

Resistance in Gram Negative Rods: KPC

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Klebsiella pneumoniae carbapenemases (KPC) are class A and group 2f β -lactamases that can hydrolyze penicillins, cephalosporins, monobactams, and carbapenem. KPC β -lactamases are inhibited by clavulanic acid and are generally considered plasmid mediated. KPC-1 was first detected through the Intensive Care Antimicrobial Resistance Epidemiology (ICARE) program in North Carolina in 1996. Although predominant in *Klebsiella pneumoniae*, KPC β -lactamases have also been discovered in other gram-negative rods, especially in species from *Enterobacteriaceae*, such as *Escherichia coli*, *Enterobacter* spp., *Salmonella enterica*, *K. oxytoca*, and *Citrobacter freundii*. In addition, KPC-2 was isolated from *Pseudomonas aeruginosa* in Colombia in 2006.

KPC β -lactamases are transferable and are generally associated with genes encoding resistance for other antimicrobial agents including aminoglycosides, fluoroquinolones, and trimethoprim/sulfamethoxazole. To date, there are four KPC enzymes (KPC-1, 2, 3, and 4) isolated mostly from the East Coast of the USA including North Carolina, Maryland, New York, and Massachusetts. Several outbreaks by KPC-producing *Klebsiella pneumoniae* have been identified in New York City hospitals. In addition, KPC β -lactamases have been detected outside the US in Scotland, Colombia, Israel, China, and France.

KPC β -lactamases can be difficult to detect for several reasons. First, KPC β -lactamases are detected in *K. pneumoniae* and other *Enterobacteriaceae* which are well known to have mechanisms of β -lactam resistance such as porin mutations and encode other β -lactamases including ESBLs and AmpCs which can hinder the detection of KPCs. Second, the minimum inhibitory concentrations (MIC) of imipenem are significantly influenced by inoculum volume in which a lower inoculum has resulted in susceptible MICs for imipenem in a KPC producing organism. Third, there is inconsistency of KPC detection using automated systems, microbroth dilution, and E-test methods. The factors mentioned above suggest the need for methodologies that are able to accurately detect KPC producing organisms.

According to the Clinical and Laboratory Standards Institute (CLSI) recommendations, *Enterobacteriaceae* that are resistant to the expanded-spectrum cephalosporins and have a carbapenem MIC ≥ 2 $\mu\text{g/ml}$ or a carbapenem intermediate or resistant zone of inhibition by disk diffusion may produce a KPC β -lactamase. For KPC detection, ertapenem is the most sensitive carbapenem while meropenem and imipenem are more specific than ertapenem. Some automated system panels have been modified to match the CLSI carbapenem MIC interpretive standards for detection of KPC β -lactamases. As examples, there are two new MicroScan (Siemens) panels, neg combo (NC) 50 and neg/urine combo (NUC) 51, with imipenem and meropenem concentrations of 1 $\mu\text{g/ml}$. In addition, NUC 51 panel has breakpoints for ertapenem. The definitive detection of a KPC encoding organism can be performed using PCR and/or a phenotypic test called the modified Hodge test (1). We are not aware of any KPC producing *Enterobacteriaceae* in Nebraska, however, if any laboratory suspects a KPC producing organism, NPHL would be happy to provide consultation for further testing.

KPC producing *Enterobacteriaceae* are generally susceptible to both colistin and tigecycline. CLSI interpretive criteria are available for colistin only for *Pseudomonas aeruginosa* but not for *Enterobacteriaceae*. In addition, there are no CLSI guidelines for tigecycline (tigecycline FDA breakpoints do exist). The accurate detection is imperative to effectively control the spread and emergence of KPC-producing *Enterobacteriaceae*.

For additional information regarding resistance in gram-negative rods: KPC, please contact Dr. Abdalhamid at 402-552-3305 or Dr. Fey at 402-559-2122.

References

- 1 Lee, K., Y. Chong, H. B. Shin, Y. A. Kim, D. Yong, and J. H. Yum. 2001. Modified Hodge and EDTA-disk synergy tests to screen metallo- β -lactamase-producing strains of *Pseudomonas* and *Acinetobacter* species. Clin. Microbiol. Infect. 7:88-91.