The MENA Typhoid Project: New Insights on Typhoid Burden and Antibiotic Resistance

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What is the MENA Typhoid Project?

• A collaboration between the American University of Beirut (AUB), WHO, and US CDC to enhance typhoid surveillance and control measures in the Middle East and North African (MENA)/Eastern Mediterranean region
• Includes non-laboratory and laboratory-focused initiatives
The MENA Typhoid project: Non-laboratory Initiatives

- Published review of typhoid fever occurrence and antibiotic resistance in the Eastern Mediterranean region from 1990-2021*
  - ~45,000 blood culture-confirmed cases identified from 12 countries
  - Limited burden data, especially from countries outside of Pakistan (22/70 or 31% of studies)
  - Of 56 studies with AMR data:
    - 68% of isolates were fluoroquinolone resistant
    - 40% MDR
    - 48% XDR of tested isolates from Pakistan

The MENA Typhoid project: Non-laboratory Initiatives

- Typhoid fever surveillance systems and vaccination policy survey
- Regional workshop on challenges and opportunities related to typhoid fever laboratory surveillance and TCV introduction
The MENA Typhoid project: Laboratory Surveillance

- Antibiotic susceptibility testing (AST)
  - Broth microdilution
  - All experiments run in duplicate
  - MDR=resistance to ampicillin, chloramphenicol, and trimethoprim/sulfamoxazole
  - XDR=MDR+resistance to fluoroquinolones and third generation cephalosporins
- Whole genome sequencing (WGS) on Illumina MiSeq sequencer
- All sequences shared publicly on NCBI

Phenotype
Genotype
Metadata
The majority of isolates were resistant to chloramphenicol (98%), ampicillin (68%), nalidixic acid (65%), and trimethoprim/sulfamethoxazole (56%).

All isolates susceptible to azithromycin, meropenem, colistin, and gentamicin.

- 67% (20/30) of isolates from Jordan were MDR.
- 100% (22/22) of isolates from Pakistan and 19% (7/36) from Oman (all Pakistan travel-associated) were XDR.
- 72% (13/18) of isolates from Iraq were ceftriaxone resistant.

*Ceftriaxone refers to ceftriaxone resistance without MDR or XDR. Ciprofloxacin refers to ciprofloxacin resistance without MDR or XDR.
Laboratory Surveillance Results to Date: WGS

• The majority (88%; 93/106) of isolates belonged to the H58 haplotype
Chloramphenicol resistance without known genetic determinants

• 43% (46/106) of isolates demonstrated chloramphenicol resistance without any relevant genetic determinants of chloramphenicol resistance

• Discordance was observed only in isolates from Iraq, Jordan, and Oman
Implications for Typhoid Control

• Chloramphenicol resistance by AST without genetic determinants underscores importance of maintaining capacity to perform culture with AST to inform empiric treatment

• Travel-associated XDR cases in Oman underscore the risk of spread of XDR S. Typhi from Pakistan

• Results highlight the continued need to improve surveillance for rapid detection and effective implementation of control measures
Next Steps: The Role of Data Moving Forward

- Continued country recruitment and results dissemination
- Continued phenotypic and genotypic analysis to accurately characterize resistance, understand linkages with regional and global strains, and anticipate future risk of drug-resistant strains
- Leverage of partnerships to encourage public sharing of surveillance data and support countries in using available data to inform control measures
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