Abstract

The molecular epidemiology and mechanism of quinolone resistance of South African human isolates of *Salmonella* Typhi for the period 2003-2007, *Salmonella* Enteritidis, *Salmonella* Isangi and *Salmonella* Typhimurium for the period 2004-2006, received by the Enteric Diseases Reference Unit (EDRU) of the National Institute for Communicable Diseases was investigated. Molecular epidemiology was investigated using pulsed-field gel electrophoresis (PFGE) analysis for all four serotypes, as well as multiple-locus variable-number tandem-repeats analysis (MLVA) for *Salmonella* Typhi and *Salmonella* Typhimurium. Three probable mechanisms for quinolone resistance were investigated which included: amino acid mutations in the quinolone resistance determining regions (QRDRs) of DNA gyrase (gyrA/gyrB) and topoisomerase IV (parC/parE), active efflux of antibiotic out the bacterial cell and plasmid-mediated resistance encoded by *qnr* genes. For the period 2003-2007, 498 human isolates of *Salmonella* Typhi were received by the EDRU, of which 27 were resistant to nalidixic acid (MICs, ≥32 µg/ml). Only 19 *Salmonella* Typhi quinolone-resistant isolates were available for analysis. For the period 2004-2006, 329 human isolates of *Salmonella* Enteritidis, 1005 human isolates of *Salmonella* Isangi and 2624 human isolates of *Salmonella* Typhimurium were received by the EDRU. Of these isolates, 119 *Salmonella* Enteritidis, 143 *Salmonella* Isangi and 532 *Salmonella* Typhimurium were invasive, nalidixic acid-resistant. Only 116 *Salmonella* Enteritidis, 137 *Salmonella* Isangi and 516 *Salmonella* Typhimurium invasive, nalidixic acid-resistant isolates were available for analysis. For each respective serotype the isolates were genetically diverse as they could be differentiated into many

PFGE types, suggesting that quinolone-resistant strains have emerged independently of one another for all four serotypes. The use of MLVA for *Salmonella* Typhi and *Salmonella* Typhimurium also illustrated the genetic diversity of the isolates by differentiating the isolates in various MLVA types. The investigation into the contributory mechanisms of resistance showed that an over-active efflux system in combination with mutations in both gyrA and parC play a major role in facilitating quinolone resistance in *Salmonella* Typhi, *Salmonella* Enteritidis and *Salmonella* Isangi. These very same mechanisms were also found to be responsible for the quinolone resistance in the majority of the *Salmonella* Typhimurium isolates along with the rarely isolated mechanism of resistance, a *qnr* plasmid. This is the first report of any kind identifying the presence of *qnr* genes in South African Enterobacteriaceae isolates. Our study also highlights the need for further work to establish the link amongst the various mechanisms of resistance as their interactions remains unclear.

Comment [A1]: spelling