Clonal diversity in CTX-M producing bacteria

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In the last decade, the distribution and prevalence of extended-spectrum beta-lactamases (ESBL) among Enterobacteriaceae has been marked by a shifting epidemiology characterized by an exponential increase in the number and diversity of CTX-M enzymes in different settings and geographic areas, mainly associated with a high clonal diversity. Nevertheless, the epidemiological success of specific variants has greatly influenced the expansion of particular clones in different species (mainly *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterobacter aerogenes*, but also *Enterobacter cloacae*, *Proteus mirabilis*, *Citrobacter freundii*, *Salmonella* spp., *Shigella* spp. or *Serratia marcescens*) and/or plasmid dissemination among different genetic backgrounds. In *E. coli*, the wide amplification of fluoroquinolone resistant lineages belonging to different phylogroups with a high colonization and transferability abilities seems to have served as substrate of $bla_{\text{CTX-M}}$ types. The CTX-M-15 pandemia has been linked to a highly virulent, *E. coli* B2-ST131 clone frequently causing urinary tract infections (UTI). This EC-ST131 clone has also been linked to the spread of other CTX-M (CTX-M-1, -2 and -9 groups), AmpC (CIT) and SHV ESBLs, and it has also been identified among non-ESBL producing healthy volunteers and ciprofloxacin resistant UTI-causing isolates. The spread of CTX-M-14, highly prevalent in South Europe, Canada and Asia, seems to be associated with *E. coli* lineages A (ST10), B1 (ST359, ST155) and D. Recently, the dispersion of CTX-M-9 throughout Japan has been linked to a sulfamethoxazole/trimethoprim resistant D-ST38 *E. coli* clone. Particular *K. pneumoniae* lineages belonging to ST11, ST15 and ST147 have been identified among CTX-M-15-producing ciprofloxacin-resistant *K. pneumoniae* isolates across Hungary. Clonal spread also plays a significant role in the local dissemination of CTX-M-3 (different species including *C. freundii* and *S. marcescens*) in Eastern Europe, CTX-M-5 (*E. coli* and *S. enterica*) in Belarus and Russia and CTX-M-2 (*P. mirabilis* and *S. enterica*) in Asia and France/Belgium. The spread of other CTX-M types seems to be associated with a high clonal diversity although sporadic outbreaks may also occur. That is the case of CTX-M-1 and CTX-M-9 in Southern Europe (mostly in *E. coli*) CTX-M-10 (*K. pneumoniae* and *E. cloacae*) in Spain or CTX-M-32 (mostly in *E. coli*) in the Mediterranean area. Despite the variability observed in multiple locations (probably related to local ecological variation), CTX-M-producing organisms are mainly associated with clonal expansion of different species which have been able to acquire antibiotic resistant genes and/or virulence factors. Early detection of these multiresistant clones constitutes a new challenge in the control of antibiotic resistance.