Comparison of Antimicrobial Susceptibility and Incidence of Extended-Spectrum Beta-Lactamase-Producing Isolates in Medical Intensive Care Units versus Surgical Intensive Care Units – Results from SMART 2008-2009

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Revised Abstract

Introduction: The Study for Monitoring Antimicrobial Resistance Trends (SMART) is a global longitudinal surveillance program that tracks antimicrobial susceptibility of aerobic gram-negative pathogens from intra-abdominal infections (IAI) to ertapenem, imipenem, amikacin, ampicillin-sulbactam, cefepime, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, ciprofloxacin, levofloxacin, and piperacillin-tazobactam. Data from this program can help in development and updating of therapy guidelines as bacterial resistance to many drugs increases. This report compares incidence of extended-spectrum beta-lactamase (ESBL) producing isolates and the susceptibility of IAI pathogens recovered from surgical ICUs (SICU) to those of isolates from medical ICUs (MICU).**Methods:** 120 hospitals in 35 countries collected 1,595 isolates representing 34 species from patients in SICU (713) or MICU (882) in 2008-2009. All isolates were sent to a central lab in the US for identification, confirmation of ESBL production, and susceptibility testing using CLSI methods. Only the 12 species with ≥10 isolates recovered from both SICU and MICU were included in this analysis. Fisher's Exact Test was used to determine statistical significance.**Results:** In 23 drug/species combinations a difference of ≥10% susceptibility between MICU and SICU was seen: *Serratia marcescens* had 8, *Morganella morganii* had 4, *Pseudomonas aeruginosa* had 4, *Proteus mirabilis* and *P. vulgaris* each had 2, and *Acinetobacter baumannii*, *Klebsiella oxytoca,* and *Citrobacter freundii* had 1 each. SICU %S values tended to be lower for *A. baumannii*, and *P. vulgaris;* MICU %S values were usually lower for *K. oxytoca, M. morganii, P. mirabilis, P. aeruginosa,* and *S. marcescens*; however, in only 9 cases were the differences significant (*P*<0.05). ESBL rates (%) in MICU/SICU for *Escherichia coli*, *K. pneumoniae*, *K. oxytoca*, and *P. mirabilis* were 21/23, 33/30, 18/8, and 9/2, respectively; however none of the differences in ESBL rates between MICU and SICU were significant (*P*>.05). Ertapenem and imipenem maintained %S values ≥85 in both MICU and SICU for all 12 species in this analysis except *A. baumannii* and *P. aeruginosa*, while amikacin did so for all species except *A. baumannii* and *C. freundii*. No other drug did so in more than 5 species. **Conclusions:** Although there were some differences observed between MICU and SICU regarding drug susceptibilities and ESBL incidence, most were not statistically significant. Among the agents included in SMART, ertapenem, imipenem, and amikacin were the most active compounds *in vitro* against IAI pathogens in both MICU and SICU.

Introduction

Levels of bacterial resistance to antimicrobial agents can vary widely, not only geographically, but even within individual hospitals. Intensive care units (ICUs) often have significantly higher rates of resistance (including multi-drug-resistance, or MDR) than other units in hospitals [1]. Because of this situation, guidelines for therapy of infectious diseases may include ICU vs. non-ICU location of patients as part of treatment algorithms to account for higher risk of resistance or MDR in the ICU [2]; however, in those guidelines that do account for patient location (ICU vs. non-ICU), no distinction is made between surgical ICU (SICU) versus medical ICU (MICU) [2].

The Study for Monitoring Antimicrobial Resistance Trends (SMART) is a global longitudinal antimicrobial surveillance study that has been monitoring susceptibility of gram-negative aerobic pathogens from intra-abdominal infections (IAI) since 2002. In this report we compare the susceptibility levels of recent (2008-2009) IAI pathogens and the rates of extended-spectrum-beta-lactamase (ESBL)-producing isolates from patients in SICUs versus MICUs to determine if significant differences exist that may necessitate different empiric therapy regimens.

Materials & Methods

- ◊ 120 hospitals in 35 countries collected 1,595 isolates from IAI infections in 2008-2009 representing 34 gram-negative aerobic species. 713 isolates were from SICU and 882 were from MICU. All isolates were sent to a central laboratory (Laboratories International for Microbiology Studies, a subsidiary of International Health Management Associates, Inc., in Schaumburg, Illinois, USA), for confirmation of identification and antimicrobial susceptibility testing.
- ◊ Susceptibility testing was performed following Clinical and Laboratory Standards Institute (CLSI) guidelines [3], using dehydrated broth microdilution panels prepared by MicroScan (Siemens Medical Solutions Diagnostics, West Sacramento, California, USA). The drugs tested were: amikacin, ampicillin-sulbactam, cefepime, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, ciprofloxacin, ertapenem, imipenem, levofloxacin, and piperacillin-tazobactam.
- ◊ ESBL testing was done according to CLSI guidelines [4], looking for a ≥3-doubling dilution decrease in MIC of ceftazidime or cefotaxime in the presence of clavulanic acid.
- ◊ Quality control testing was done following CLSI [4] and manufacturer (MicroScan) guidelines, using quality control strains *E. coli* ATCC 25923, *E. coli* ATCC 35218, *P. aeruginosa* ATCC 27853, and *K. pneumoniae* ATCC 700603.
- ◊ Only the 12 species with ≥10 isolates in both SICU and MICU were included in this analysis.
- ◊ Fisher's Exact Test (two-tailed) was used to determine statistical significance.

References

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Acknowledgements

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Results

Figure 1. Relative frequency of isolation of gram-negative aerobic IAI pathogens in MICUs.

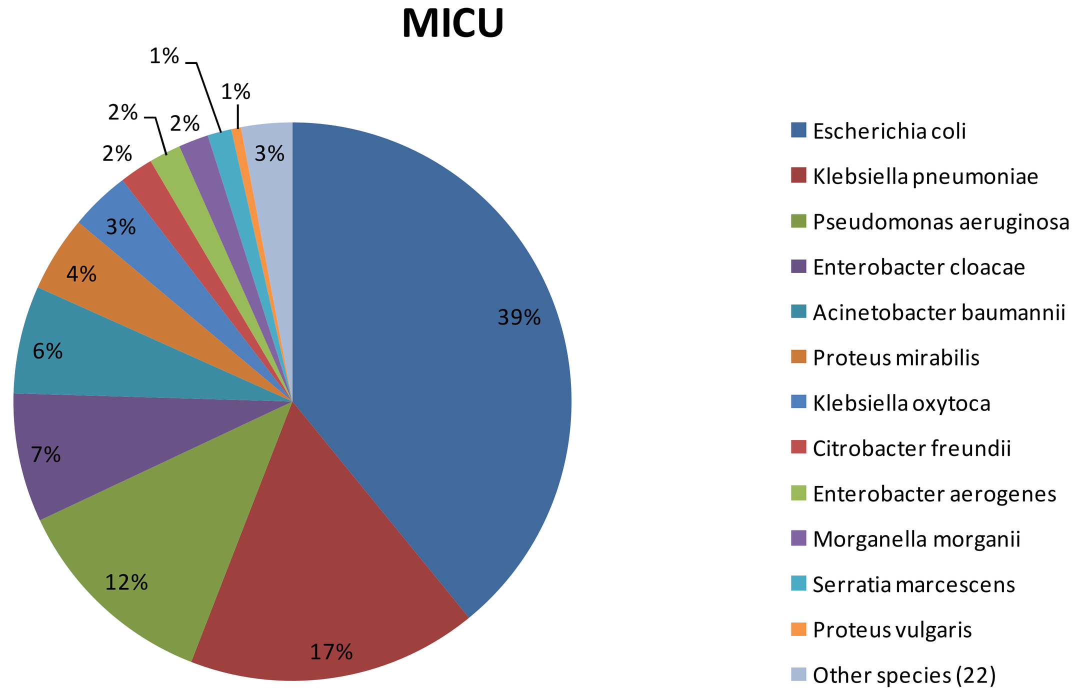

Figure 2. Relative frequency of isolation of gram-negative aerobic IAI pathogens in SICUs.

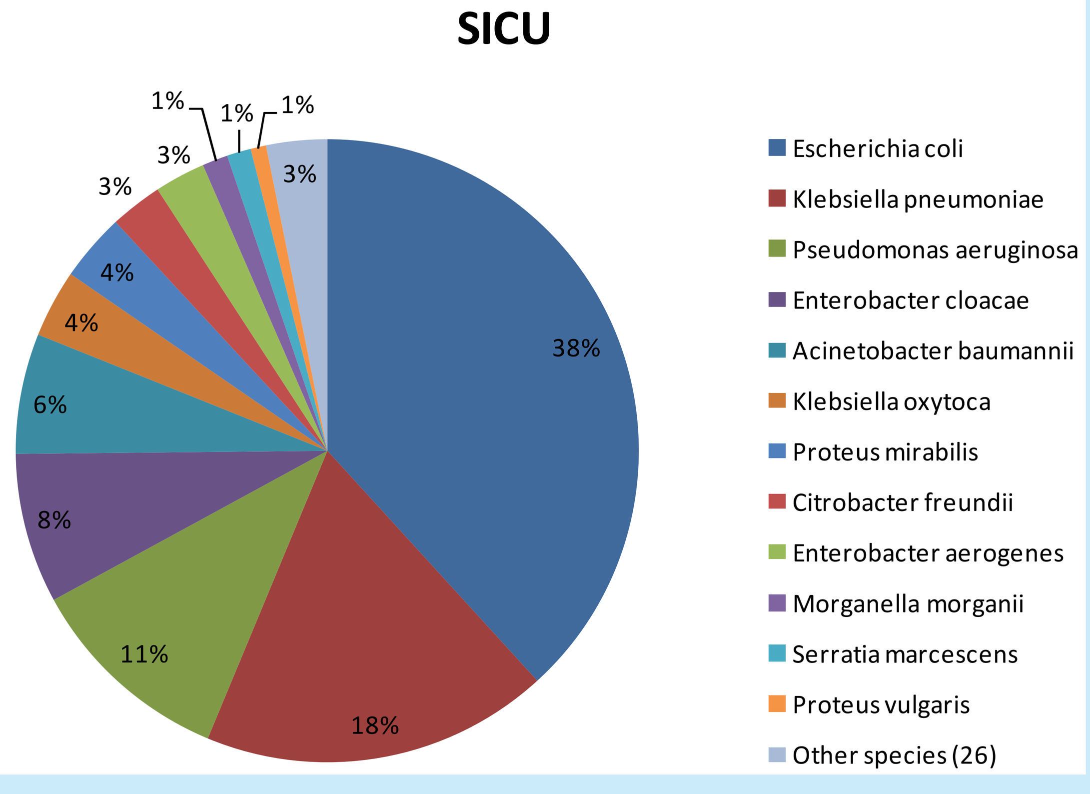

Figure 3. Comparison of relative frequency of isolation of gram-negative aerobic IAI pathogens in MICUs versus SICUs.

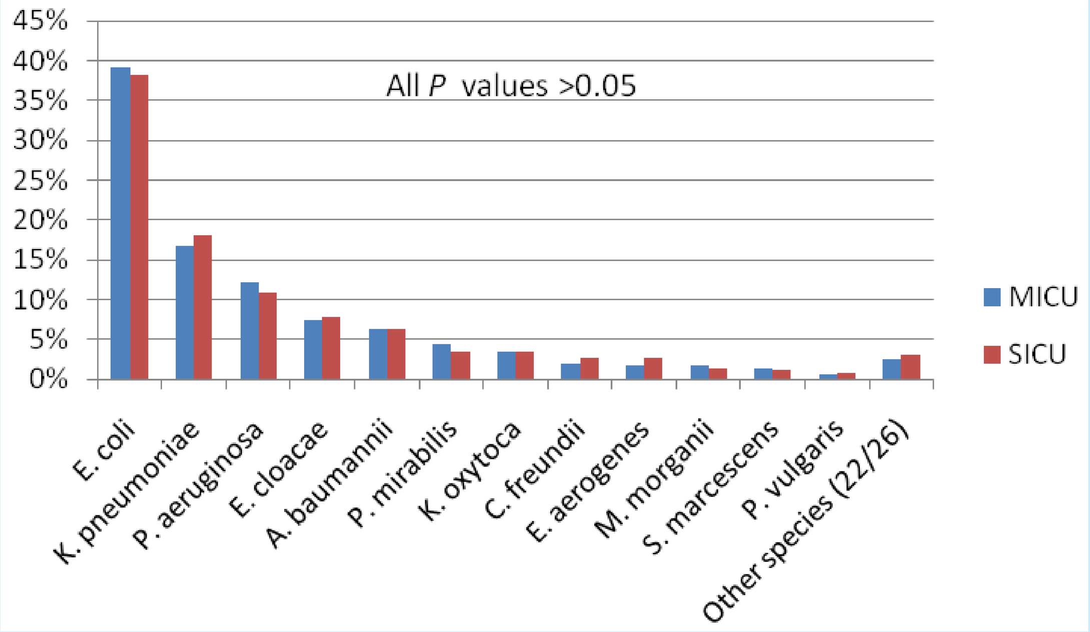

Figure 4. Comparison of ESBL-positive rates of *E. coli*, *K. pneumoniae*, *K. oxytoca*, and *P. mirabilis* in MICUs and SICUs.

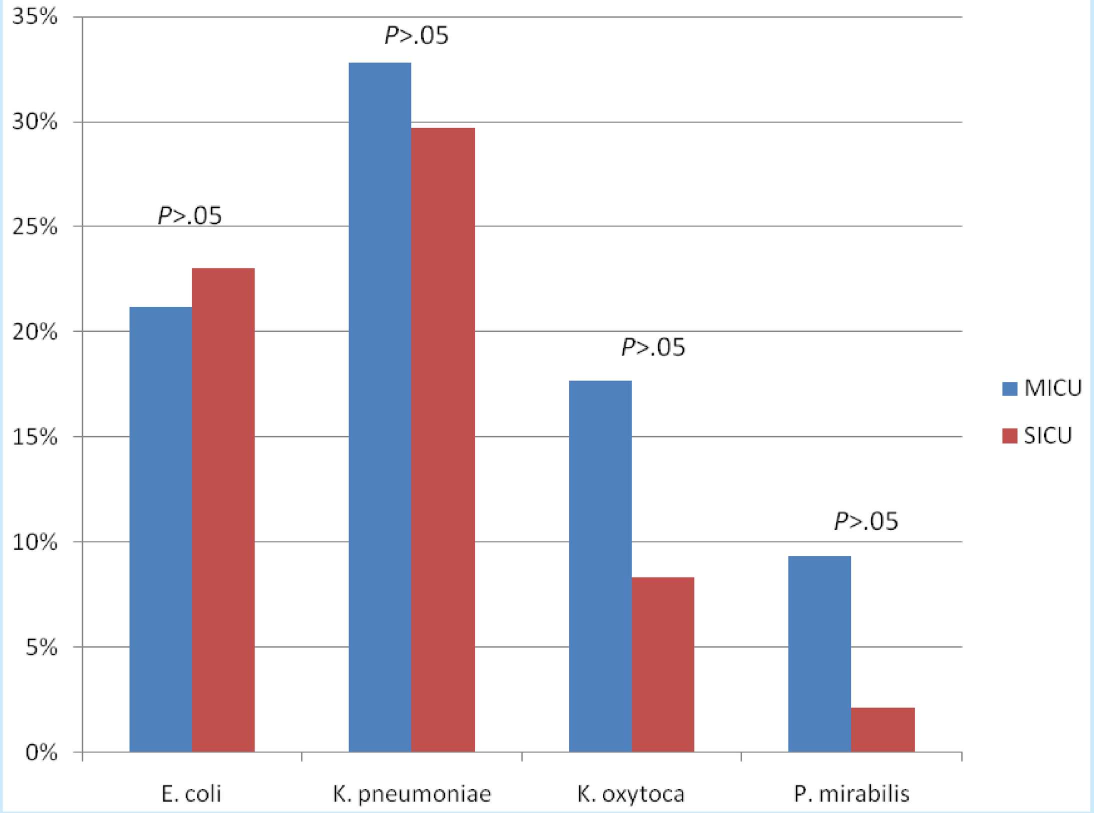

Table 1. Antimicrobial susceptibility* percentages of the most commonly isolated gram-negative aerobic IAI pathogens in MICU versus SICU (gray-shading denotes differences of >10%; yellow-highlighting denotes pairs where *P*<0.05).

Organism	Location	N	Ak	AS	Cpe	Cft	Cfx	Caz	Cax	Cp	Etp	Imp	Lvx	PT
Acinetobacter baumannii	MICU	122	30.3	21.3	16.4	16.4	-	18.9	15.6	13.1	-	32.0	18.0	18.0
	SICU	85	28.2	10.6	10.6	9.4	-	12.9	9.4	12.9	-	36.5	15.3	14.1
Citrobacter freundii	MICU	38	84.2	29.0	81.6	50.0	5.3	50.0	50.0	76.3	97.4	100	81.6	68.4
	SICU	37	94.6	21.6	83.8	46.0	2.7	46.0	46.0	81.1	97.3	97.3	86.5	62.2
Enterobacter aerogenes	MICU	36	100	19.4	86.1	55.6	13.9	55.6	55.6	88.9	86.1	91.7	94.4	61.1
	SICU	36	100	27.8	77.8	58.3	8.3	58.3	58.3	88.9	86.1	94.4	91.7	61.1
Enterobacter cloacae	MICU	146	95.9	15.8	89.0	54.1	5.5	56.2	54.8	86.3	95.9	97.3	88.4	66.4
	SICU	106	98.1	14.2	84.0	57.6	3.8	58.5	56.6	82.1	91.5	98.1	86.8	66.0
Escherichia coli	MICU	765	95.0	37.3	80.0	76.2	88.4	79.2	75.6	63.8	99.1	99.6	65.5	87.1
	SICU	521	95.8	35.7	77.9	74.7	86.0	79.1	74.1	59.1	98.9	99.6	59.3	86.6
Klebsiella oxytoca	MICU	68	97.1	55.9	91.2	83.8	89.7	85.3	77.9	85.3	100	100	88.2	85.3
	SICU	48	100	60.4	89.6	89.6	95.8	97.9	81.3	91.7	100	100	95.8	85.4
Klebsiella pneumoniae	MICU	329	88.2	42.9	70.2	65.1	77.2	66.6	65.1	69.3	95.1	97.0	75.7	69.6
	SICU	246	86.2	51.2	72.8	66.7	74.8	68.7	67.1	64.2	91.5	95.9	69.1	72.4
Morganella morganii	MICU	34	100	0.0	91.2	82.4	76.5	85.3	88.2	64.7	100	100	73.5	97.1
	SICU	18	100	5.6	100	94.4	77.8	77.8	100	88.9	100	100	88.9	94.4
Proteus mirabilis	MICU	86	94.2	72.1	93.0	88.4	93.0	91.9	88.4	62.8	100	100	79.1	94.2
	SICU	48	93.8	79.2	97.9	97.9	93.8	97.9	95.8	85.4	100	100	91.7	100
Proteus vulgaris	MICU	11	100	45.5	100	100	100	90.9	72.7	100	100	100	100	100
	SICU	11	100	36.4	100	90.9	90.9	100	81.8	63.6	100	100	63.6	100
Pseudomonas aeruginosa	MICU	238	86.6	-	59.7	4.2	-	66.0	6.7	57.6	-	57.6	56.7	78.2
	SICU	147	87.8	-	71.4	8.8	-	75.5	12.9	76.9	-	68.0	73.5	87.1
Serratia marcescens	MICU	25	92.0	8.0	84.0	72.0	24.0	80.0	72.0	84.0	88.0	88.0	84.0	80.0
	SICU	17	94.1	11.8	100	88.2	23.5	94.1	88.2	82.4	100	100	94.1	94.1

*Susceptibility based on CLSI M100-S19 (2009).
N=number of isolates; 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.

Table 2. Antimicrobial susceptibility* of gram-negative aerobic IAI pathogens in MICUs and SICUs (percentages ≥85 highlighted in green).

Organism	Location	N	Ak	AS	Cpe	Cft	Cfx	Caz	Cax	Cp	Etp	Imp	Lvx	PT
Acinetobacter baumannii	MICU	122	30	21	16	16		19	16	13		32	18	18
	SICU	85	28	11	11	9		13	9	13		36	15	14
Citrobacter freundii	MICU	38	84	29	82	50	5	50	50	76	97	100	82	68
	SICU	37	95	22	84	46	3	46	46	81	97	97	86	62
Enterobacter aerogenes	MICU	36	100	19	86	56	14	56	56	89	86	92	94	61
	SICU	36	100	28	78	58	8	58	58	89	86	94	92	61
Enterobacter cloacae	MICU	146	96	16	89	54	5	56	55	86	96	97	88	66
	SICU	106	98	14	84	58	4	58	57	82	92	98	87	66
Escherichia coli	MICU	765	95	37	80	76	88	79	76	64	99	100	65	87
	SICU	521	96	36	78	75	86	79	74	59	99	100	59	87
Klebsiella oxytoca	MICU	68	97	56	91	84	90	85	78	85	100	100	88	85
	SICU	48	100	60	90	90	96	98	81	92	100	100	96	85
Klebsiella pneumoniae	MICU	329	88	43	70	65	77	67	65	69	95	97	76	70
	SICU	246	86	51	73	67	75	69	67	64	91	96	69	72
Morganella morganii	MICU	34	100	0	91	82	76	85	88	65	100	100	74	97
	SICU	18	100	6	100	94	78	78	100	89	100	100	89	94
Proteus mirabilis	MICU	86	94	72	93	88	93	92	88	63	100	100	79	94
	SICU	48	94	79	98	98	94	98	96	85	100	100	92	100
Proteus vulgaris	MICU	11	100	45	100	100	100	91	73	100	100	100	100	100
	SICU	11	100	36	100	91	91	100	82	64	100	100	64	100
Pseudomonas aeruginosa	MICU	238	87		60	4		66	7	58		58	57	78
	SICU	147	88		71	9		76	13	77		68	73	87
Serratia marcescens	MICU	25	92	8	84	72	24	80	72	84	88	88	84	80
	SICU	17	94	12	100	88	24	94	88	82	100	100	94	94

*Susceptibility based on CLSI M100-S19 (2009).

Conclusions

- ◊ There were no significant differences in frequency of isolation of gram-negative aerobic species from IAI between MICU and SICU, and the antimicrobial susceptibility patterns observed in IAI pathogens from MICU and SICU were very similar overall, with only 9 drug/organism combinations being significantly different (*P*<0.05); in 8 of those, SICU susceptibility rates were higher than MICU.
- ◊ Among the drugs evaluated in the SMART program, ertapenem, imipenem, and amikacin exhibited the broadest *in vitro* efficacy against the species accounting for >97% of gram-negative aerobes causing IAI.
- ◊ Unless local susceptibility and epidemiologic data indicate otherwise, this report suggests that a single set of guidelines for empiric therapy of IAI infections in SICU and MICU should suffice.