Analysis of the antimicrobial susceptibility patterns of Salmonella enterica serotype Typhi following Mass-targeted typhoid conjugate vaccine immunization campaigns in Harare City, Zimbabwe, 2023

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Globally, typhoid fever is a major cause of mortality and morbidity.

Annually 215,000 deaths result from over 26 million cases.

Southern Asia and sub-Saharan Africa are the most affected regions.

Up to 4% of typhoid fever patients become chronic carriers.
Epidemiology of Typhoid in Zimbabwe 2012 - 2023

<table>
<thead>
<tr>
<th>Year</th>
<th>Suspected Typhoid cases</th>
<th>Culture-confirmed Typhoid cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>5829</td>
<td>103</td>
</tr>
<tr>
<td>2013</td>
<td>1707</td>
<td>61</td>
</tr>
<tr>
<td>2014</td>
<td>1653</td>
<td>101</td>
</tr>
<tr>
<td>2015</td>
<td>1236</td>
<td>45</td>
</tr>
<tr>
<td>2016</td>
<td>2352</td>
<td>85</td>
</tr>
<tr>
<td>2017</td>
<td>2032</td>
<td>155</td>
</tr>
<tr>
<td><strong>2018</strong></td>
<td><strong>4195</strong></td>
<td><strong>223</strong></td>
</tr>
<tr>
<td>2019</td>
<td>2137</td>
<td>138</td>
</tr>
<tr>
<td>2020</td>
<td>875</td>
<td>36</td>
</tr>
<tr>
<td>2021</td>
<td>144</td>
<td>7</td>
</tr>
<tr>
<td>2022</td>
<td>153</td>
<td>9</td>
</tr>
</tbody>
</table>

Typhoid has been endemic in Zimbabwe, particularly Harare City since 2010.

Highest number of cases in 2018: 4195 cases with 223 culture confirmed cases.

754 cases in 2023 with 29 culture confirmed cases.

- Limited diagnostic capacity in Microbiology
- Limited diagnostic access

Source: District Health Information System (DHIS2)
National Microbiology Reference Laboratory
Proportion of Children under 5 years suspected of having Typhoid in Zimbabwe 2013-2023

Source: District Health Information System Zimbabwe (DHIS2)
Typhoid Conjugate Vaccine Rollout in Zimbabwe

- Increased emergence and spread of drug resistance
  - Genomic characterization of 29 samples identified S. Typhi H58 with reduced susceptibility to ciprofloxacin (*T. Mashe, et al, 2021*)

- First typhoid conjugate vaccination (TCV) campaign in 2019
  - Introduced Harare’s nine high-density suburbs
  - Targeted children aged 6 months -15 years
  - Extended up to 45 years in some areas due to high attack rate

- Second nationwide mass TCV was conducted in 2021
  - Incorporation of TCV in the country's routine immunisation programme
Objectives

- Determine the antimicrobial susceptibility patterns of Salmonella Typhi isolated in Harare City from October 2022 to May 2023
- Assess the antimicrobial susceptibility pattern following two distinct TCV campaigns in Harare City
- Inform future public health interventions to control typhoid fever in Harare City
Methods

Study Location: National Microbiology Reference Laboratory (NMRL)

Salmonella Typhi Identification
- 55 blood culture isolates from suspected Salmonella cases
- BioMerieux VITEK® MS (MALDI-TOF)
- Serotyping
- 31 confirmed as Salmonella typhi

Antimicrobial Susceptibility Testing
- BioMerieux VITEK® 2 COMPACT
- To determine Minimum Inhibitory Concentration

Statistical Analysis
- Stata® to calculate frequencies and proportions
Demographic Distribution of Salmonella Typhi Confirmed Cases

- Males were 19/31 (61%)
- Median age was 19 years (IQR, 12-24)
- 23/31 (74.2%) did not have their vaccination status stated
- 6/31 (19.4%) were unvaccinated whilst 2/31 (6.4%) reported previous vaccination
Antimicrobial resistance pattern in Zimbabwe, 2022-2023

Percentage (%)
### Ratio of MDR Salmonella Typhi in Zimbabwe, 2023

<table>
<thead>
<tr>
<th></th>
<th>n/N</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDR</td>
<td>2/31</td>
<td>6%</td>
</tr>
<tr>
<td>Non MDR/XDR</td>
<td>29/31</td>
<td>94%</td>
</tr>
</tbody>
</table>

- Overall, 2/31 (6%) of analysed isolates had multi-drug resistance
- No isolates phenotypically showed extensive drug resistance
Comparison of antibiograms 2018 versus 2023

Ampicillin

- 2018 n=82:
  - R: 89%
  - I: 1%
  - S: 10%
- 2023 n=31:
  - R: 100%
  - I: 0%
  - S: 0%

Ceftriaxone

- 2018 n=82:
  - R: 0%
  - I: 0%
  - S: 100%
- 2023 n=31:
  - R: 0%
  - I: 0%
  - S: 100%

Trimethoprim/Sulfamethoxazole

- 2018 n=82:
  - R: 90%
  - I: 0%
  - S: 10%
- 2023 n=31:
  - R: 94%
  - I: 0%
  - S: 6%

Ciprofloxacin

- 2018 n=82:
  - R: 9%
  - I: 61%
  - S: 30%
- 2023 n=31:
  - R: 6%
  - I: 3%
  - S: 94%
Study Limitations

- Limited statistical power inference based on a small sample size
- Small sample size may be more susceptible to selection bias
- Confounding variables (e.g., different Salmonella Typhi strains)
The study suggests increased susceptibility to ciprofloxacin following the introduction and integration of TCV in Harare City.

- Previous studies conducted in Zimbabwe have shown increased resistance to ciprofloxacin (*Mashe et al, 2019*).
- Zimbabwe treatment guidelines:
  - 1st line – Ciprofloxacin, Ceftriaxone
  - 2nd line - Azithromycxin

Ampicillin and cotrimoxazole resistance in *Salmonella Typhi* isolates has remained persistent in Zimbabwe between 2018 and 2023.
Recommendations

Continued integration of TCV in the national immunization program

Whole-genome sequencing to identify the presence and mechanisms of antimicrobial resistance

Genetic characterization to determine phylogenetic relatedness
Acknowledgements
Thank you