Analysis of Trends in Resistance to Fluoroquinolones and Extended Spectrum β-lactams among *Salmonella* Typhi Isolates Obtained From Patients at Four Outpatient Clinics in Nairobi County, 2012-2016, Kenya

Susan Kavai
Kenya Medical Research Institute
Typhoid fever → 25 million illnesses & >200,000 deaths per yr.

S. Typhi → international public health problem esp in SubSaharan Africa.
Global spread of H58 MDR Typhi genotype

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A single dominant MDR lineage, H58, has emerged and spread throughout Asia and Africa over the last 30 years
Distribution of MDR Typhi in recent surveillance studies

History and Background of TF in Kenya

- TF→ a disease mostly affecting adults and older children (>10 years).
- Typhoid fever → **Consumption of contaminated foods, drinks, or water**
- **MDR in S. Typhi** isolates collected in hospitals within Nairobi county was 77% (Kariuki *et al.*, 2015).
Distribution of the Sampling Sites
Results: *S. Typhi* resistance trends from 2012 to 2016 (N=287)

- Most common resistance phenotype **AMP, SXT, TCY & CHL**.
- Trends increasing and decreasing depending on the *S. Typhi* isolated annually.
- **SXT, CHL & AMC** resistance high among recommended drugs for Typhoid fever.
- Generally low resistance observed among **Cephalosporins**.
**S. Typhi Resistance to fluoroquinolones and β-lactams (N=34)**

- Resistance to fluoroquinolones and β-lactams was observed at an average of 18.2% and 15.4% respectively.

- Thirty four (11.85%) isolates had combined resistance to fluoroquinolones and β-lactams.

*N=34, resistance levels of MDR S. Typhi against recommended drugs of treatment for various age distributions. Ceftazidime(CAZ), Cefpodoxime(CPD), Cefotaxime(CTX), Amoxicillin Clavulanate(AMC), Ciprofloxacin(CIP).*
PCR Results for confirmation of Beta-lactam resistance

Gel electrophoresis of PCR assays for the identification of resistance bla genes

Plates (A) bla\textit{INT} gene 650bp, (B) bla\textit{CTX-M} gene 593bp and (C) bla\textit{TEM} gene 865bp

M-Molecular weight Ladder; NC-\textbf{Negative Control} (Sterile distilled water); PC-\textbf{Positive Control} (known positive control strains).

*Numbers at the top represent DNA numbers of the isolate
PCR Results for confirmation of Fluoroquinolone resistance

Plates (D) *PARC gene 412bp*, and (E) *PARE gene 272 bp*.
M-Molecular weight Ladder; NC-Negative Control (Sterile distilled water); PC-Positive Control (known positive control strains). Numbers at the top represent DNA numbers of the isolate.

- A total of 27 (80%) isolates subjected to PCR were found to have resistance genes for both β-lactams and fluoroquinolones.
Discussion

- The overall prevalence of MDR S. Typhi in this study was 55.5%. In 2008-2012 a study done in Kenya from hospital isolates found the MDR in S. Typhi to be 77% (Kariuki et al., 2015).

- Data from this study confirms there is resistance in the recommended drugs for typhoid fever such as SXT (59.2%), CHL (54.8%) and AMC(11.3%).

- The increased prevalence of MDR S. Typhi strains resistant to nalidixic acid should be of public health concern as it is a marker for possible complete fluoroquinolone resistance arising.

- Presence of ESBL producers among the isolates tested is a confirmation of the rising resistance against beta lactams.

- Presence of the bla genes was a confirmation of resistance posed by these isolates and possible transmission to other enteric bacteria in the gut microflora.
Variations in prevalence rates over time can be attributed to environmental, economic and social settings of a community.

The observed prevalence of MDR *S. Typhi* in Kenya though showing a decrease over time is still something to worry about as *S. Typhi* showed resistance to recommended drugs of treatment.

There is evidence of transferability of resistance genes among these isolates hence an indication that resistance is likely to increase over time.
Conclusion

- All isolates were resistant to at least one drug used in the panel. Indicates that levels of resistance were quite alarming.

- Among drugs recommended for typhoid treatment, Resistance mostly observed in AMP, SXT, CHL, and AMC.

- With increasing prevalence of MDR strains that have decreased ciprofloxacin susceptibility and resistance to nalidixic acid, careful observation to be made on outcome of therapy for typhoid fever.

- Transferrable resistance bla genes indicates possible horizontal transfer of resistance.
Recommendations

1. Prevention measures: **provision of clean water and sanitation improvements**, as well as **health education**.

2. **Routine surveillance to monitor antimicrobial resistance patterns** for typhoid outbreaks.

3. **Surveillance data → inform policy on trends** in effectiveness of current drugs of choice for treatment of typhoid.

4. **Review on the drugs of choice for treatment** of typhoid fever especially fluoroquinolones and third generation cephalosporins.
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