Genomic Characterization of Invasive *Salmonella enterica* Isolated in Severe Typhoid In Africa Surveillance In Ibadan, Nigeria

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Background

- Typhoidal and invasive non-typhoidal *Salmonella* (iNTS) infections cause high morbidity and mortality in Africa (Smith *et al.*, 2016).
- Globally, iNTS causes 94 million cases of gastroenteritis (Majowicz *et al.*, 2010).
- An estimated 17.8 million cases of typhoid occur annually in low- and middle income countries (LMICs) annually (Antillon *et al.*, 2017).
- 26% of global typhoid mortality occurs in Africa (Mogasale *et al.*, 2014).

**The Severe Typhoid in Africa (SETA) program**

- High typhoid incidence in Africa (Jeon *et al.*, 2019)

- Nigeria had the highest proportion (4%) of investigated cases of typhoid intestinal perforation among SETA sites (Birkhold *et al.*, 2023)

Figure 1: SETA country sites
Blood culture based surveillance is very useful to investigate/assess bacterial invasive infections (Ombelet et al., 2019).

Unfortunately, genomic surveillance of invasive Salmonella in Nigeria is insufficient (Ikhimiukor et al., 2022)

4 hospital facilities in Ibadan
- University College Hospital (UCH) – tertiary
- Our Lady Apostle (OLA) Hospital – secondary
- Adeoyo Maternity Teaching Hospital (AMTH) - secondary
- Kola Daisi Foundation (KDF) Hospital - primary
Methodology

Antimicrobial susceptibility testing (Vitek2 System)

Extraction of *Salmonella* genomes

Whole genome sequencing (Illumina platform)

Sequence data analysis
Figure 2: *Salmonella* serovars recovery across age groups
Figure 3: *Salmonella* serovars distribution across local government areas
Figure 4: S. Typhi and iNTS recovery in tertiary versus primary/secondary facilities

*Salmonella* serovars

- **S. Typhi**
  - Tertiary
  - Primary/secondary

- **iNTS**
  - Tertiary
  - Primary/secondary

*p = 0.02*
**Table 1: Salmonella lineages in Ibadan**

<table>
<thead>
<tr>
<th>Sequence Type</th>
<th>Serovar</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Typhi</td>
<td>38</td>
</tr>
<tr>
<td>11</td>
<td>Enteritidis</td>
<td>9</td>
</tr>
<tr>
<td>313</td>
<td>Typhimurium</td>
<td>3</td>
</tr>
<tr>
<td>365</td>
<td>Weltevreden</td>
<td>6</td>
</tr>
<tr>
<td>2562</td>
<td>Stanleyville</td>
<td>1</td>
</tr>
</tbody>
</table>

33/38 (86.8%) of the S. Typhi isolates are of the 3.1.1 genotype showing the predominance of the genotype among S. Typhi strains in Ibadan.

**Figure 5: S. Typhi genotypes distribution**
Salmonella recovery was least in 2020. This is likely attributable to the hiatus in subject recruitment owing to COVID-19.

Majority of the recovered Salmonella were from UCH although none was recovered from UCH in 2021.

Figure 6a: Recruitment per year across facilities

Figure 6b: Salmonella serovars recovery per year
Figure 7: Pairwise core genome SNPs threshold of *Salmonella* serovars
Figure 8: Potential clonal transmission timeline and clusters of *Salmonella* serovars across facilities
Figure 9: Antimicrobial resistance determinants, point mutations and plasmid replicons in *Salmonella* serovars.
Conclusion

• The prominent *Salmonella* lineage in Ibadan is the genotype 3.1.1, sequence type (ST) 2.

• The alarming detection of quinolone resistance determining regions (QRDRs) in this lineage suggests that ciprofloxacin, often used for empiric treatment of typhoid fever, may soon become obsolete.

• The recovery of multidrug resistant *Salmonella* is worrisome particularly as some of the antimicrobial resistance combinations were associated with certain plasmid replicons and the possibility that *Salmonella* acquire resistance from circulating mobile elements.

• The endemicity of both S. Typhi and iNTS may be driven by mini-outbreaks from a point source.
Recommendations

- There is a need for more water, sanitation and hygiene (WASH) programmes in Ibadan to abate the risk of *Salmonella* infections.

- Nigeria needs to adopt typhoid conjugate vaccines especially as the therapeutic value of ciprofloxacin against typhoid fever is being threatened.

- Surveillance efforts should be intensified to ensure active monitoring of MDR *Salmonella* serovars in Ibadan.
Acknowledgments

• This work was supported by Bill & Melinda Gates Foundation Award (Grant number OPP1127988) to the International Vaccine Institute (IVI), South Korea

• This research work was supported in part by the UK National Institute of Health and Care Research (NIHR) Global Health Research Unit on Genomics and enabling data for Surveillance of Antimicrobial Resistance Consortium Award NIHR project #NIHR133307.

• INO is a Calestous Juma Science Leadership Fellow Supported by the Bill & Melinda Gates Foundation.

• GHRU-GSAR staff – Anderson Oaikhena, Gabriel Temitope Sunmonu.

• Ifiok Udofia, Jesutofunmi Odeyemi and other SETA Research Assistants and lab staff.

• College of Medicine, University of Ibadan.

• University College Hospital, Ibadan.
THANK YOU FOR YOUR ATTENTION