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.