Trends in Susceptibility and Multi-Drug Resistance in *K. pneumoniae* from Intra-Abdominal Infections in Western Europe 2009-2013

EV0089

S. Lob, R. Badal, D. Biedenbach, A. Johnson, D. Sahm
IHMA, Inc., Schaumburg, IL, USA

IHMA, Inc.
2122 Palmer Drive
Schaumburg, IL 60173 USA
Phone: +1.847.303.5003
Fax: +1.847.303.5601
www.ihmainc.com

Objectives

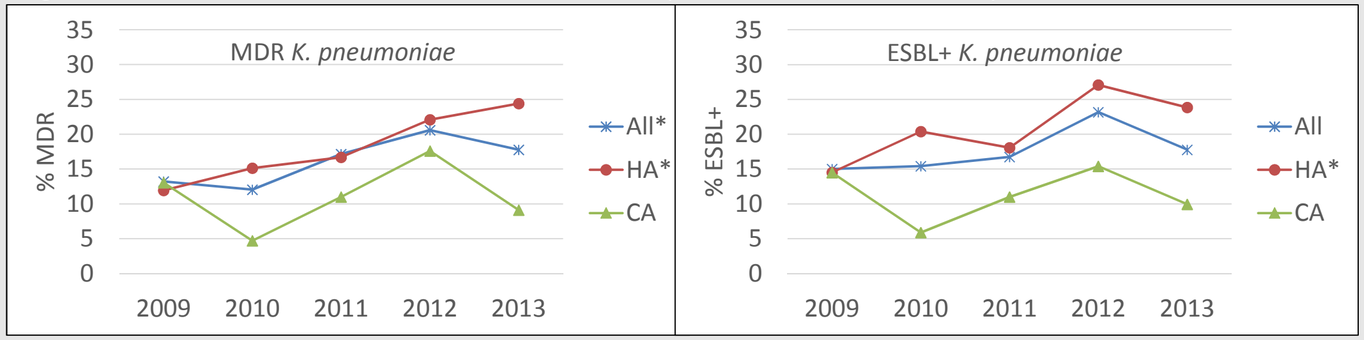
Increasing resistance in gram-negative pathogens, especially due to extended-spectrum β-lactamases (ESBLs), has been reported worldwide, seriously limiting treatment options in some regions. This report uses data from the Study for Monitoring Antimicrobial Resistance Trends (SMART) to examine resistance patterns in *Klebsiella pneumoniae* from intra-abdominal infections (IAI) collected in Western Europe from 2009 to 2013.

Materials and Methods

34 laboratories in France (6 sites), Germany (5), Italy (4), Portugal (3), Spain (12), and the UK (4) collected up to 100 consecutive gram-negative IAI isolates each year. Susceptibility was determined for 1,367 *K. pneumoniae* using CLSI broth microdilution and EUCAST breakpoints [1, 2]. ESBL status was determined phenotypically using the CLSI method [3]. Linear trends in susceptibility and MDR and ESBL rates were assessed with the Cochran-Armitage test. An IAI was defined as hospital-associated (HA) or community-associated (CA) if cultured ≥48 hours or <48 hours post-admission, respectively. Multi-drug resistance (MDR) was defined as resistance to three or more of the tested drug classes.

Results

Figures 1a and 1b. Trends in rates of MDR and ESBL+ *K. pneumoniae*, Western Europe, 2009-2013.



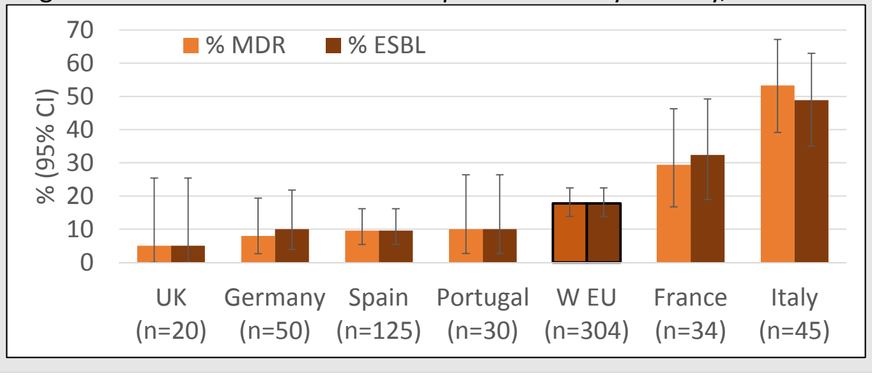
* Significant increasing trend (p<0.05).

Table 1. Susceptibility of *K. pneumoniae*, Western Europe, 2009-2013. Decreasing trends are shaded yellow.

	All					Hospital-associated					Community-associated				
	2009	2010	2011	2012	2013	2009	2010	2011	2012	2013	2009	2010	2011	2012	2013
Ertapenem	95.0	98.9	92.7	97.1	96.1	96.9	98.7	93.8	96.7	94.8	94.2	98.8	96.7	97.8	97.7
Imipenem	98.2	99.6	93.5	97.8	97.4	98.5	100	93.8	97.2	95.9	97.1	98.8	98.9	98.9	99.2
Amp-Sulb	59.3	64.7	62.0	57.7	63.8	61.1	56.6	56.3	51.9	54.7	62.3	78.8	75.8	69.2	75.8
Cefepime	85.0	85.7	80.4	75.7	79.6	87.1	81.6	79.2	72.4	72.1	84.1	94.1	89.0	82.4	89.4
Ceftriaxone	83.6	85.7	81.2	76.5	79.6	85.0	81.6	80.6	73.5	73.3	84.1	94.1	89.0	82.4	87.9
Ceftazidime	78.2	83.1	79.6	73.9	79.9	80.3	77.6	77.8	70.2	72.7	78.3	94.1	89.0	81.3	89.4
Ciprofloxacin	78.9	81.2	75.9	72.4	75.3	79.8	75.7	75.7	69.6	66.9	81.2	90.6	82.4	78.0	86.4
Levofloxacin	84.3	83.1	83.3	78.3	80.6	87.1	79.0	84.0	77.9	72.7	82.6	90.6	89.0	79.1	90.9
Pip-Tazo	78.2	82.3	78.4	82.0	82.2	78.8	76.3	76.4	79.6	77.3	81.2	94.1	87.9	86.8	88.6
Amikacin	95.0	95.1	93.9	94.5	94.4	95.3	94.1	93.1	93.4	92.4	98.6	97.7	100	96.7	97.0
n	280	266	245	272	304	193	152	144	181	172	69	85	91	91	132

Amp-sulb, ampicillin-sulbactam; pip-tazo, piperacillin-tazobactam

Figure 2. MDR and ESBL+ rates of *K. pneumoniae* by country, 2013.



Sensitivity analyses were conducted for regional trends using only the 21 sites that submitted isolates in all 5 years. The increasing trends for MDR rates were significant overall (13.6 in 2009 to 18.5% in 2013) and in HA IAI (11.3 to 27.3%), as was the increasing ESBL rate in HA IAI (13.8 to 26.6%; all p<0.05).

Results Summary

- *K. pneumoniae* MDR rates increased significantly in Western Europe from 2009 to 2013, with an especially sharp increase in isolates from HA IAI (p<0.05, Figure 1a). ESBL rates showed a similar pattern as MDR rates (Figure 1b).
- Interestingly, *K. pneumoniae* susceptibility overall did not show a statistically significant decrease for most agents when the drugs were analyzed individually. In contrast, in isolates from HA IAI, significant decreasing susceptibility was seen in all cephalosporins and fluoroquinolones (Table 1).
- MDR rates varied widely between countries in Western Europe with highest rates in France and Italy and lowest in UK and Germany (Figure 2).

Conclusions

- MDR and ESBL rates in *K. pneumoniae* from IAI increased and susceptibility decreased in Western Europe from 2009 to 2013, especially in HA IAI isolates.
- Of the tested agents, only amikacin, ertapenem, and imipenem showed susceptibility >90%.
- Monitoring of MDR and ESBL rates must continue in Western Europe, and national and preferably local resistance patterns should be taken into account when making empiric treatment decisions for IAI patients.

References & Acknowledgements

1. Clinical Laboratory Standards Institute. 2012. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standards -- Ninth Edition. CLSI document M07-A9. Wayne, PA.
2. European Committee on Antimicrobial Susceptibility Testing (EUCAST). 2013. Breakpoint tables for interpretation of MICs and zone diameters, version 3.1, http://www.eucast.org.]
3. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Fourth Informational Supplement. Wayne, PA: Clinical and Laboratory Standards Institute; 2014. CLSI Document M100-S24.

The SMART surveillance program is funded by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. Whitehouse Station, NJ. The authors thank all the participants in the SMART program for their continuing contributions to its success.