tr>
<tr>
<td>Kabale</td>
<td>0</td>
</tr>
<tr>
<td>Tororo</td>
<td>0</td>
</tr>
</tbody>
</table>
Salmonella serotypes by site
Uganda AFI Project: Jul 2016 – Nov 2017
n=47

Number of Salmonella isolates

Arua: n=25 (Enteritidis: 15, Typhimurium: 10)
Mubende: n=5 (Enteritidis: 3, Typhimurium: 2)
Jinja: n=3 (Enteritidis: 2, Typhimurium: 1)
Kabale: n=2 (Typhi: 2)
Apac: n=2 (Typhi: 2)
Tororo: n=1

Legend:
- Enteritidis
- Typhimurium
- I 4,5,12:i:-
- Typhi
Antimicrobial Resistance
Antimicrobial resistance of *Salmonella* isolates
Uganda AFI Project: Jul 2016 – Nov 2017
n=49

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Percentage of isolates resistant (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ampicillin</td>
<td>61%</td>
</tr>
<tr>
<td>chloramphenicol</td>
<td>59%</td>
</tr>
<tr>
<td>TMP-SMX*</td>
<td>59%</td>
</tr>
<tr>
<td>nalidixic acid</td>
<td>29%</td>
</tr>
<tr>
<td>ceftriaxone</td>
<td></td>
</tr>
</tbody>
</table>

*trimethoprim-sulfamethoxazole (TMP-SMX)
Antimicrobial resistance patterns by serotype
Uganda AFI Project: Jul 2016 – Nov 2017
n=49

- Multidrug Resistant (MDR) - resistant to ampicillin, chloramphenicol, and TMP-SMX
- Fluoroquinolone nonsusceptible

Serotype
- Enteritidis (n=21)
- Typhimurium (n=13)
- I 4,[5],12:i:- (n=1)
- Typhi (n=14)
Antimicrobial resistance patterns, grouped as nontyphoidal or typhoidal
Uganda AFI Project: Jul 2016 – Nov 2017
n=49
Discussion
Limitations

- Blood culture collection proportions
Limitations

- Blood culture collection proportions
  - Staffing
  - Stockouts
  - Clinician discretion
Limitations

- Blood culture collection proportions
  - Staffing
  - Stockouts
  - Clinician discretion
- Laboratory challenges
Conclusions

- *Salmonella* is the most commonly detected cause of bacteremia in febrile hospitalized children in Uganda.
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- 71% of *Salmonella* serotypes causing bacteremia were identified as nontyphoidal
Conclusions

- *Salmonella* is the most commonly detected cause of bacteremia in febrile hospitalized children in Uganda
- 71% of *Salmonella* serotypes causing bacteremia were identified as nontyphoidal
- Antimicrobial resistance continues to threaten our ability to properly treat invasive *Salmonella* infections
Acknowledgments

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Arua Regional Referral Hospital
Jinja Regional Referral Hospital
Kabale Regional Referral Hospital
Mubende Regional Referral Hospital
Tororo District Hospital

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
Extra Slides
Risk factors previously associated with iNTS

- HIV infection
- Malnutrition
- Malaria
- Young age
- Anemia
- Rural setting
Contaminants

- CONS
- Corynebacterium
- Bacillus
- Micrococcus
- Strep viridans
- "bloodcultureresult" = 2 “contaminant” with no organism identified
Number of children with *Salmonella* bacteremia by site
(Uganda AFI project: Jul 2016 – Nov 2017)
n=57
Number of blood cultures done by site

### Number of cultures

<table>
<thead>
<tr>
<th>Site</th>
<th>Number of Cultures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jinja</td>
<td>2,440</td>
</tr>
<tr>
<td>Arua</td>
<td>963</td>
</tr>
<tr>
<td>Mubende</td>
<td>759</td>
</tr>
<tr>
<td>Kabale</td>
<td>517</td>
</tr>
<tr>
<td>Tororo</td>
<td>355</td>
</tr>
<tr>
<td>Apac</td>
<td>245</td>
</tr>
</tbody>
</table>
Malaria
Proportion of *Salmonella* bacteremia patients positive for malaria
Uganda AFI Project: Jul 2016 – Nov 2017
n=54

- Malaria positive: 30%
- Malaria negative: 70%
Proportion of tested patients positive for malaria, by site
Uganda AFI Project: Jul 2016 – Nov 2017
n=19,882

- Arua
- Mubende
- Apac
- Jinja
- Tororo
- Kabale
Diagnoses/Antibiotics
Most common admission diagnoses of all children
Uganda AFI Project: Jul 2016 – Nov 2017
n=20,762*

*8% missing data
Most common antibacterial medications given to all hospitalized children
Uganda AFI Project: Jul 2016 – Nov 2017
n=21,544
Admission diagnoses in children with *Salmonella* bacteremia
Uganda AFI Project: Jul 2016 – Nov 2017
n=51*

*12% missing data
Antibacterial medications received by children with *Salmonella* bacteremia
Uganda AFI Project: Jul 2016 – Nov 2017
n=55

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Percentage of children with <em>Salmonella</em> bacteremia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone</td>
<td>61%</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>44%</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>32%</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>7%</td>
</tr>
<tr>
<td>Penicillin</td>
<td>7%</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>7%</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>5%</td>
</tr>
<tr>
<td>Doxycyclin</td>
<td>4%</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>2%</td>
</tr>
<tr>
<td>Cotrimoxazole</td>
<td>2%</td>
</tr>
</tbody>
</table>
Salmonella deaths
## Description of deaths with *Salmonella* bacteremia

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Sex</th>
<th>Location</th>
<th>Length of stay in days</th>
<th>Lab test positive for malaria</th>
<th>Diagnoses</th>
<th>Medications given</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Male</td>
<td>Arua</td>
<td>16</td>
<td>Yes</td>
<td>Severe malaria, Sickle cell disease, Anemia, Respiratory infection</td>
<td>artesunate IV, penicillin IV, amoxicillin oral</td>
</tr>
<tr>
<td>1</td>
<td>Male</td>
<td>Arua</td>
<td>6</td>
<td>Yes</td>
<td>Severe malaria, Septicaemia</td>
<td>artesunate IV</td>
</tr>
<tr>
<td>3</td>
<td>Male</td>
<td>Jinja</td>
<td>1</td>
<td>No</td>
<td>Pneumonia</td>
<td>artesunate IV, gentamicin, ampicillin</td>
</tr>
</tbody>
</table>
### Antimicrobial Susceptibility Patterns of Children Who Died with *Salmonella* Bacteremia

<table>
<thead>
<tr>
<th></th>
<th>Ampicillin</th>
<th>Cotrimoxazole</th>
<th>Ciprofloxacin</th>
<th>Ceftriaxone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child 1</td>
<td>resistant</td>
<td>resistant</td>
<td>susceptible</td>
<td>resistant</td>
</tr>
<tr>
<td>Child 2</td>
<td>susceptible</td>
<td></td>
<td>susceptible</td>
<td></td>
</tr>
<tr>
<td>Child 3</td>
<td>susceptible</td>
<td>resistant</td>
<td>susceptible</td>
<td>intermediate</td>
</tr>
</tbody>
</table>
Seasonality
Salmonella cases by month

- Jan: 1 case
- Feb: 6 cases
- Mar: 4 cases
- Apr: 5 cases
- May: 2 cases
- Jun: 4 cases
- Jul: 9 cases
- Aug: 1 case
- Sep: 7 cases
- Oct: 10 cases
- Nov: 7 cases
- Dec: 3 cases

Stockouts and Staffing limitations indicated.
Children included in Uganda AFI project in Arua, by month (average)
Number of children diagnosed with *Salmonella* bacteremia in Arua, by month (average)