

0205

Changing trends of antimicrobial susceptibility and resistance mechanisms to quinolones in typhoidal salmonellae isolated from India in last 5 years

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Background: Antimicrobial resistance in enteric fever is a major therapeutic challenge and there is a need to monitor the pattern of resistance to the antityphoidal agents and detection of molecular mechanisms of resistance. The study was designed to monitor the antimicrobial susceptibility of *Salmonella enterica* serovars Typhi and Paratyphi A isolated from patients of enteric fever during 2014 to 2019 and detection of antimicrobial resistance mechanisms to quinolones.

Methods and materials: Total 281 strains isolated from January 2014 to September 2019 were selected for the study. Antimicrobial susceptibility was done as per CLSI guidelines (2019) for amoxicillin, chloramphenicol, co-trimoxazole, ciprofloxacin, ceftriaxone and azithromycin. Minimum inhibitory concentration (MIC) determination for ciprofloxacin, ceftriaxone and azithromycin were done by E-Test method according to manufacturer's (ABs Biodisk, Sweden) instructions. DNA sequencing was done for *gyrA*, *gyrB*, *parC* and *parE* genes to find mutations in quinolone resistance determining region (QRDR).

Results: Out of total 281 strains included in the study 214 (76.2%) were *S. Typhi* and 67 (23.8%) were *S. Paratyphi A*. As per CLSI 2019, antimicrobial susceptibility for chloramphenicol, ampicillin and cotrimoxazole was 0.7% (2/281), 1.42% (4/281) and 1.06% (3/281) respectively. Only 6/214 (2.8%) were susceptible for *S. Typhi* and no strain was found to be susceptible in *S. Paratyphi A*. Azithromycin susceptibility was 100% in *S. Typhi*, for *S. Paratyphi* there is no breakpoint available. Ciprofloxacin MIC₅₀ and MIC₉₀ values found to be 0.25 µg/mL and 1 µg/mL in *S. Typhi* and 0.5 µg/mL and 6 µg/mL in *S. Paratyphi A*. Ceftriaxone MIC₅₀ and MIC₉₀ values found to be 0.023 µg/mL and 0.5 µg/mL in both *S. Typhi* and *S. Paratyphi A*. For azithromycin MIC₅₀ and MIC₉₀ were 2 µg/mL and 6 µg/mL for *S. Typhi* and 4 µg/mL and 12 µg/mL for *S. Paratyphi A* respectively. All quinolone resistance strains had mutations in QRDR of *gyrA* and *parC* genes.

Conclusion: Ciprofloxacin is no longer a drug of choice for treatment of enteric fever in India. Although susceptibility to ceftriaxone is 100% but MIC is creeping towards resistance. Azithromycin can be a promising treatment option for uncomplicated enteric fever.

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0206

Antimicrobial resistance diagnostic use accelerator – Behavioural determinants of point-of-care diagnostic uptake, and adherence to prescription

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Background: Targeting both diagnostic capacity and behaviours has the potential for decreasing unnecessary antibiotic prescriptions in acute febrile patients, thereby improving patient health outcomes, supporting actions against AntiMicrobial Resistance (AMR) and contributing to Universal Health Coverage (UHC).

Methods and materials: The clinical study of the 'AMR Diagnostic Use Accelerator' based at 9 sites in 6 LMICs comprises a qualitative behavioural component to answer the question: "What are the behavioural determinants of the uptake of diagnostic algorithms, PoC tests and associated prescribing practices, by healthcare workers and adherence to antibiotic prescriptions by patients presenting with acute fever and respiratory tract infections at outpatient clinics in LMICs."

A baseline qualitative study is being conducted to understand the contextual factors and behavioural determinants towards adherence to prescriptions. The findings will form part of the clinical intervention arm consisting of diagnostic algorithms, PoC tests, prescribing decision trees, clinic process flow, training and communication on adherence to prescription. This is compared with a control of current practice.

Results: Data collection includes adherence to prescription by study participants, future intentions regarding antibiotics in clinic visits, and the effects of communication intervention on patients. The information we are gathering will inform a training and communication package which will be rolled out during the clinical intervention.

Conclusion: Further research will investigate the long-term effects of behavioural determinants for healthcare workers who will use the clinical algorithms, new PoC rapid diagnostic tests



and associated prescribing practices. Using the COM-B (Capacity, Opportunity and Motivation) and TDF (Theoretical Domains Framework) models, findings on behavioural determinants will be used to develop recommendations for behaviour change interventions to address the key areas of uptake of PoC diagnostic tests, algorithms, associated prescribing practices, and adherence to prescriptions by patients.

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0208

The UK Fleming Fund: Developing microbiology laboratory capacity for AMR surveillance



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Background: The Fleming Fund is a UK Overseas Development Aid programme aiming to improve Antimicrobial Resistance (AMR) surveillance in low- and middle-income countries in Africa and Asia. The Fund has placed Country Grants in over 20 countries, to support implementation of the surveillance component of country AMR National Action Plans. Grants provide funding and technical assistance to develop AMR governance systems, and to improve country capacity for bacteriology diagnostics, AMR reporting and data analysis. In rolling out the programme, we have accumulated a substantial dataset on clinical microbiology capacity across a broad range of settings.

Methods and materials: A standardised questionnaire was developed to assess the key laboratory components for bacterial culture, identification and antimicrobial susceptibility testing. The questionnaire addressed infrastructure, equipment, staff capacity, clinical reporting, and reporting into the National Surveillance System. The questionnaire was administered in laboratories to be supported by the Fleming Fund Country Grant programme.

Results: Over 100 laboratories were assessed. The most common factors hindering delivery of diagnostic service were a lack of reliable power supply, unreliable consumable/reagent supply chains, budget constraints (either due to limited country budget for healthcare, or lack of dedicated laboratory budget within hospital funding mechanisms), and a lack of laboratory staff with specific microbiology training. We also identified a universal lack of clinical engagement with laboratory services, resulting in poor use of laboratories and a predominantly syndromic approach to management even where laboratory services were judged to be adequate.

Conclusion: Clinical microbiology laboratory capacity was extremely limited across the sites and countries assessed, meaning that most cases of infection in these countries are managed in the absence of any reliable microbiology data to inform individual treatment or empiric guidelines. The Fleming Fund aims to improve capacity through the Grant programme, but additional solutions are needed to ensure that efforts to improve use of antimicrobials as part of the global response to AMR are supported by adequate laboratory services. Clinician engagement is urgently needed to drive demand for better services and data, in conjunction with laboratory

investment to break the vicious spiral of unreliable results, poor trust, reduced sample throughput and further lowering of quality.

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0210

Linezolid for staphylococcus! Is resistance on the rise in Egypt?



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Background: Staphylococci can cause a wide range of infections, ranging in severity from mild skin infections to invasive life threatening ones. In the era of methicillin resistance, it is becoming more challenging for clinicians to find suitable agents to treat infections due to resistant strains. Linezolid is one of the agents recently introduced in clinical practice for the management of resistant staphylococcal infections. The global prevalence of linezolid resistance is still low, however, little is known about the situation in Egypt. We are investigating the prevalence and mechanisms of resistance among Egyptian staphylococcal clinical isolates.

Methods and materials: Methods: Linezolid resistance among staphylococcal isolates obtained from Alexandria Main University Hospital between 2011 and 2015 was determined using disc diffusion and confirmed by minimum inhibitory concentration determination. To study resistance mechanisms, polymerase chain reaction (PCR) was used to detect *cfr* gene, and PCR and sequencing were carried out to investigate the mutations in the V domain of different alleles of 23S rRNA gene. Linezolid resistant mutants were selected through serial passages in linezolid sub-inhibitory concentrations. Combinations of linezolid with other antimicrobial agents or anti-inflammatory agents were investigated using time kill and modified checkerboard assays.

Results: Results: Among the 232 clinical staphylococcal isolates tested, three *Staphylococcus haemolyticus* isolates (1.3%) were found to be linezolid resistant and they were among the 2015 collection. Only one resistant isolate was shown to carry *cfr* gene which was plasmid borne. Sequencing of the V domain of the different alleles of 23S rRNA gene revealed a G2603T point mutation in two isolates. Successive exposure to linezolid sub-inhibitory concentrations selected for three resistant *Staphylococcus aureus* mutants out of nine susceptible staphylococcal isolates. These mutants were also more resistant towards antibiotics from different classes than their susceptible parents. Combinations of linezolid with doxycycline, imipenem, ibuprofen or aspirin were synergistic against the tested isolates and mutants.

Conclusion: Conclusions: Despite unregulated use of linezolid and its ready availability on the market, resistance remains fairly low among the Egyptian isolates. However, strict antimicrobial stewardship guidelines need to be observed in Egyptian hospitals and the community to guard against the evolution of resistant mutants.

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