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### **In vitro susceptibility and resistance phenotypes in contemporary *Enterobacter* isolates in a university hospital in Crete, Greece**

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**Background:** *Enterobacter* spp. are Gram negative bacilli that cause infections globally, primarily in the hospital and particularly in the intensive care unit (ICU), in neonates and debilitated patients. Development of resistance has been associated with administration of broad spectrum cephalosporins and quinolones. We sought to study the evolution in the susceptibility of *Enterobacter* spp. in various antibiotics and relevant resistance mechanisms at the University Hospital of Heraklion during a six year period (2010-2015).

**Material/methods:** *Enterobacter* spp. isolated from outpatients and inpatients at the University Hospital of Heraklion, Crete, Greece during a six year period (2010-2015) were included in the study. Non-duplicate isolates from intensive care unit (ICU) and non-ICU patients were studied using automated systems (Advanced Expert System in conjunction with the VITEK 2). Phenotypic confirmatory tests were applied for detection of extended-spectrum beta-lactamases (ESBLs), AmpCs and carbapenemases.

**Results:** A total of 939 *Enterobacter* spp. isolates from unique patients were included in the analysis. *Enterobacter* spp. were isolated from 756 inpatients and 183 outpatients. *E. cloacae* (655, 69.8%)

followed by *E. aerogenes* (275, 29.3%) were the most commonly isolated species. *E. gergoviae* (6), *E. amnigenus* (1) and *E. asburiae* (1) were the remaining isolates. Pus (248, 26.4%) and urine (239, 25.5%) were the most commonly cultured specimens. Colistin was the most active antibiotic (97.9%) followed by imipenem (96.1%), gentamicin (95.7%), tigecycline (91.8%), cefepime (89.4%) chloramphenicol (85.8%), fosfomycin (85.5%), trimethoprim/ sulfamethoxazole (83.3%), and piperacillin/tazobactam (73.3%). Antibiotic resistance did not increase during the study period for most antibiotics. Lower susceptibility was observed among multi-drug resistant strains (table 1) and carbapenem non-susceptible isolates. AmpC was the most common resistant mechanism (21%); carbapenemases (3.7%) and aminoglycoside modifying enzymes (6.5%) were also detected. Almost all AmpC producers were resistant to cephalosporins and 25% of them were also resistant to carbapenems. In all but three isolates aminoglycoside resistance was accompanied by acquired  $\beta$ -lactamases.

**Conclusions:** Although most *Enterobacter* spp. isolates remain susceptible to a number of antibiotics, a significant proportion was resistant to several antibiotics, most notably  $\beta$ -lactams.

**Table 1. Susceptibility to selected antibiotics and MICs of all and 275 MDR *Enterobacter* spp. isolated from clinical specimens during the period 2010-2015 in the University Hospital of Heraklion, Crete, Greece.**

Antibiotic	All N = 939					MDR N=275				
	MIC range	MIC50	MIC90	% S	% R	MIC range	MIC50	MIC90	% S	% R
piperacillin/ tazobactam	≤1 - >128	4	>128	73.3	26.0	≤4 - >128	128	>128	14.9	82.5
imipenem	≤0.25 - 32	1	1	96.1	3.4	≤0.25 - 32	1	4	87.6	11.3
ciprofloxacin	≤0.25 - >4	≤0.25	≤0.25	92.9	6.4	≤0.25 - >4	≤0.25	>4	76.7	21.1
amikacin	≤0.25 - >64	2	2	95.4	4.2	2 - >64	2	>64	85.5	13.5
tigecycline	≤0.5 - >8	1	2	91.8	4.9	≤0.5 - >8	1	>8	78.9	14.5
colistin	≤0.25 - >16	0.5	0.5	97.9	2.1	≤0.25 - >16	0.5	0.5	95.6	4.4
fosfomycin	4 - >1024	32	128	85.5	8.6	4 - >1024	24	256	82.2	9.8

**Abbreviations:** MDR multi-drug resistant, MIC minimum inhibitory concentration, S susceptible, R resistant