Abstract of

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Title: Biochemical and molecular characterization of extended spectrum beta-lactamases (ESBL) producing enterobacteria isolated from clinical samples

Plasmid mediated extended spectrum β lactamases (ESBLs) usually confer resistance to penicillins, cephalosporins and aztreonam. At present, CTX-M ESBLs in *Enterobacteriaceae* have increased significantly in most regions of the world. Globally, the members of *Enterobacteriaceae* are of the most significant etiological agents both for hospital and community acquired infections by causing systemic and urinary tract infections in humans. Therapeutic possibilities are few as a result of rise in CTX-M-type ESBL production, fluoroquinolone resistance and multidrug resistance. In this study we aimed to investigate the genotypic characterization of ESBLs and other associated resistances among clinical isolates from two Pakistani cities. Moreover, we studied the prevalence of the ST131 *E. coli* clone, the prevalence of plasmid mediated quinolone resistance genes, and of 16S rRNA methylases. Lastly, we characterized CTX-M phylogroups, plasmid replicon types, molecular typing of isolates by pulse field gel electrophoresis (PFGE), multilocus sequence typing (MLST), serotyping and virulence factors among ESBL producing isolates. Out of 245 collected isolates, 144 (59%) bacterial pathogens were ESBL producers. CTX-M genes were detected in all isolates by PCR and all these ESBL producing bacteria were multidrug resistant. All isolates were from phylogenetic group CTX-M 1 and 13% ESBL producing isolates were carrying *rmtB* genes which confer resistance against aminoglycosides. 39% and 6% ESBL producing pathogens carried *qnr* and *qepA* alleles, respectively which are responsible for resistance against quinolones while 69% ESBL producers harbored *aac(6´)-Ib-cr* which reduced the susceptibility of fluoroquinolones. Molecular typing by PFGE revealed very distinctive genotypes showing the genetic diversity among ESBL producing organisms. 18% ESBL producing *E. coli* were ST131 as worldwide distributed clone, phylogenetic group D was most prevalent and group B2 was most virulent among ESBL producing *E. coli*. Prevalence of multiple extraintestinal virulence factors among *E. coli* isolates was detected. Variants of IncF replicons were mostly detected which could carry these multiple resistance and disseminate these resistances to other bacteria by horizontal transfer gene. Animal originated ST215 *Klebsiella pneumoniae* was detected by MLST first time from clinical samples collected from human beings. Conclusively, highly virulent and genetically divergent strains with different types of resistance mechanisms were involved in hospital and community acquired infections in the region, but amikacin and carbapenems still retained excellent activity.