KPC-producing *Klebsiella pneumoniae* resistant to tigecycline: epidemiology and risk factors for colonization during Intensive Care Unit stay

[1]Matthaios Papadimitriou-Olivgeris, [2]Christina Bartzavali, [3]Fotini Fligou, [4]Christina Sklavou, [2]Sophia Vamvakopoulou,
[2]Myrto Christofidou, [3]Kriton S. Filos, [1]Markos Marangos, [2]Evangelos D. Anastassiou
[1]Division of Infectious Diseases, [2]Department of Microbiology, [3]Anaesthesiology and Critical Care Medicine, School of Medicine, University of Patras, Greece

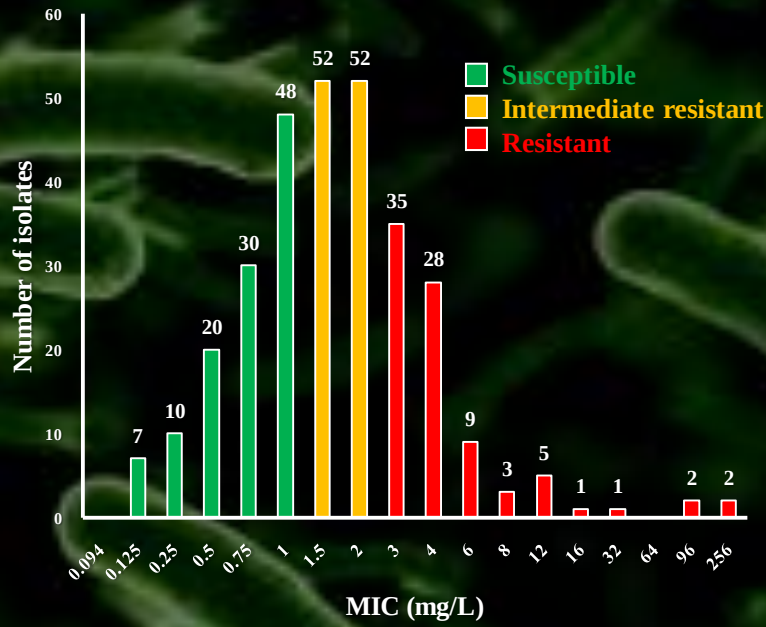
Objective: Tigecycline remains one of the last treatment options against carbapenemases-producing Gram negative bacteria. The emergence of tigecycline resistance poses a serious threat. The objective is to identify risk factors for colonization by KPC-producing *Klebsiella pneumoniae* resistant to tigecycline (TR-Kp) of Intensive Care Unit (ICU) patients.

Methods: During a 2-year period, rectal samples were taken from each patient, initially upon ICU admission and then once a week. Rectal swabs were inoculated in chromogenic agar and *K. pneumoniae* isolates were thereafter identified by standards methods (Enterotube II, BD, BBL). Antibiotic susceptibility test was performed by the agar disk diffusion method according to CLSI guidelines. MIC to tigecycline was determined by Etest (AB Biodisk). The presence of *bla*KPC gene was confirmed by PCR. Epidemiologic data were collected from the ICU computerized database and patient´s chart reviews. Statistical analysis was performed by SPSS ver. 19.0.

Table I: Univariate analysis for tigecycline-resistant KPC-producing *K. pneumoniae* colonization risk factors during Intensive care unit stay.

Characteristics	Infection (n=24)	Controls (n=102)	*P*
Age (years)	54.8 ± 17.8	57.5 ± 18.3	0.520
Male gender	16 (66.7%)	73 (71.6%)	0.627
Chronic diseases (number)	0.8 ± 1.0	0.9 ± 1.0	0.883
Hospitalization during summer months	14 (58.3%)	25 (24.5%)	0.003
APACHE II Score upon admission	16.0 ± 8.1	17.1 ± 7.1	0.493
Mean antibiotic use per day	2.6 ± 0.6	2.6 ± 1.0	0.326
Tracheostomy	16 (66.7%)	46 (45.1%)	0.071
Resistance	2.3 ± 1.5	1.2 ± 1.1	<0.001
Imipenem resistance	18 (75.0%)	52 (51.0%)	0.001
Gentamicin resistance	14 (58.3%)	34 (33.3%)	0.034
Colistin resistance	14 (58.3%)	21 (20.6%)	0.001
Tigecycline resistance	9 (37.5%)	16 (15.7%)	0.023
Increase (>5 points) of SAPS II score during the first 7 days of ICU stay	18 (75.0%)	46 (45.1%)	0.012
Increase (>2 points) of SOFA score during the first 7 days of ICU stay	8 (33.3%)	30 (29.4%)	0.805

Figure 1: Mean inhibitory concentration (MIC) to tigecycline of 305 KPC-producing *K. pneumoniae*



Results: Among 257 patients, who were hospitalized for more than 6 days, 152 (59.1%) became colonized by susceptible to tigecycline KPC-producing *K. pneumoniae*, 39 (15.2%) by TR-Kp while 66 (25.7%) were not colonized. During the study period 305 KPC-producing *K. pneumoniae* isolates were collected. All isolates were resistant to standard antibiotics, while 197 (64.6%), 117 (38.4%), 103 (33.8%), and 88 (28.9%) were resistant to imipenem, gentamicin, colistin and tigecycline, respectively. The MIC distribution of the 305 KPC-Kp strains is depicted in Figure 1. Multivariate analysis identified administration of tigecycline, obesity, days at risk and the presence of colonized patients in nearby beds as important risk factors for TR-Kp colonization (Table I).

Conclusion: There exists a high percentage of TR-Kp colonization. As it was expected, administration of tigecycline predisposes to colonization. The presence of colonized patients in nearby beds also constitutes a risk factor, indicating the importance of patient-patient transmission via the staff.