ABSTRACT

Quinolone Resistance and Gene Regulation in Uropathogenic *Escherichia coli*

Stacy Ann-Marie Stephenson

Urinary tract infections are among the most frequently encountered infections in clinical practice. *Escherichia coli*, the most ubiquitous pathogen implicated in UTIs among females has evolved to become highly adaptable in circumventing host defenses. Up to the commencement of this study in 2007, the emergence of quinolone resistance, virulence factor distribution and putative epigenetic effect of DNA adenine methylation had not been investigated in Jamaica. This body of work sought to (i) investigate the prevalence and genetic environment of *qnr* genes (ii) determine the distribution of various virulence factors and; (iii) determine the *dam*'s influence on gene expression in uropathogenic *E. coli* clinical isolates. Plasmid-mediated *qnr* resistance genes amplified by PCR from 174 non-duplicate UPEC clinical isolates were detected in 43.5% of strains; *qnr*A (93%) and *qnr*S (26%) most frequently. Of 58 *qnr*-positive isolates identified, 91.4%, 90% and 55% correspondingly harboured class I integrases, Orf513 and 5'CS/3'CS. Sixteen subtypes documented from RFLP analysis of conserved segments revealed heterogeneity. Further examinations for virulence determinants distribution among antimicrobial-susceptible and resistant strains confirmed 14 subtypes with *fimH* (97.1%) and *cnfI* (75.3%) as dominating epidemiological indicators. To monitor the influence of *dam* on attachment and FQ resistance, selected *E. coli Dam* mutants created via one-step allelic exchange were transformed with cloned *qnr*A and *dam* complement plasmid for comparative analysis of fitness, antimicrobial susceptibility, biofilm formation, gene expression and mammalian cell attachment. The absence of DNA methylation among *dam* mutants were apparent. Varying deficiencies in cell growth, antimicrobial resistance, biofilm formation and gene expression alongside low-level increases in adherence to HEK-293 and HTB-9 mammalian cells were also detected. Phenotypic characteristics of cured parental strains were restored in *dam* complement strains. Therefore, *dam*'s vital role in DNA methylation and gene expression in local UPEC isolates was confirmed. Further investigations are warranted to shed light into the post-transcriptional influence of *dam* on the regulatory network of virulence genes central to pathogenesis.

Keywords: Stacy Ann-Marie Stephenson; quinolone resistance; *Escherichia coli*; *dam* methylation.