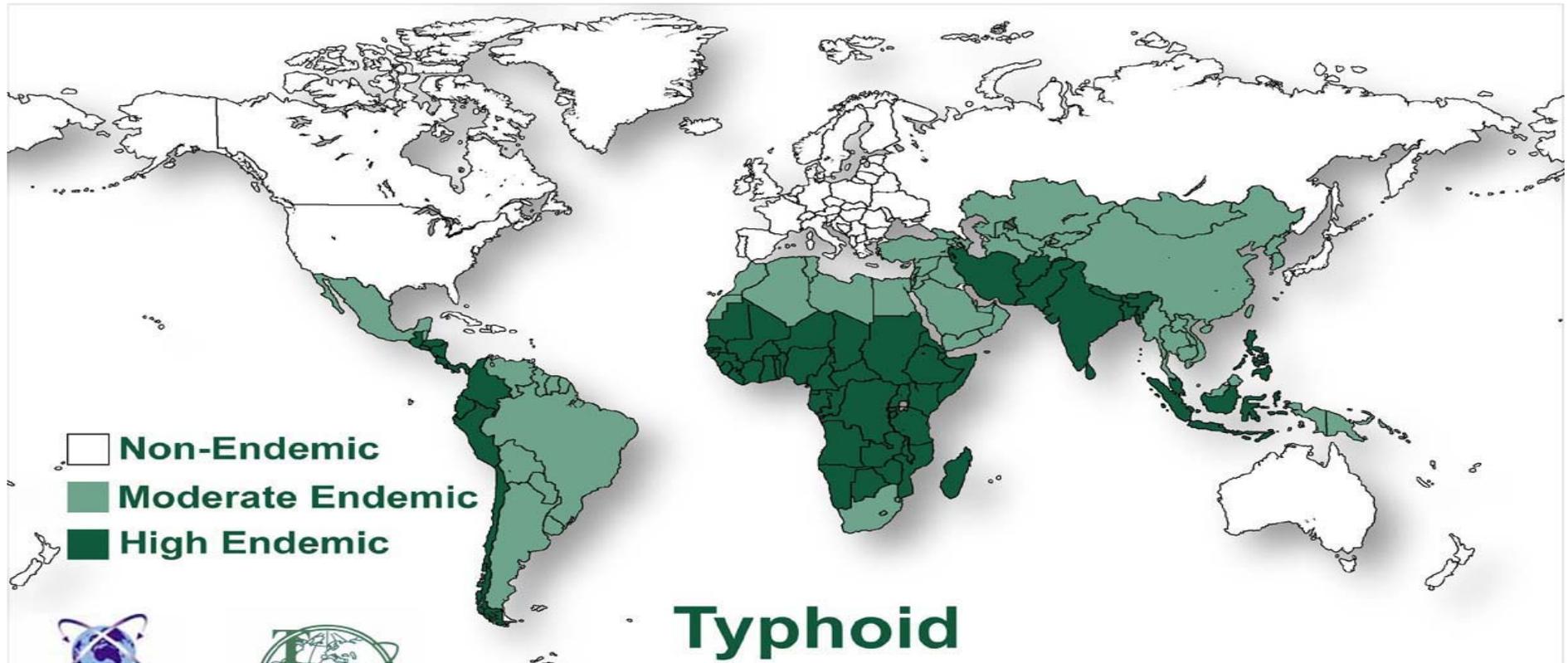




**Analysis of Trends in Resistance to Fluoroquinolones and Extended Spectrum  $\beta$ -lactams among *Salmonella* Typhi Isolates Obtained From Patients at Four Outpatient Clinics in Nairobi County, 2012-2016, Kenya**

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## Introduction



- ❖ Typhoid fever → **25 million illnesses** & >200 000 deaths per yr.
- ❖ *S. Typhi* → international public health problem esp **in SubSaharan Africa**.

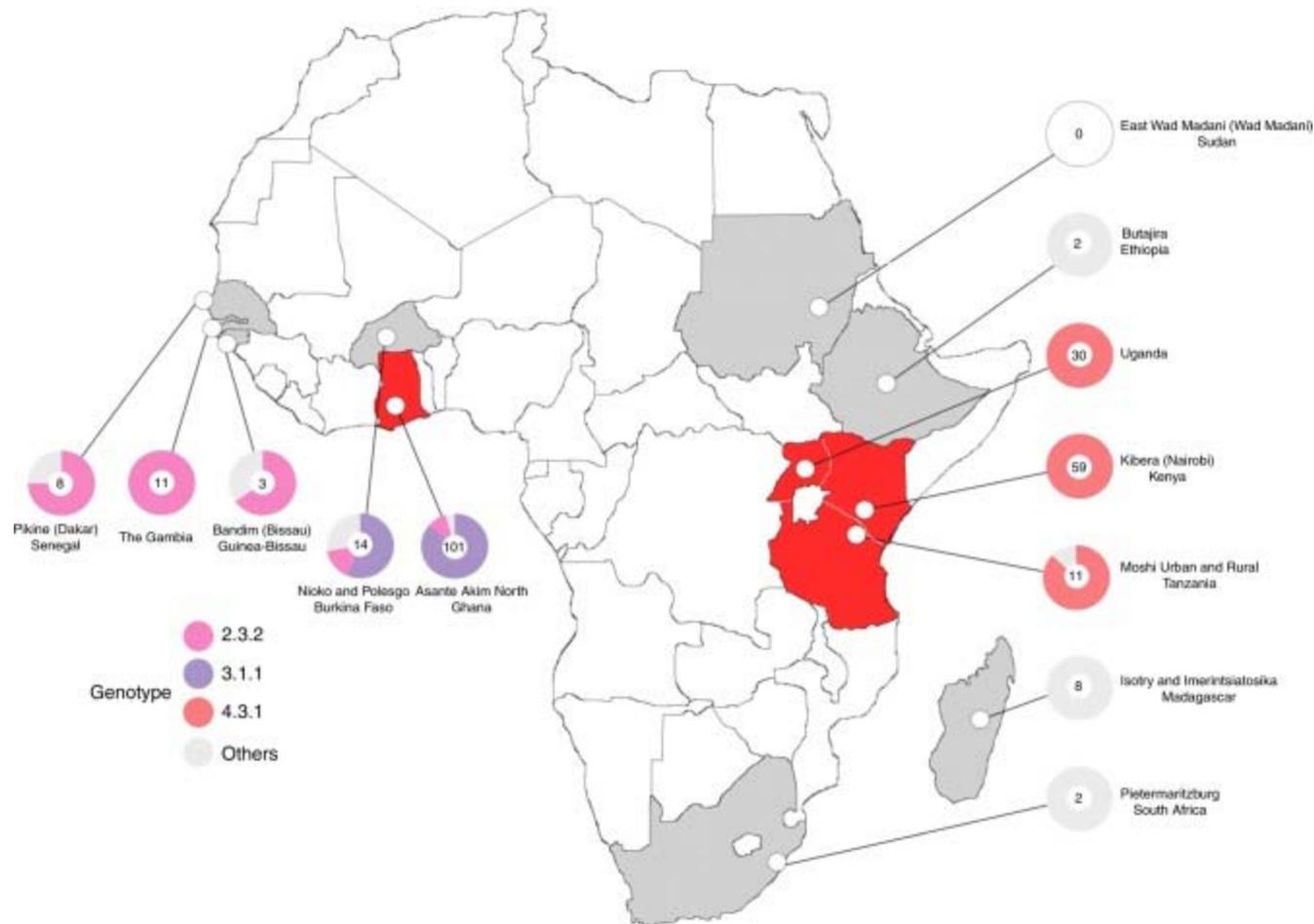
# Global spread of H58 MDR Typhi genotype



**WTAC 9-14 Sept 2018**

**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



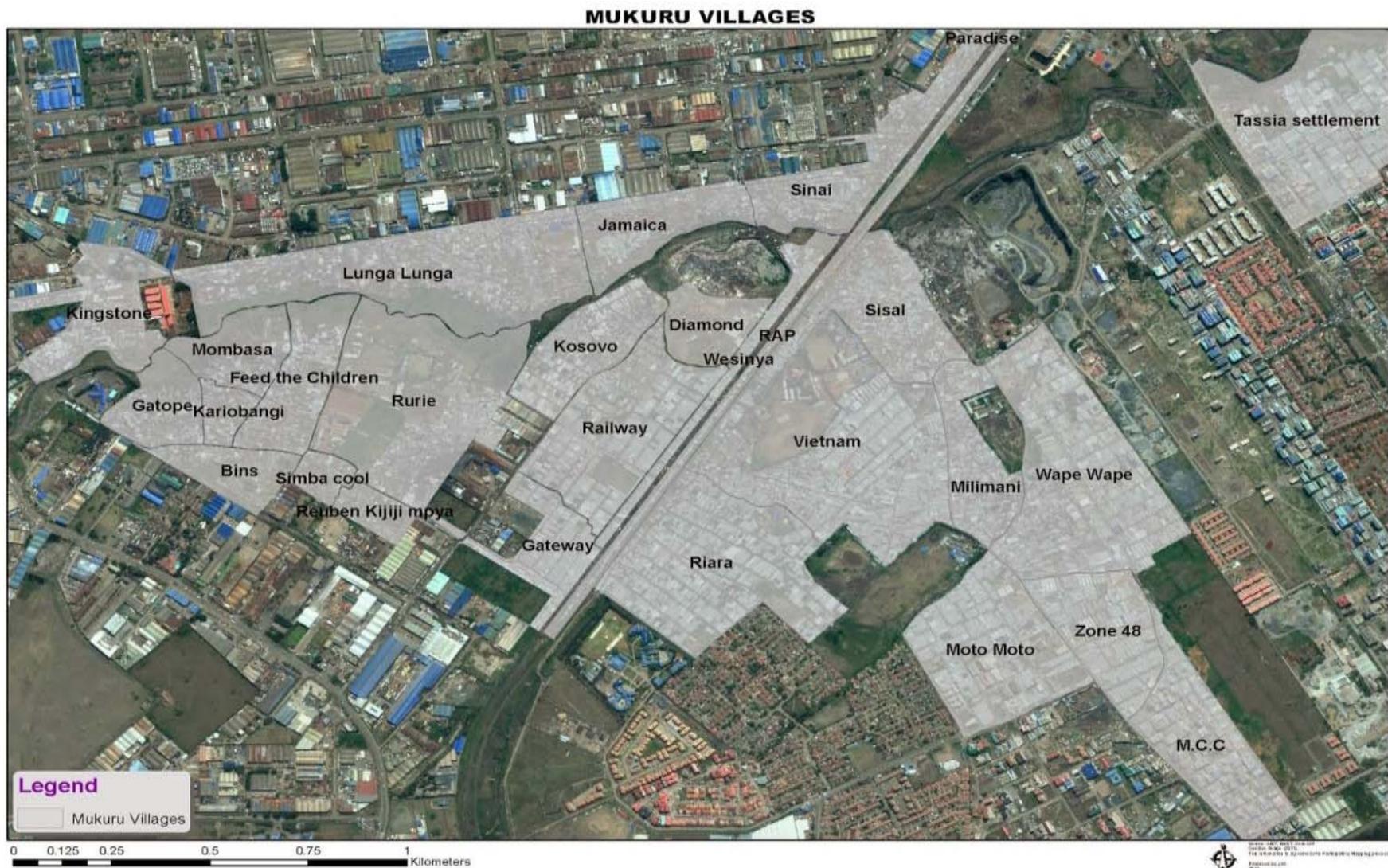
Park *et al.* Nat Commun. 2018 Nov 30;9(1):5094

## History and Background of TF in Kenya

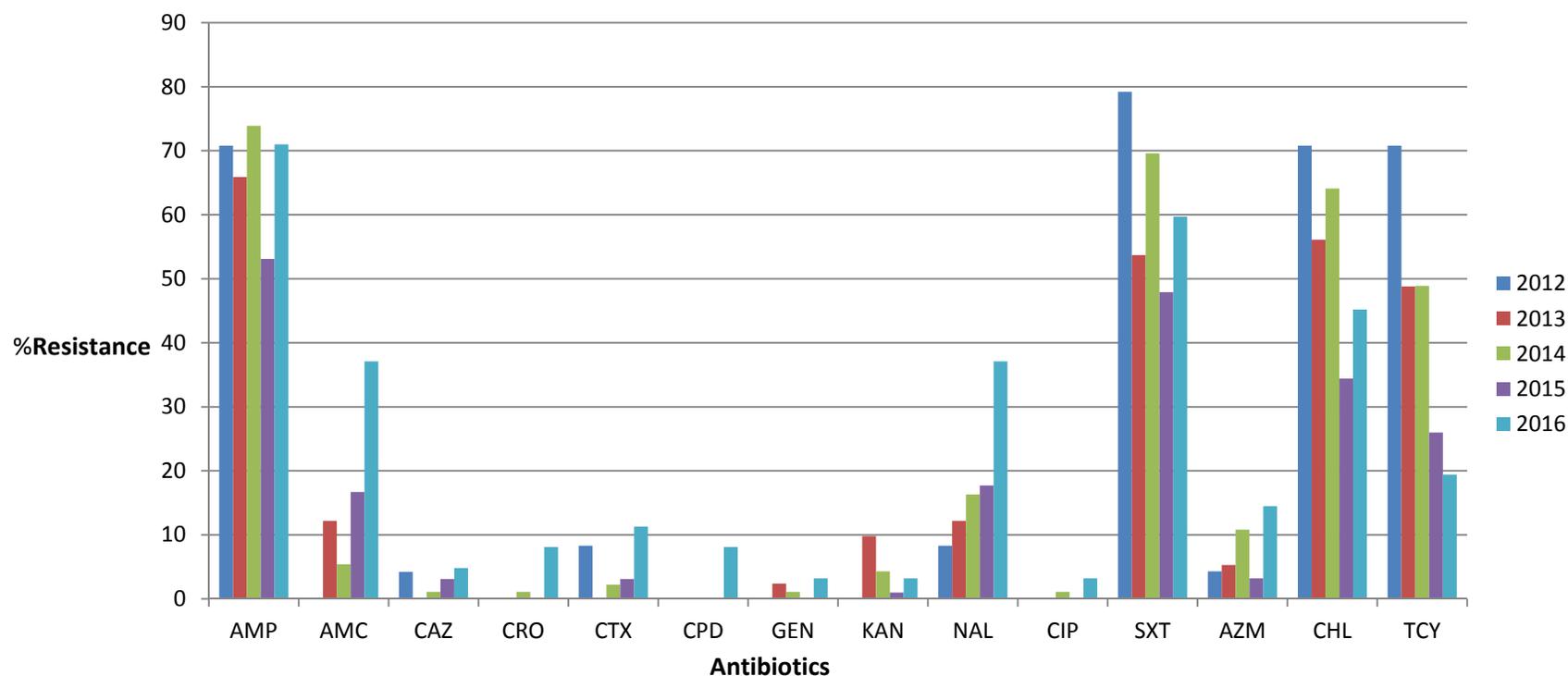


- ❖ TF → a disease mostly affecting adults and older children (>10 years).
- ❖ Typhoid fever → **Consumption of contaminated foods, drinks, or water**
- ❖ **MDR in *S. Typhi*** isolates collected in hospitals within Nairobi county was 77% (Kariuki *et al.*, 2015).

# Distribution of the Sampling Sites

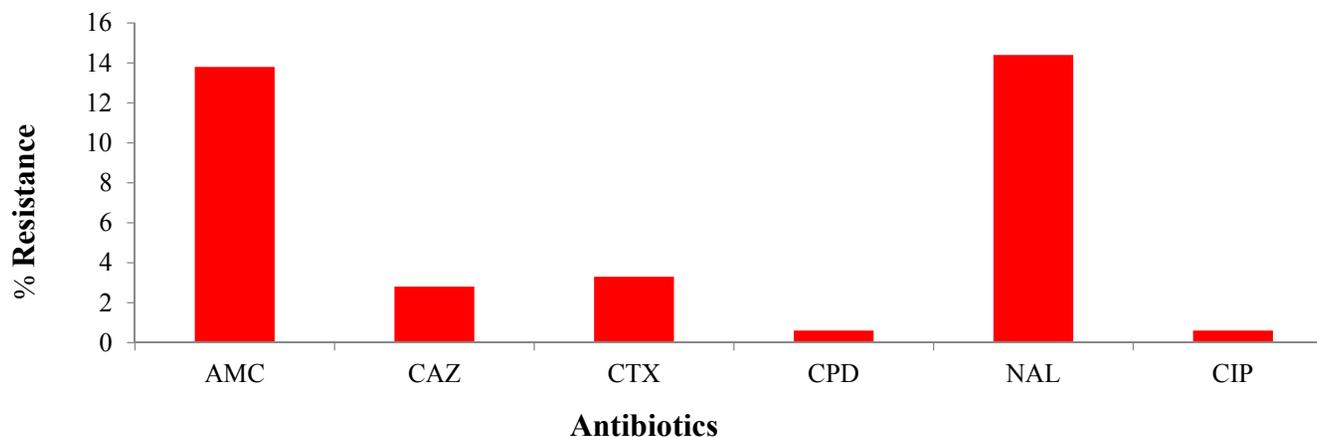


## Results: *S. Typhi* resistance trends from 2012 to 2016 (N=287)



- ❖ 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**

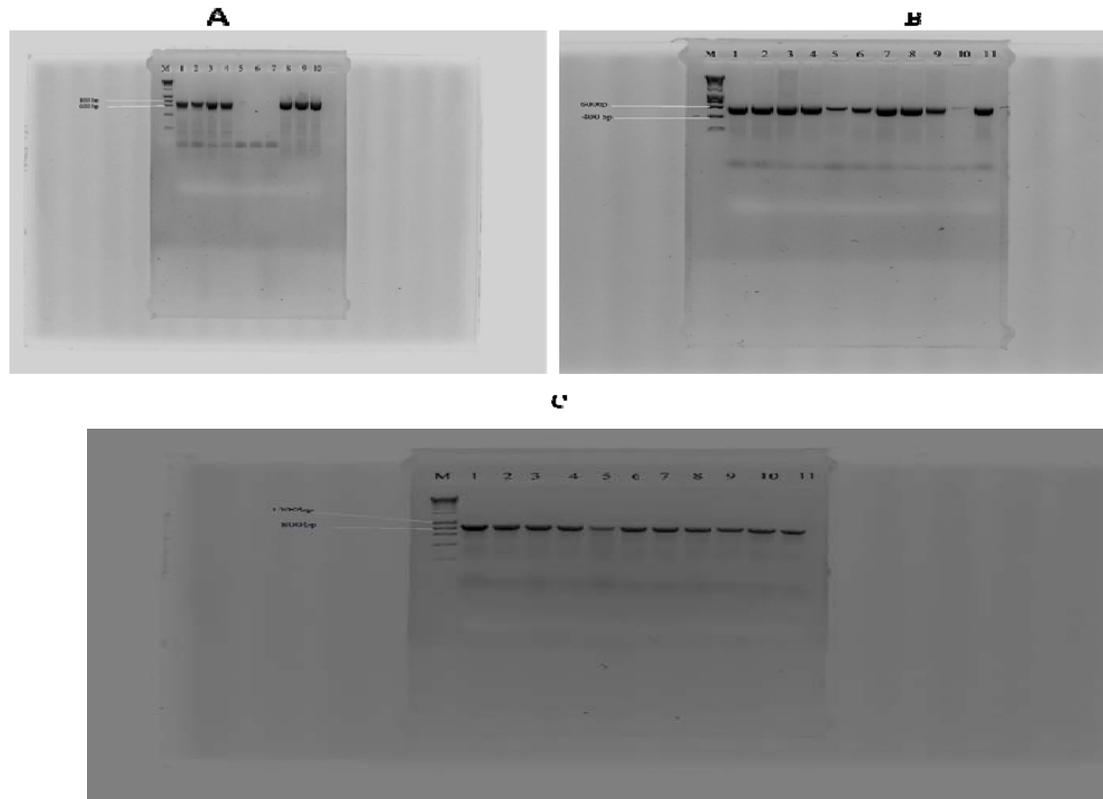
## **S. Typhi Resistance to fluoroquinolones and $\beta$ -lactams (N=34)**



- ❖ Resistance to fluoroquinolones and  $\beta$ -lactams was observed at an **average of 18.2% and 15.4% respectively.**
- ❖ **Thirty four (11.85%)** isolates had **combined resistance** to fluoroquinolones and  $\beta$ -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



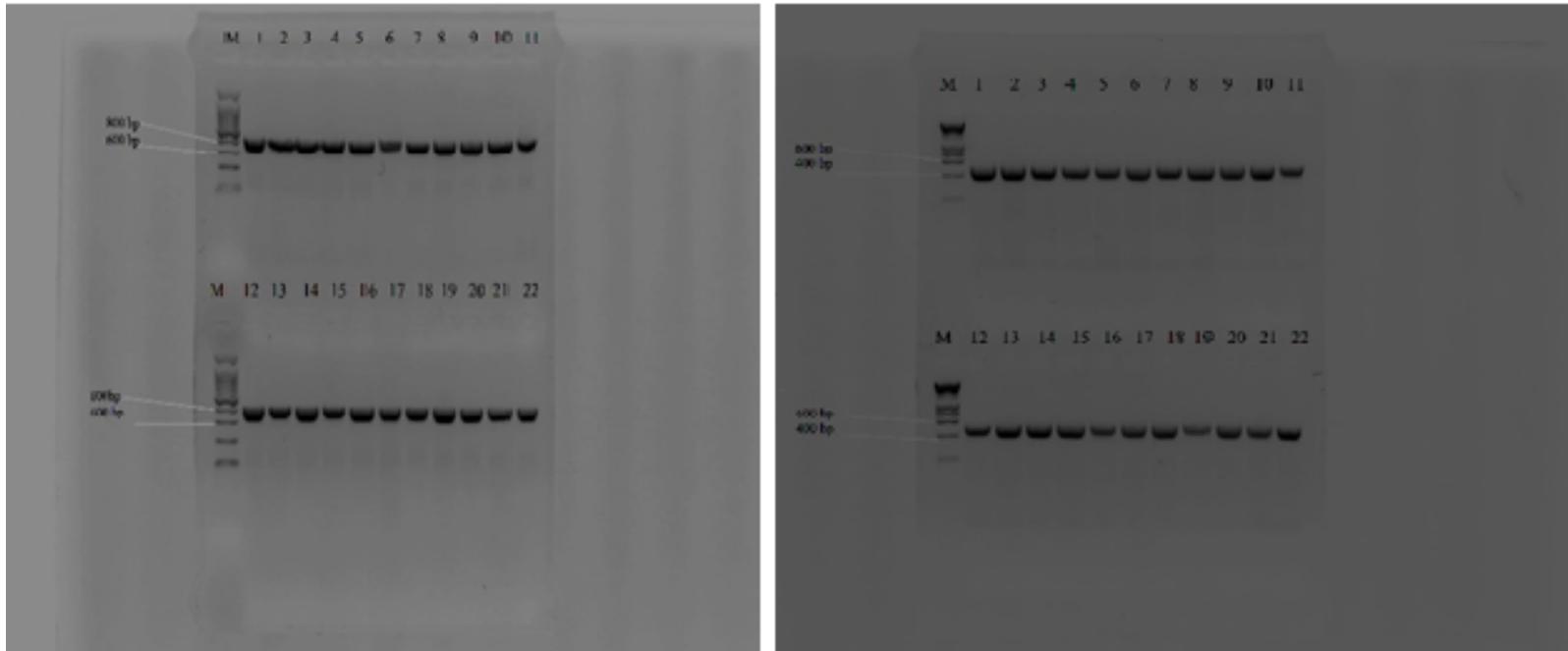
**Gel electrophoresis of PCR assays for the identification of resistance bla genes**

Plates **(A) blaINT** gene 650bp, **(B) blaCTX-M** gene 593bp and **(C) blaTEM** gene 865bp

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

## PCR Results for confirmation of Flouroquinolone 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  **$\beta$ -lactams and flouroquinolones.**

## 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.

## Discussion

- ❖ **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** overtime.

## 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 flouoroquinolones and third generation cephalosporins.

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