

**Characterization of Antibiotic Resistance Plasmids in *Salmonella Enterica*  
*Serovar Typhi* Isolated in Nairobi, Kenya**

**Winnie Chepkurui Mutai**

**A Thesis Submitted in Partial Fulfilment for the Degree of Master of Science in  
Medical Microbiology in the Jomo Kenyatta University of Agriculture and  
Technology**

2009

## ABSTRACT

Typhoid fever caused by *Salmonella enterica* serotype Typhi (*S. Typhi*) is a significant cause of morbidity and mortality among children and adults in developing countries, where the disease burden is high and cost constraints prevent the widespread use of newer, more effective but more expensive agents. The emergence and global dissemination of Multiple Drug Resistant (MDR) *S. Typhi* has posed major public-health problems and is a challenge in health care in the developing countries. The aim of this study was to characterise plasmids that encode multi-drug resistance among the *S. Typhi* isolates and explore their role in the genetic diversity of *S. Typhi* strains using antibiotic susceptibility, plasmid profiling, incompatibility grouping and Polymerase Chain Reaction (PCR) of resistance genes.

A representative sample of 144 archived isolates from cultures of blood and cerebrospinal fluid of patients visiting Kenyatta National Hospital and Aga Khan University Hospital in Nairobi, Kenya were tested for their susceptibilities to 10 antimicrobial agents; ampicillin (10 µg), tetracycline (30 µg), chloramphenicol (30 µg), gentamicin (10 µg), co-amoxycylav (30 µg), ciprofloxacin (5 µg), cefuroxime (30 µg), ceftriaxone (30 µg), and nalidixic acid (10 µg). A total of 16% of the isolates were susceptible to all the drugs tested while 84% were resistant to one or more of the 10 drugs tested. Of main concern was a high prevalence of 75% of MDR *S. Typhi* strains. A high percentage of resistance was observed for the first-line antibiotics (ampicillin (71%), chloramphenicol (72%), and tetracycline (74%) which are the main drugs used to treat infectious diseases in Kenya owing to their inexpensive nature. Approximately 80% of the drug resistance in *S. Typhi* analysed was associated with presence of plasmid DNA. Class 1 integrons and transposon Tn21, was also detected. Chromosomal mediated resistance was also evidenced by the presence of *gyrA*, *gyrB*, *parE*, and *parC* genes encoding for quinolone and floroquinolone resistance. A proportion of 80% of the MDR *S. Typhi* strains selected for conjugation experiment

transferred one or all their resistance phenotypes to the recipient strain *E. coli* K12 suggesting that resistance genes can easily be transferred or acquired rapidly among the bacterial population. This study revealed that the plasmids encoding antibiotic resistance genes have a high degree of genetic similarity since 95% of the MDR isolates carried plasmids of incompatibility group HI1. It appears that a single strain type containing a plasmid conferring multidrug-resistance has emerged within the *S. Typhi* bacterial population in Kenya and has been able to adapt and survive the challenge of antibiotics as they are introduced into clinical use. The other replicons identified included IncI1, IncP, and IncFIC.

Unfortunately, there are still gaps in our understanding of how new multi-resistance plasmids evolve and the genetic relatedness among them. This therefore calls for a need to carry out more studies that will address the dynamics of antibiotic resistance genes.