Laboratory and molecular surveillance of Paediatric Enteric Fever in Bengaluru, India reveals a dominance of fluoroquinolone resistant H58 Lineage II without Multi Drug Resistance (MDR)

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Background and Aims

- India is endemic for enteric fever, caused by *Salmonella* serovars Typhi and Paratyphi A, and affects children disproportionately
- MDR enteric fever refers to infection with isolates that are collectively resistant to chloramphenicol, ampicillin and co-trimoxazole
- This study aims to characterize the antibiogram and population structure of circulating *S. Typhi* and *S. Paratyphi A* strains among children in South India

Methods

- Isolates were obtained from children attending the St. John's Medical College Hospital in Bengaluru from June 2016 until June 2017.
- Antibiotic sensitivity testing was performed using Kirby- Bauer disk diffusion tests and interpreted using the Clinical Laboratory Standards Institute (CLSI) criteria.
- Demographic data were linked to individual isolates to identify their temporal and age distribution
- Whole genome sequencing (WGS) was performed to identify the molecular structure of circulating strains in comparison with adult strains and to identify mechanisms implicated in antimicrobial resistance (AMR)

Results

- H58 lineage II (4.3.1.2) was dominant across all ages and throughout the duration of the study. Twenty-five strains belonged to H58 lineage II, 9 to lineage I (4.3.1.1) and 3 to non-H58 genotypes. Two Paratyphi A strains which belonged to lineage A and C respectively (**Fig. 1A and 1B**)
- The majority of patients (81%) were treated on an inpatient basis (**Fig. 2**)
- All 36 isolates tested, were resistant to fluoroquinolones. SNPs in *gyrA* conferring reduced susceptibility to fluoroquinolones were seen in all 36 isolates. Nine *S. Typhi* isolates encoded SNPs in 3 quinolone resistance determining (QRDR) sites simultaneously, namely *gyrA*-S83F, *gyrA*-D87N, and *parC*-S80I as shown in **Fig. 3**
- No phenotypic resistance to first-line antimicrobials (MDR) or cephalosporins was observed
- The phylogeny in **Fig. 3** shows that strains from both children and adults are intermingled suggesting ongoing transmission between these groups

Conclusions

- Fluoroquinolones have little role to play in the treatment of enteric fever in this region owing to widespread resistance mediated by the H58 lineage II strains
- The re-emergence of strains sensitive to chloramphenicol and cotrimoxazole could be exploited during treatment regimes to conserve cephalosporins from the emergence of resistance
- The transmission of isolates between adults and children necessitates a broad vaccine strategy to effectively deal with endemic disease

Figure 1A. Temporal distribution of Bengaluru *S. Typhi* and *S. Paratyphi A* lineages.

Figure 1B. Patient age distribution of Bengaluru *S. Typhi* and *S. Paratyphi A* lineages.

Figure 2. Age distribution and patient status of Bengaluru *S. Typhi* and *S. Paratyphi A*.

Figure 3. Phylogenetic structure and AMR status of both adult and child Bengaluru *S. Typhi* strains.