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Meropenem-resistant *Klebsiella pneumoniae* in the USA: Data from TEST 2009

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Revised Abstract

Background: Carbapenem-resistant clinical isolates of *Klebsiella pneumoniae* (KPC) have been detected in various countries worldwide. However, there are few reports related to the incidence of these isolates in large-scale surveillance studies in the USA. As part of the Tigecycline Evaluation and Surveillance Trial (TEST), this study investigated the incidence of carbapenem resistance in the USA during 2009.
Methods: A total of 781 clinical isolates of *K. pneumoniae* were collected during 2009 from multiple infection sources in the USA. The majority of isolates were from respiratory (n=180), cardiovascular (n=232) and genito-urinary (n=213) sources.
Results: 34 (4.4%) from nine states were identified as being meropenem-resistant, using recently revised clinical breakpoints published by the CLSI during 2010.
Susceptibility of these isolates is shown below:

Drug	MIC $_{50}$	MIC $_{90}$	%S	%I	%R
Amikacin	16	64	64.7	20.6	14.7
Amox-Clav	>32	>32	0.0	0.0	100
Ampicillin	>32	>32	0.0	0.0	100
Cefepime	32	>32	26.5	14.7	58.8
Ceftazidime	>32	>32	5.9	2.9	91.2
Ceftriaxone	>64	>64	8.8	2.9	88.2
Levofloxacin	>8	>8	8.8	0.0	91.2
Meropenem	16	>16	0.0	0.0	100
Minocycline	8	16	41.2	29.4	29.4
Pip-Tazo	>128	>128	11.8	2.9	85.3
Tigecycline	1	2	94.1	5.9	0.0

%S, %I, %R; percent susceptible, intermediate, or resistant calculated using CLSI M100-S20-U.

Conclusions: The meropenem resistance rate in *K. pneumoniae* for the USA in 2009 was 4.4%. The most active antimicrobial against these isolates was tigecycline which had an MIC$_{90}$ of 2 mcg/ml; 94% of isolates were susceptible. All other antimicrobials exhibited susceptibilities that were <65%.

Introduction

There is tremendous variability of antimicrobial resistance not only in pathogens causing various clinical infections, in different geographic regions, but also over time. These situations make continuous surveillance of the extent and trends of antimicrobial resistance crucial to provide guidance in choosing optimal therapy. While most *Enterobacteriaceae* remain susceptible to the carbapenem class of antibiotics, non-susceptibility to these agents appears to be emerging especially so in *Klebsiella pneumoniae* [1, 2]. The present study describes the frequency of meropenem-resistant *K. pneumoniae*, collected throughout the United States during 2009 as part of the Tigecycline Evaluation and Surveillance Trial (TEST).

Materials & Methods

- **Clinical isolates:** Isolates collected from multiple infection sources were identified to the species level and MICs determined at each participating laboratory. All organisms were deemed clinically significant by local participant criteria. Isolate inclusion was independent of medical history, antimicrobial use, age or gender. All sites identified each study isolate utilizing local laboratory criteria. All isolates were from 2009 and originated from throughout the United States (a total of 9 states).
- **Susceptibility testing:** Minimum inhibitory concentrations (MICs) were determined using panels manufactured by Trek Diagnostics, following manufacturer and Clinical and Laboratory Standards Institute (CLSI) instructions for broth microdilution testing [3]. Susceptibility was determined using clinical breakpoints published by the CLSI [4,5]. FDA breakpoints were used for tigecycline [6]. Tigecycline was supplied by Pfizer, Inc. (Collegeville, PA, USA). All other agents were supplied by the panel manufacturers, MicroScan (Siemens Medical Solutions Diagnostics., West Sacramento, CA, USA) and Trek (TREK Diagnostic Systems, Cleveland, OH). The following antimicrobial agents were included on the panels with their dilution ranges (expressed in mcg/ml): amikacin (0.5-64); amoxicillin/clavulanic acid (0.12/0.06-32/16); ampicillin (0.06-16); cefepime (0.5-32); ceftazidime (8-32); ceftriaxone (0.06-64); meropenem (0.12-16); levofloxacin (0.008-8); minocycline (0.5-16); tigecycline (0.008-16); piperacillin/tazobactam (0.06/4-128/4). *K. pneumoniae* ATCC 700603, *E. coli* ATCC 25922 and ATCC 35218 and *P. aeruginosa* ATCC 27853 were tested as quality control organisms.

References

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Acknowledgements

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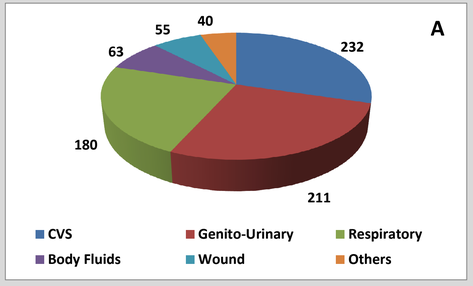
Results

Figure 1.

(A) Infection source of all isolates (n = 781).



(B) Infection source of meropenem-resistant isolates (n = 34).

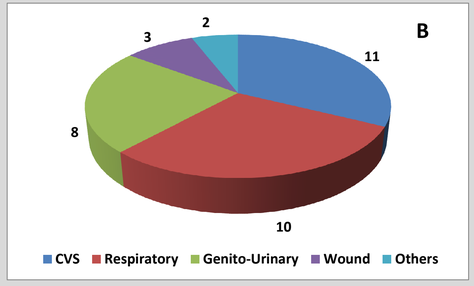


Figure 2. Number of meropenem-resistant isolates (n = 34) by state.

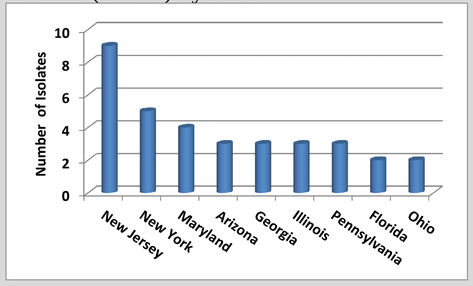


Figure 3. Susceptibility of all isolates (n = 781) to antimicrobial agents.

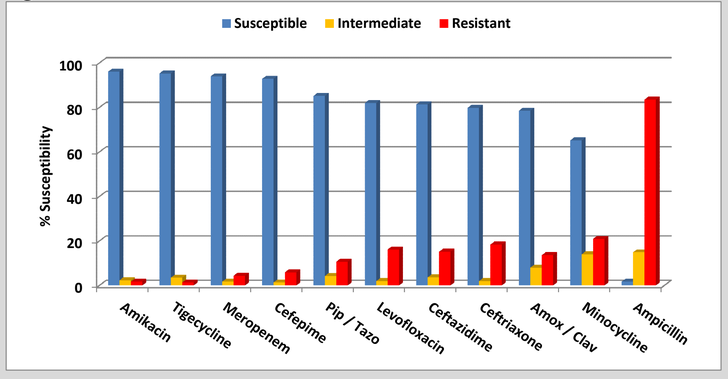
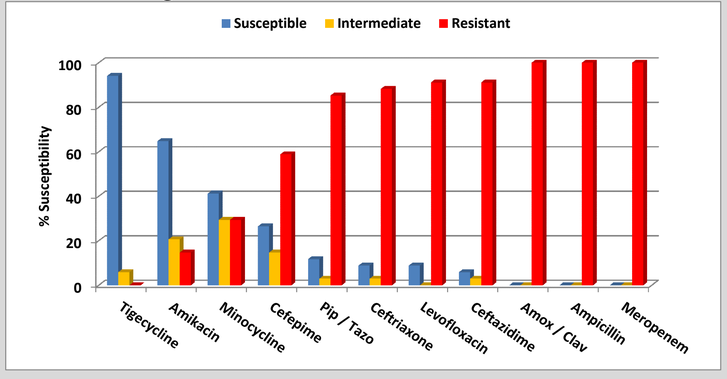


Figure 4. Susceptibility of meropenem-resistant isolates (n = 34) to antimicrobial agents.



Conclusions

- Of the total of 781 isolates collected during 2009, 4.6 % (34 isolates) were meropenem-resistant.
- Meropenem-resistant isolates were detected in nine different states within the United States with the highest number coming from New Jersey.
- The most active agents tested against meropenem-resistant isolates were tigecycline (94% susceptible), followed by amikacin (65%) and minocycline (41%). Co-resistance to other drug classes and agents was very high in meropenem-resistant isolates.