Invasive Salmonellosis in Central Nigeria

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Objectives

• Background
• Bacteremia surveillance of young children
• Preliminary results
• Gaps in knowledge
• Way forward
Child Mortality in Nigeria-General Facts

• About 5.3 million children are born yearly in Nigeria—11,000 everyday
  – 1 million of these children die before the age of 5 years

• Nigeria’s newborn death rate (NMR)-528 per day— is one of the highest in the world
  – About 9 of ten of newborn deaths are preventable
Lack of Etiologic Data for Bacteremic Syndromes

Limitations of previous studies

- Sub optimal laboratory Methods
- Culture media
- Agar preparation- suboptimal blood agar source
- Identification of isolates- misidentification
- Incomplete characterization
Community Acquired Bacteremic Syndrome in Young Nigerian Children (CABS SYNC)

A COLLABORATIVE STUDY
National Hospital Abuja
Zankli Medical Center
MRC Laboratories, The Gambia
Michigan State University
CDC, ATLANTA

Objectives
- To introduce automated blood culture system to pediatric clinical care
- Pilot study of the etiologic agents of bacteremia in young children in central Nigeria
Equipping the Laboratory
Surveillance

- Enrolment from Sept 2008-
- All children aged 2 months-5 years
- Fever or hypothermia (temp greater or equal to 38.5°C or less than 34.5°C plus prostration, respiratory distress, convulsion or diarrhea
- Informed consent
Methods II

• Blood drawn aseptically into culture bottle with other clinically indicated tests
• Culture bottles incubated for 5 days (max)
• Positive cultures Gram stained and sub cultured on appropriate agar plates
• Identification by standard biochemical method (API)
Pre-Consultation Antibiotic Exposure in FCT

Fig 2. Serum Antimicrobial Activity in Sub-Population by Site

(Obaro et al. 2011 BMC infectious Diseases)
Childhood Bacteremia in FCT, Central Nigeria

- 969 children aged 2 months - 5 years. Mean age was 21 ± 15.2 months.
- Salmonella spp were the leading cause of bacteremia - 28.5% with *S. typhi* accounting for 20.9% and non-typhi salmonella - 7.6%)
- *S. aureus* - 20.2%
- *S. pneumoniae* - 11.9%
- Acinetobacter - 11%.

*Obaro et al. BMC Infect Dis 2011*
Nigeria—Culturally Diverse
Bacteremia Surveillance in Young Children
Surveillance Sites in Kano
Facilities in Kano
Etiologic Agents of Childhood Bacteremia in North Central Nigeria

### Isolate Count 3/22/2015

- **Streptococcus Pneumoniae**: 78
- **Streptococcus Specie**: 18
- **Staphylococcus Aureus**: 86
- **Salmonella Typhi**: 306
- **Salmonella Non Typhi**: 94
- **Pseudomonas Specie**: 7
- **Pseudomonas Aeruginosa**: 27
- **Providential Specie**: 5
- **Proteus Specie**: 22
- **Klebsiella Specie**: 49
- **Haemophilus Influenza**: 14
- **Escherichia Coli**: 35
- **Enterococcus Faecalis**: 12
Seasonal Trend of Invasive Salmonellosis

Number of S. Typhi and NTS isolated by month

<table>
<thead>
<tr>
<th>Month</th>
<th>S. Typhi</th>
<th>NTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feb-13</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Mar-13</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Apr-13</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>May-13</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Jun-13</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Jul-13</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Aug-13</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>Sep-13</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>Oct-13</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Nov-13</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Dec-13</td>
<td>27</td>
<td>9</td>
</tr>
<tr>
<td>Jan-14</td>
<td>40</td>
<td>27</td>
</tr>
<tr>
<td>Feb-14</td>
<td>42</td>
<td>40</td>
</tr>
<tr>
<td>Mar-14</td>
<td>51</td>
<td>42</td>
</tr>
<tr>
<td>Apr-14</td>
<td>17</td>
<td>51</td>
</tr>
</tbody>
</table>

Legend:
- Blue: S. Typhi
- Red: NTS
# Age Distribution of Bacteremic Children

<table>
<thead>
<tr>
<th></th>
<th>Mean Age (Months)</th>
<th>Median</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.Typhi</td>
<td>32.5</td>
<td>31.5</td>
<td>260</td>
</tr>
<tr>
<td>NTS</td>
<td>24.3</td>
<td>22</td>
<td>73</td>
</tr>
<tr>
<td>Other bacteria spp</td>
<td>13.7</td>
<td>9</td>
<td>333</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>686</td>
</tr>
</tbody>
</table>
## Isolates from Neonates

<table>
<thead>
<tr>
<th>Isolates from Infants &lt; 1 month</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALKALIGENS SPECIE</td>
<td>1</td>
<td>1.1%</td>
</tr>
<tr>
<td>Aeromonas Hydrophila</td>
<td>1</td>
<td>1.1%</td>
</tr>
<tr>
<td>HAEMOLYTIC STREPTOCOCCUS SPECIES</td>
<td>3</td>
<td>3.2%</td>
</tr>
<tr>
<td>Candida specie</td>
<td>5</td>
<td>5.4%</td>
</tr>
<tr>
<td>ENTEROCOCCUS FAECALIS</td>
<td>4</td>
<td>4.3%</td>
</tr>
<tr>
<td>ESCHERCHIA COLI</td>
<td>9</td>
<td>9.7%</td>
</tr>
<tr>
<td>KLEBSIELLA PNEUMONIAE</td>
<td>14</td>
<td>15.1%</td>
</tr>
<tr>
<td>MORGANELLA MORGANII</td>
<td>1</td>
<td>1.1%</td>
</tr>
<tr>
<td>NON HAEMOLYTIC STREPTOCOCCUS SPECIE</td>
<td>2</td>
<td>2.2%</td>
</tr>
<tr>
<td>PROTEUS MIRABILIS</td>
<td>2</td>
<td>2.2%</td>
</tr>
<tr>
<td>PROTEUS SPECIE</td>
<td>5</td>
<td>5.4%</td>
</tr>
<tr>
<td>PROVIDENTIAL SPECIE</td>
<td>1</td>
<td>1.1%</td>
</tr>
<tr>
<td>PSEUDOMONAS AERUGINOSA</td>
<td>9</td>
<td>9.7%</td>
</tr>
<tr>
<td>SALMONELLA TYPHI</td>
<td>2</td>
<td>2.2%</td>
</tr>
<tr>
<td>SERRATIA SPECIE</td>
<td>1</td>
<td>1.1%</td>
</tr>
<tr>
<td>STAPHYLOCOCCUS AUREUS</td>
<td>28</td>
<td>30.1%</td>
</tr>
<tr>
<td>STREPTOCOCCUS PNEUMONIAE</td>
<td>5</td>
<td>5.4%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>93</strong></td>
<td></td>
</tr>
<tr>
<td>Salmonellae</td>
<td>N</td>
<td></td>
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<tr>
<td>-----------------------------------------</td>
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<td></td>
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<tr>
<td>Salmonella brendeney</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Salmonella dublin</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Salmonella durban</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Salmonella enteritidis</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>Salmonella Galiema</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Salmonella group B</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Salmonella Group C</td>
<td>2</td>
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</tr>
<tr>
<td>Salmonella group D</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Salmonella Paratyphi C</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Salmonella Pasing</td>
<td>1</td>
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<tr>
<td>Salmonella poona</td>
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<tr>
<td>Salmonella ser. Pullorum Grp D</td>
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<td></td>
</tr>
<tr>
<td>Salmonella spp</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Salmonella typhimurium</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>100</strong></td>
<td></td>
</tr>
</tbody>
</table>
Resistance Pattern of Invasive *S. typhi* Isolates
Regional Differences in S. Typhi

Abuja - percent resistant

- Azithromycin: 2.63%
- Imipenem: 0.00%
- Chloramphenicol: 61.54%
- Tetracycline: 47.44%
- Sulfamethoxazole: 92.31%
- Trimethoprim/Sulfamethoxazole: 58.97%
- Streptomycin: 24.36%
- Kanamycin: 0.00%
- Gentamicin: 0.00%
- Ciprofloxacin: 0.00%
- Nalidixic Acid: 3.85%
- Ceftriaxone: 0.00%
- Cefoxitin: 5.13%
- Ampicillin: 55.13%

Kano - percent resistant

- Azithromycin: 22.56%
- Imipenem: 0.00%
- Chloramphenicol: 35.76%
- Tetracycline: 62.42%
- Sulfamethoxazole: 92.12%
- Trimethoprim/Sulfamethoxazole: 73.94%
- Streptomycin: 55.76%
- Kanamycin: 0.61%
- Gentamicin: 1.21%
- Ciprofloxacin: 0.00%
- Nalidixic Acid: 4.24%
- Ceftriaxone: 2.42%
- Cefoxitin: 1.82%
- Ampicillin: 69.70%
Terminal Ileal Perforation (TIP)

- **Mortality**: Dickson et al. (Br. J Surg 1964) 58%
- Adesunkanmi et al. (Ann Coll Surg Hong Kong 2003) 28%
- Ugochukwu et al. (Int J Surg 2013) 19%
Typhoid Perforation-CFR

Case Fatality rates of patients with typhoid intestinal perforation:

- Nigeria (1986 - 2009) n=1427: 19.8%
- Africa (1978 - 2005) n=1818: 15.46%
- ASIA (1987 - 2008) n=1080: 11.48%
- Others (1987 - 2010) n=301: 5.98%

*unweighted

Source: Mogasale V, Desai SN, Mogasale VV, Park JK, Ochiai RL, et al. (2014) Case Fatality Rate and Length of Hospital Stay among Patients with Typhoid Intestinal Perforation in Developing Countries: A Systematic Literature Review
TIP

• A complication of treatment?
• An unusual manifestation of TF?
• Host genetic and/or bacterial virulence?

Need for improved understanding of TIP
Sickle Cell Disease

• 300x more likely to develop bacterial meningitis
• 600x more likely to develop pneumococcal meningitis
• 116x more likely to develop *H.influenzae* meningitis
• 25x more likely to develop NTS sepsis than non-SCD children from same community

2. Booth, Inusa, Obaro IJID 2011
Public Water Supply
Public Water Supply
Health Care Seeking Behavior

Alternative Medicine

Patient

CP

Chemist Pharmacy

Diagnosis

Rx → N/A → Chemist Pharmacy

?Lab diagnosis
?Availability
?Quality control
?Reliability
?Timeliness
Rising Abx Resistance

- OTC abx
- Poor quality abx

Rising Antimicrobial Resistance

- Unguided choice of abx

- Prolonged hospital stay
- Increased cost of care
- Increased mortality
Conclusions

- High prevalence of S. typhi over NTS
- Overall high prevalence of MDR (NTS>Typhi)
- High prevalence of infant disease, including neonates
- Significant regional difference in the epidemiology of invasive salmonellosis
- High prevalence of TIP
- Rare disease by Paratyphi
- Surveillance
  - population-based surveillance
  - Multi-disciplinary research teams
“The microbe that felled one child in a distant continent yesterday can reach yours today and seed a global pandemic tomorrow”

Nobel Laureate
Dr. Joshua Lederberg
Acknowledgement

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  – NIAID (NIH)
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  – AKTH
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Thank you!