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Susceptibility of Intra-abdominal Pathogens in Asia – SMART 2009

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Revised Abstract

Background: The Study for Monitoring Antimicrobial Resistance Trends (SMART) has monitored susceptibility of intra-abdominal infection (IAI) pathogens since 2002. During that time, antimicrobial resistance has increased alarmingly, with some of the highest resistance rates in Asia. This report summarizes Asian data from SMART in 2009. **Methods**: 38 hospitals in 12 countries each collected up to 100 consecutive isolates of gram-negative aerobic bacilli from IAI. Isolate identification and susceptibility testing was done at a central laboratory, and interpreted using CLSI M100-S20 guidelines. **Results:** 3,303 isolates were collected, of which 75% were *E. coli* (48%), *K. pneumoniae* (19%), and *P. aeruginosa* (8%). 23% of all IAI pathogens (37% of *E. coli* and 26% of *K. pneumoniae*) were ESBL+ with the reduced susceptibility profiles normally associated with that phenotype. Individual country ESBL+ *E. coli* rates ranged from 2% (Australia) to 65% (China and India). Susceptibility of organisms with n>20 are shown in the table below. Shading denotes % susceptible values ≥90%.

Organism	N	Ak*	AS	Cpe	Cft	Cfx	Caz	Cax	Cp	Etp	Imp	Lvx	PT
E. coli, all	1577	94	31	62	54	81	62	55	50	98	99	52	89
E. coli ESBL+	586	91	7	5	0	77	19	1	16	99	100	17	87
E. coli ESBL-	989	97	46	95	87	84	87	87	71	98	98	73	91
K. pneumoniae, all	641	91	57	72	66	77	69	66	69	93	96	79	79
K. pneumo. ESBL+	169	82	2	11	1	66	9	1	20	90	95	49	46
K. pneumo. ESBL-	468	94	77	94	89	82	90	89	87	94	96	90	90
P. aeruginosa	257	86	-	74	11	-	77	12	80	-	78	79	89
E. cloacae	188	93	11	76	45	5	49	43	73	96	98	81	68
A. baumannii	135	31	22	22	22		25	22	23	-	30	29	23
P. mirabilis	100	92	79	94	87	94	94	85	82	100	99	88	100
K. oxytoca	76	97	59	86	79	83	86	76	87	99	99	88	86
C. freundii	48	92	44	83	65	15	67	60	71	96	98	79	79
E. aerogenes	46	100	24	87	59	4	63	61	89	100	100	96	78
M. morganii	42	81	2	86	43	62	67	57	67	98	98	76	93
S. marcescens	31	100	0	97	61	35	87	71	90	100	100	90	87
A. hydrophila	27	93	11	89	85	48	85	85	93	78	52	100	78
S. maltophilia	22	-	-	-	-	-	14	-	-	-	-	77	-

*Ak=amikacin, AS=ampicillin-sulbactam, Cpe=cefepime, Cft=cefotaxime, Cfx=cefoxitin, Caz=ceftazidime, Cax=ceftriaxone, Cp=ciprofloxacin, Etp=ertapenem, Imp=imipenem, Lvx=levofloxacin, PT=piperacillin-tazobactam.

Conclusions: Although ESBL rates and susceptibility vary greatly among countries in Asia, the two species accounting for 2/3 of all IAI pathogens (*E. coli* and *K. pneumoniae*) were <90% susceptible to all study drugs except ertapenem, imipenem, and amikacin. Although *A. baumannii* represented only 4% of IAI isolates, this species was <32% susceptible to all drugs for which it has breakpoints. Increasing resistance requires ongoing monitoring to help control the rapid spread of multi-drug resistant pathogens.

Introduction

Increasing antimicrobial resistance is a critical problem in infectious disease, and has been shown to vary significantly from region to region. The Study for Monitoring Antimicrobial Resistance Trends (SMART) is a global and longitudinal surveillance study that has tracked susceptibility and resistance patterns of aerobic or facultative gram-negative organisms causing intra-abdominal infections (IAI) since 2002. Previous reports from SMART and other surveillance studies have shown that countries in the Asia/Pacific (AP) region often have the highest rates of antimicrobial resistance in IAI pathogens such as *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa,* and *Acinetobacter baumannii*. One of the most important goals of surveillance is to identify changes and trends in antimicrobial susceptibility levels, especially regionally, thereby providing physicians with current data which may be used to tailor empiric therapy to reflect local resistance levels. This report presents the 2009 results from SMART regarding susceptibility to ertapenem and several comparator agents of commonly isolated gram-negative IAI pathogens.

Materials & Methods

- A total of 38 labs in 12 countries in AP collected and identified 3,303 non-repeat gram-negative bacilli (GNB) from IAI in 2009. Only one isolate per species per patient was accepted into the study.
- All isolates were sent to a central laboratory (International Health Management Associates, Inc., Schaumburg, Illinois, USA) for confirmation of identification, antimicrobial susceptibility testing, detection of extended-spectrum beta-lactamase (ESBL) production, and long-term storage.
- Susceptibility testing and ESBL detection was done using custom MicroScan dehydrated broth microdilution panels (Siemens Medical Solutions Diagnostics, West Sacramento, California, USA), following Clinical and Laboratory Standards Institute (CLSI) guidelines [1], and interpreted using CLSI January 2010 guidelines [2]. The following antimicrobial agents were included on the panels with their dilution ranges (expressed in mcg/ml): ertapenem 0.03-4, imipenem 0.06-8, cefepime 0.5-32, ceftazidime 0.5-128, ceftazidime-clavulanic acid 0.12-16, cefoxitin 2-16, ciprofloxacin 0.25-2, amikacin 4-32, levofloxacin 0.5-4, cefotaxime 0.5-128, cefotaxime-clavulanic acid 0.12/2-16/2, piperacillin-tazobactam 2/4-64/4, ampicillin-sulbactam 2/2-16/2, and ceftriaxone 1-32.
- Quality control was done on each day of susceptibility testing, using CLSI ranges for *E. coli* ATCC 25922, *E. coli* ATCC 35218, *P. aeruginosa* ATCC 27853, and *K. pneumoniae* ATCC 700603 (positive ESBL control) [2].
- *E. coli*, *K. pneumoniae, K. oxytoca*, and *Proteus mirabilis* isolates were classified as ESBL producers if there was at least an eight-fold reduction of MIC for ceftazidime or cefotaxime tested in combination with clavulanic acid versus their MICs when tested alone as described by the CLSI [2].
- Development of a centralized database of study results was managed by International Health Management Associates, Inc. located in Schaumburg, Illinois, USA.

References

1. Clinical and Laboratory Standards Institute, 2009. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard—Eighth Edition*, in Document M7-A8. Clinical and Laboratory Standards Institute (CLSI), Wayne, PA 19087-1898 USA.
2. Clinical and Laboratory Standards Institute, 2010. *Performance Standards for Antimicrobial Susceptibility Testing; Twentieth Informational Supplement*. CLSI document M100-S20. Clinical and Laboratory Standards Institute (CLSI), Wayne, PA 19087-1898 USA.

Acknowledgements

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Results

Figure 1. Relative proportions of gram-negative pathogens from IAI in Asia/Pacific in 2009.

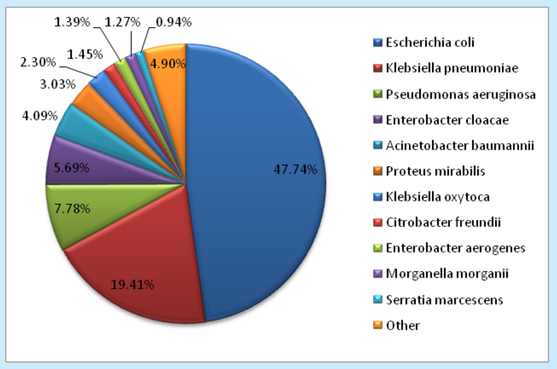


Figure 2. ESBL+ rates for *E. coli* from IAI in Asia/Pacific countries in 2009.

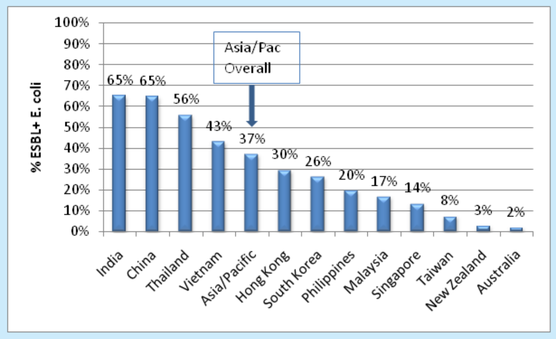


Figure 3. ESBL+ rates for *K. pneumoniae* from IAI in Asia/Pacific countries in 2009.

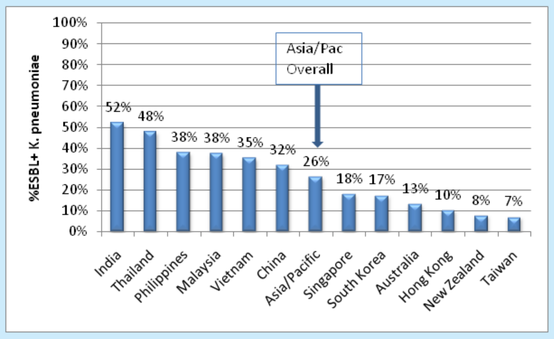
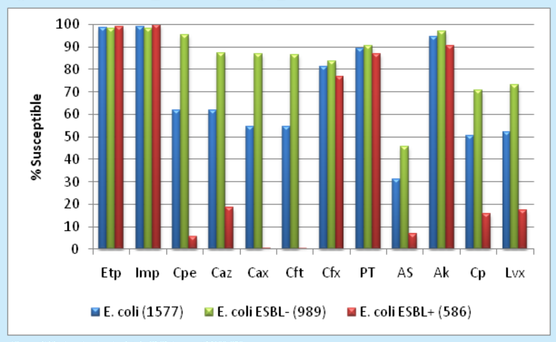
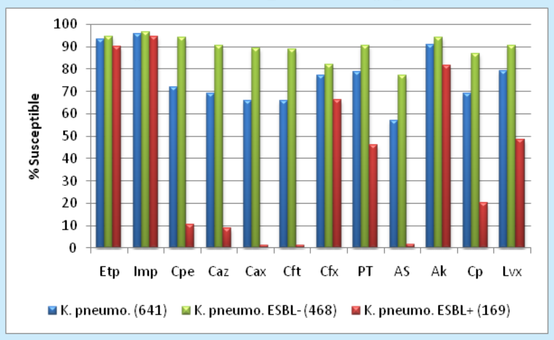


Figure 4. Susceptibility* of *E. coli* overall and by ESBL phenotype.



*Susceptibility based on breakpoints in CLSI document M100-S20.
Etp=ertapenem, Imp=imipenem, Cpe=cefepime, Caz=ceftazidime, Cax=ceftriaxone, Cft=cefotaxime, Cfx=cefoxitin, PT=piperacillin-tazobactam, AS=ampicillin-sulbactam, Ak=amikacin, Cp=ciprofloxacin, Lvx=levofloxacin.

Figure 5. Susceptibility* of *K. pneumoniae* overall and by ESBL phenotype.



*Susceptibility based on breakpoints in CLSI document M100-S20.
Etp=ertapenem, Imp=imipenem, Cpe=cefepime, Caz=ceftazidime, Cax=ceftriaxone, Cft=cefotaxime, Cfx=cefoxitin, PT=piperacillin-tazobactam, AS=ampicillin-sulbactam, Ak=amikacin, Cp=ciprofloxacin, Lvx=levofloxacin.

Table 1. Susceptibility (%)* of IAI pathogens in Asia/Pacific in 2009 for species with n>20.

Organism	N	Ak	AS	Cpe	Cft	Cfx	Caz	Cax	Cp	Etp	Imp	Lvx	PT
E. coli	1577	94	31	62	54	81	62	55	50	98	99	52	89
E. coli ESBL+	586	91	7	5	0	77	19	1	16	99	100	17	87
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A. hydrophila	27	93	11	89	85	48	85	85	93	78	52	100	78
S. maltophilia	22						14					77	

*Susceptibility based on breakpoints in CLSI document M100-S20; — means breakpoints are not defined for this drug and species.
Ak=amikacin, AS=ampicillin-sulbactam, Cpe=cefepime, Cft=cefotaxime, Cfx=cefoxitin, Caz=ceftazidime, Cax=ceftriaxone, Cp=ciprofloxacin, Etp=ertapenem, Imp=imipenem, Lvx=levofloxacin, PT=piperacillin-tazobactam.
Values ≥90% are boldened and green-shaded for emphasis.

Conclusions

- Although ESBL rates and susceptibility vary greatly among countries in Asia, overall, the two species accounting for 2/3 of all IAI pathogens (*E. coli* and *K. pneumoniae*) were <90% susceptible to all study drugs except ertapenem, imipenem, and amikacin.
- *A. baumannii* represented only 4% of IAI isolates, but this species was <32% susceptible to all drugs for which it has breakpoints, making for very challenging therapeutic options when this pathogen is present in an IAI.
- Increasing resistance requires ongoing monitoring to help control the rapid spread of multi-drug resistant pathogens, and to ensure the most effective use of available antimicrobials to optimize patient outcomes.