

P1060 Epidemic diffusion of OXA-48 beta-lactamase in Croatia

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Background: : Carbapenemases involved in resistance to carbapenems in *Enterobacteriaceae* belong to Ambler class A, class B metallo- β -lactamases (MBL), or OXA-48-(class D.) The OXA-48 positive isolates emerged first in 2013 in two large hospitals in Croatia. During 2016 epidemic diffusion of OXA-48 positive *Enterobacteriaceae* to smaller hospitals was noticed.

Materials/methods: In total 46 enterobacterial isolates from six hospital centers located in different geographic regions in Croatia, were analyzed: 38 *Klebsiella pneumoniae*, 5 *Enterobacter cloacae*, 2 *Escherichia coli* and 1 *Citrobacter freundii*. Antibiotic susceptibility was determined by broth microdilution test. Hodge and carbapenemase inactivation test (CIM) were used to detect carbapenemase activity. Combined disk tests with clavulanic acid, phenylboronic acid (PBA) and EDTA were applied to detect extended-spectrum β -lactamases (ESBLs), KPC and MBLs. PCR was used to detect genes encoding ESBLs, plasmid-mediated AmpC β -lactamases, carbapenemases of class A, B and D, qnr and IS1999.

Results: Out of 38 *K. pneumoniae* 26 (68,4%) were ESBL positive. All isolates were uniformly resistant to amoxicillin alone and combined with clavulanic acid and piperacillin/tazobactam. ESBL positive isolates showed resistance to expanded-spectrum cephalosporins (ESC), gentamicin and ciprofloxacin. ESBL negative strains were susceptible to ESC but 75% showed reduced susceptibility to ciprofloxacin. The isolates showed variable susceptibility/resistance to imipenem and meropenem. Two isolates were resistant to colistin. Hodge and CIM test were positive in all but one and seven strains, respectively, indicating the production of carbapenemase. Combined disk tests with PBA and EDTA were negative demonstrating the lack of KPC and MBL. PCR was positive for OXA-48 gene in all strains. All ESBL positive strains were found to harbour *bla*_{CTX-M} genes of group 1. *QnrB* and *qnrA* were found in 18 and 2 isolates, with reduced susceptibility to ciprofloxacin, respectively. Twenty-six isolates were found to harbour IS1999. Plasmid of L/M inc group was found in 12 ESBL negative isolates. The isolates exhibited different PFGE patterns.

Conclusions: The study showed dissemination of OXA-48 β -lactamase in all geographic regions of Croatia. A large proportion of isolates harboured ESBL contributing to resistance and complicating therapy. The emergence of colistin resistance is worrisome. IS1999 was responsible for the mobilization of *bla*_{OXA-48} gene.