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Paper Poster Session
Surveillance of carbapenemases: they will not stop!

Emergence of OXA-48 beta-lactamase in Enterobacteriaceae in Croatia

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Background: Previous studies found VIM-1, NDM-1 and KPC-2 among CRE in Croatia with VIM-1 being the most prevalent. Recently OXA-48 was identified in three hospital centers.

Material/methods: Since 2012 surveillance system for CRE was implemented in University Hospital Center (UHZ) in Croatia which inluded phenotypic and molecular identification of carbapenemases in *Enterobacteriaceae*. In total four carbapenem non-susceptible strains of *K. pneumoniae* were found to be positive for OXA-48 in three hospital centers (University Hospital Center Zagreb-UHZ, University Hospital Center Sisters of Mercy-UHM, University Hospital Split-UHS). The antimicrobial susceptibility was determined by broth microdilution method. Double-disk-synergy test (DDST) was performed to detect ESBLs and modified Hodge test (MHT) was used to screen for production of carbapenemases. MBL E-test was used to screen for metallo-β-lactamases (MBLs). Additionally the isolates were tested by combined disks test with EDTA or 3-aminophenylboronic to screen for KPC, MBLs or simoultaneous production of MBL and KPC respectively. The transferability of meropenem resistance was determined by conjugation employing *E. coli* A15R$^-$ strain resistant to sodium-azide. The presence of genes encoding broad and extended-spectrum β-lactamases (*bla*$_{SHV}$, *bla*$_{TEM}$, *bla*$_{CTX-M}$ and *bla*$_{PER-1}$), plasmid-mediated AmpC β-lactamases, group A carbapenemases (*bla*$_{KPC}$, *bla*$_{SME}$, *bla*$_{IMI}$,

bla$_{NDM}$), metallo β-lactamases (*bla*$_{VIM,}$ *bla*$_{IMP}$ and *bla*$_{NDM)}$, and carbapenem hydrolyzing oxacillinases (*bla*$_{OXA-48),}$ was determined by PCR.

Results: The strains were uniformly resistant to amoxicillin alone and combined with clavulanate, cefazoline, cefuroxime, ceftazidime, cefotaxime, ceftriaxone, but uniformly susceptible to colistin and had variable resistance patterns to carbapenems. Modified Hodge test was positive indicating the production of carbapenemase. Phenotypic testing was positive for ESBL but negative for, MBL, KPC and AmpC. Meropenem resistance was not transferred to *E. coli* recipient strain. PCR revealed the strains to be positive also for CTX-M-15 and TEM-1. The strains from UHZ coproduced OXA-48 and VIM-1. Two strains from UHZ had identical rep-PCR patterns but different from those from UHS and UHM. The patients did not have a travel history to the countries where OXA-48 is endemic

Conclusions: The study demonstrated emergence of OXA-48 β-lactamase in three hospital centers located in different geographic regions in Croatia The strains from different hospitals displayed different rep_PCR patterns and thus it could be concluded that they occurred as independent events. OXA-48 was first report in Turkey in 2001 but later spread in Mediterranean and western European countries such as Israel, France, Italy, Spain, Germany, Switzerland, Belgium and the Netherlands. . Most of the strains in western Europe were imported from Turkey, Morocco, Egypt, Algeria or Lybia. Croatia was spared from this type of carbapenemas until 2014. In our study there was no link to the endemic areas.