

# Multi-drug-resistant and extensively –drug-resistant *Klebsiella pneumoniae* bloodstream infections: epidemiology and outcomes

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## Introduction:

Treatment and outcomes of bloodstream infections represent one of the most challenging therapeutic problem in the intensive care unit (ICU) setting, particularly because of the increasing prevalence of Multi-Drug Resistant (MDR) pathogens. *Klebsiella pneumoniae* (KP) represents one of the most dreadful nosocomial pathogens due to the widespread emergence of multidrug-resistant (MDR) clones, exhibiting resistance to almost all available antibiotics, including carbapenems.

## Objectives:

We sought to investigate epidemiologic trends and outcomes of bloodstream infections (BSIs) by KP, in ICU patients in a geographic area with high prevalence of antimicrobial resistance.

## Methods:

In a prospective observational study, first episodes of BSI were recorded in a registry, with the participation of 12 Greek ICUs. Bacteraemias with isolation of a coagulase-negative *Staphylococcus* were excluded. The observation period was the first half of 2012 and 2013. All treatment decisions were made by the treating physicians, without interference by the study investigators. Demographics, comorbidities, microbiology and treatment data were captured in an electronic database. Statistical analysis was performed with SPSS18; p values <0.05 were considered as significant. Student's t-test,  $\chi^2$  and Fischer's exact, and non-parametric tests were used, according to the variable distribution patterns.

## Results:

A total of 79 patients (61.5% male) with BSIs by KP were analyzed. Median (interquartile range) age was 64 years (45- 75), APACHE II, SOFA and SAPSII scores were 21 (16-26), 9 (7-11) and 50 (39-59) respectively; prior to the BSI use of antibiotics was 18 days (8-27).

The reason of ICU admission was medical (44.3%), surgical (36.7%, 87.1% of them emergent), or trauma (6.3%). BSIs were classified as primary (63.5%), catheter related/CRBSI (15.9%) and secondary (20.6%, most frequent source respiratory), Figure 1A and 1B. Crude and attributable ICU mortality of the cohort was estimated at 42.5 and 20.3% respectively. The majority of KP isolates (84.9%) were MDR with 73.8% exhibiting carbapenem resistance; colistin, tigecycline and gentamicin resistance was detected in 7.7, 29.5 and 38.4% respectively. ICU-acquired BSIs (80.4%) were less likely associated (p 0.038) with a piperacillin/tazobactam-susceptible KP strain compared to the nosocomial+healthcare- acquired counterparts (16.1%); no significant difference was recorded in any other variable or outcome. In 49.4% of cases KP was a copathogen, more frequently recovered along with another Gram-negative (25.3%), mostly Enterobacteriaceae (n=9) or *Acinetobacter baumannii* (n=6) or *Pseudomonas aeruginosa* (n=6); a Gram-positive was recovered in 12.7% (mostly coagulase-negative staphylococci) and *Candida* spp in 6.3%. Non-survival was associated with the number of comorbidities (p 0.007), the recovery of a copathogen in blood culture (p 0.027) and the type of the copathogen (p 0.010). Higher SAPSII score was associated with 28day ICU crude mortality in this subset with multiple recovered pathogens (p 0.025).

## Conclusion:

In a cohort of Greek ICU patients *Klebsiella pneumoniae* strains causing bloodstream infections showed an extensively drug-resistant profile with two thirds of them being carbapenem resistant. A considerable crude mortality of 42.5% was recorded, along with an attributed mortality of 20.3%. In almost half of the KP BSIs, there was a second or a third co-pathogen recovered, a fact that affected adversely mortality.

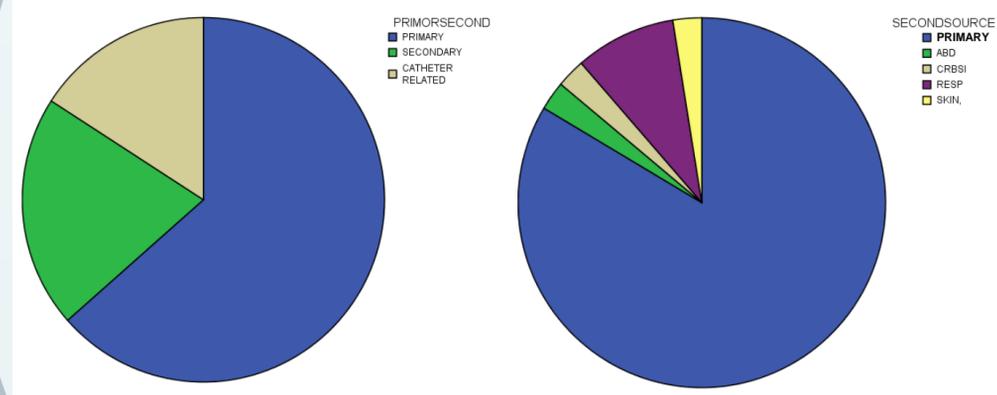


Figure 1: Type of bacteraemia (A) and source (B) of secondary bacteraemia  
ABD: ABDOMINAL INFECTION; CRBSI: Catheter related- Bloodstream infection; RESP: RESPIRATORY INFECTION; SKIN: SKIN AND SOFT TISSUE INFECTION

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