WHICH PATIENTS DEVELOP BLOODSTREAM INFECTION DUE TO KPC-PRODUCING *Klebsiella pneumoniae* WITHIN TWO DAYS FROM RECTAL COLONIZATION?

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

Objective: KPC-producing *Klebsiella pneumoniae* (KPC-Kp) provokes serious infections especially in previously colonized critically ill patients. The aim of the study was to identify risk factors for the development of KPC-Kp bacteremia within two days after rectal colonization of Intensive Care Unit (ICU) hospitalized patients.

Methods: During a 2-year period, rectal samples were taken from ICU patients upon admission and at day 4 and 7 and were inoculated in chromogenic agar for the detection of KPC-Kp colonization. KPC-Kp isolates, from bacteremic ICU patients (one per patient), at a University Hospital, were studied. Antibiotic susceptibility test was performed by the agar disk diffusion method according to CLSI guidelines. MIC was determined by the Etest (AB Biodisk). Isolates were tested by meropenem-boronic acid synergy disk test for KPC detection. The presence of *bla*KPC gene was confirmed by PCR. Molecular typing was performed by PFGE of *Xba*I restricted genomic DNA. Epidemiologic data were collected from the ICU computerized database and patient´s chart reviews. Statistical analysis was performed with SPSS ver. 19.0, as appropriate.

Table I: Univariate analysis of risk factors for KPC-Kp bloodstream infection within two days from enteric colonization during Intensive Care Unit (ICU) hospitalization.

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

Table II: Multivariate analysis of risk factors for KPC-Kp bloodstream infection within two days from enteric colonization during Intensive Care Unit (ICU) hospitalization.

Characteristics	*P*	OR (95% CI)
Tracheostomy	0.001	5.9 (2.0-17.4)
Mechanical ventilation at day of colonization	0.034	5.5 (1.1-26.2)
Number of catheters inserted after 3rd day of ICU stay	0.034	1.8 (1.0-3.1)
Colonization at day 7	0.013	4.5 (1.4-14.7)
Colistin resistance	0.002	4.4 (1.7-11.2)

Results: Among 245 ICU patients who had not KPC-Kp colonization upon admission, no one became colonized at day 4, while, 126 (51%) ~~patients~~ became colonized at day 7. Among colonized patients, 24 (19%) developed ~~the~~ bloodstream infection within two days after rectal colonization. All KPC-Kp bacteremic isolates ~~(100%)~~ were resistant to standard antibiotics, while, 18 (75%) were additionally resistant to carbapenems, 14 (58%) to gentamicin, 14 (58%) to colistin and 9 (38%) to tigecycline. bla_{KPC-2} gene was found in all KPC-Kp bacteremic isolates while the majority belonged to PFGE type A (n=15, 63%). Multivariate analysis identified hospitalization during summer months (*P*=0.030), increase (>5 points) of SAPS II score as compared to admission's (*P*=0.019), and resistance of the colonizing KPC-Kp isolate to colistin (*P*=0.003) as risk factors of KPC-Kp bacteremia immediately after enteric colonization (Tablea I and II).

Conclusion: There was a high percentage of KPC-Kp bacteremia in previously colonized ICU patients. The evolution from colonization to infection was affected by the increased temperatures during summer months, and the resistance of the colonizing isolates to colistin.