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Geographic Antimicrobial Resistance Variability Among Bacterial Pathogens Causing Nosocomial Pneumonia in North America (NA): An Eight-Year Analysis from the SENTRY Antimicrobial Surveillance Program, 1997-2004

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SENTRY ANTIMICROBIAL SURVEILLANCE

ABSTRACT

Background: To determine the geographic variability of antimicrobial resistant (R) pathogens which cause nosocomial pneumonia within the USA and Canada (CA), data from SENTRY was compared over 8-years. *S. aureus* (SA) and 7 Gram-negative species were evaluated for R patterns in 5 USA regions and CA.
Methods: *P. aeruginosa* (PSA, 3,380), *Klebsiella* spp. (KSP, 1,358), *Enterobacter* spp. (EBS, 1,100), *E. coli* (EC, 698), *Serratia* spp. (SER, 656), *Acinetobacter* spp. (ASP, 466), *S. maltophilia* (SM, 633) and SA (4,647) were common isolates from hospitalized pneumonia patients. Antimicrobial-R determination was performed using CLSI broth microdilution. R was compared in NA regions [47 centers]: southeast [SE;6], west, [W;11], south [S;5], midwest [MW;10], northeast [NE;8] and CA [7].
Results: The MRSA rate in the USA was higher in the NE and SE (50.4 - 60.2%) compared to others (42.3 - 45.6%) and was much lower in CA (5.2%). Other SA agents showed lower R rates in CA compared to USA. MLS_B-R phenotypes in SA was more commonly due to target modification in the NE, MW and W (73.4 - 76.3%) > S, SE (64 - 64.1%) > CA (43.4%). Rates of R to anti-PSA agents were similar in all regions except for ciprofloxacin, USA (18.3 - 23.9%) > CA (12.0%). EC and KSP with ESBL-phenotypes were similar across regions 2.8 – 6.3% and 4.2 - 5.4%, except NE (21.1%) which was due to endemicity of a persistent clone in one center. Except for one strain from CA, imipenem-R ACB strains were only recovered in the NE (25.2%) from 2 centers in NYC. Overall, R among EBS and SER was higher in the NE for ciprofloxacin, cephalosporins and gentamicin. Among SM, R was highest in the MW to ticar/clav (24.2%) and trim/sulfa (6.3%).
Conclusions: There is R variability among key hospital acquired pneumonia pathogens within the USA and CA with a significant difference in the MRSA rate between countries. Regional variability is likely due to prescribing practices and the endemic clones within the local environments.

INTRODUCTION

Hospital-acquired pneumonia is a common cause of serious illness associated with high morbidity and mortality, and the increasing resistance rates among bacterial pathogens is a major concern among physicians that must often make empiric therapy decisions. Thus, local data on the frequency of occurrence and susceptibility profiles of these pathogens are often used to guide empiric antimicrobial therapy. In addition, regional surveillance data can be helpful in determining resistance rates among common bacterial pathogens on a larger scale. Many studies have documented that there can be large differences in the rates of antimicrobial resistance and pathogen occurrence between countries and worldwide regions.

The SENTRY Antimicrobial Surveillance Program has monitored the pathogen occurrence and the susceptibility profiles among species that commonly cause nosocomial pneumonia since 1997. This investigation provided data collected from this program during 1997 - 2004 to determine if there were regional trends in bacterial occurrence and susceptibility profiles among the common causes of hospital-acquired pneumonia infections. This study focuses on five geographic regions in the United States and Canada.

MATERIALS AND METHODS

A total of 47 medical centers contributed isolates to the SENTRY Program from patients with hospital-acquired pneumonia during the 1997 - 2004 period. These included six sites in the southeast (FL, KY, NC, VA), 11 sites in the west (AZ, CA, HI, CO, NM, OR, UT, WA), five sites in the south (AR, MS, TX), 10 sites in the Midwest (IA, IL, IN, MI, MO, NE, WI), eight sites in the northeast (DE, MA, NY, OH, PA) and seven sites in Canada located in Ontario, Alberta, Manitoba and Nova Scotia. Eight of the 10 top rank order pathogens were analyzed in this study to determine the regional variation of these common pathogens and the associated resistance rates for each of the six regions (Tables 2 - 4). The isolates analyzed included: *Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella* spp., *Enterobacter* spp., *Escherichia coli, Serratia* spp., *Stenotrophomonas maltophilia* and *Acinetobacter* spp. The rank order of the regions according to the total number of isolates from these eight species was (no. of isolates): Northwest (3,497) > Midwest (2,388) > Canada (2,185). West (1,841) > South (1,546) > Southeast (1,481).

Species identifications were performed by the individual medical centers and confirmed at JMI Laboratories as necessary. All isolates were susceptibility tested at JMI Laboratories using a reference broth microdilution method with panels prepared by TREK Diagnostics (Cleveland, OH) according to CLSI guidelines.

RESULTS

- *S. aureus, P. aeruginosa, Klebsiella* spp. and *Enterobacter* spp. were consistently the most common bacterial causes of pneumonia in hospitalized patients for all regions of the United States and Canada (Table 1). The frequency of the remaining Gram-negative species were more variable region to region. Fastidious pathogens including *S. pneumoniae* and *H. influenzae* were also reported.
- Among the non-enteric Gram-negative bacilli listed in Table 2, the following results were observed: 1) *Acinetobacter* spp. isolated in the Northeast were more resistant to ß-lactam antimicrobials, particularly carbapenems, while fluoroquinolone and aminoglycoside resistance rates varied among regions; 2) resistance rates among *P. aeruginosa* isolates were relatively similar in all regions of the United States and Canada; and 3) resistance to commonly prescribed antimicrobial agents to treat *S. maltophilia* infections was highest in the Midwest.
- The MRSA rate was highest in the Northeast (60.2%), ranged from 42.3 to 50.4% in other regions of the United States and was very low in Canada (6.0%). This trend was similar for MLS_B agents and fluoroquinolones (Table 2).
- Among the Enterobacteriaceae, no significant resistance rate trends were noted for *E. coli* or *Serratia* spp. Conversely, *Klebsiella* spp. and *Enterobacter* spp. isolated in the Northeast showed higher resistance rates to most antimicrobial agents listed compared to other regions.
- The variability of resistance to MLS_B agents among *S. aureus* isolates is shown in Table 3. In all regions of the United States, the MLS_B-resistance was higher for strains exhibiting a ribosomal target modification phenotype (64.0 - 76.3%). However, the majority of erythromycin-resistant strains (55.7%) isolated in Canada remained susceptible to clindamycin although testing for inducible resistance rate was not determined.
- The frequency of isolates with an ESBL phenotype among *E. coli* (Table 4) was fairly similar in all United States regions (2.4 - 8.5%) and much lower in Canada (0.6 - 3.0%). Among *Klebsiella* spp. strains, the frequencies of an ESBL phenotype were similar in all United States regions and Canada, except for the US Northeast region, where a highly elevated occurrence rate compared to other regions was due to an endemic clone in one medical center.

Table 1. Regional distribution of common pathogens causing nosocomial pneumonia in North America (1997 - 2004).

	Regional rank order (no. tested)					
Organism (total in all regions)	Northeast	Southeast	Midwest	South	West	Canada
S. aureus (4,647)	1 (1,416)	1 (629)	1 (756)	1 (481)	1 (682)	1 (683)
P. aeruginosa (3,380)	2 (852)	2 (344)	2 (691)	2 (446)	2 (462)	2 (585)
Klebsiella spp. (1,358)	3 (370)	4 (120)	3 (298)	3 (162)	3 (186)	3 (222)
Enterobacter spp. (1,100)	4 (239)	3 (142)	4 (223)	4 (145)	4 (156)	4 (195)
E. coli (698)	6 (162)	6 (72)	6 (118)	6 (83)	6 (96)	6 (167)
Serratia spp. (656)	7 (151)	5 (81)	5 (134)	7 (75)	5 (105)	7 (110)
S. maltophilia (633)	5 (172)	7 (52)	7 (95)	8 (58)	7 (88)	5 (168)
Acinetobacter spp. (466)	8 (135)	8 (41)	8 (73)	5 (96)	8 (66)	8 (55)

Table 2. Regional variability among key pathogens causing nosocomial pneumonia from patients hospitalized in North America (1997 - 2004).

	Region (% susceptible/resistant)[a]					
Organism/antimicrobial agent	Northeast	Southeast	Midwest	South	West	Canada
Acinetobacter spp.						
Amp/Sul[c]	40.6/46.9	62.5/12.5	100.0/0.0	75.0/12.5	77.8/16.7	NT[b]
Ceftazidime	37.8/57.0	58.5/31.7	43.8/35.6	68.8/16.7	43.9/39.4	85.5/7.3
Cefepime	34.8/40.0	56.1/31.7	50.7/37.0	56.3/24.0	60.6/22.7	80.0/10.9
Imipenem	74.8/12.6	100.0/0.0	100.0/0.0	100.0/0.0	98.5/0.0	98.2/1.8
Meropenem	64.4/26.7	100.0/0.0	97.3/0.0	97.9/0.0	92.4/4.5	96.4/1.8
Amikacin	75.6/14.1	87.8/7.3	74.0/20.5	74.0/20.8	89.4/1.5	90.9/3.6
Tobramycin	70.4/26.7	80.5/12.2	49.3/43.9	74.0/19.8	83.3/16.7	85.5/10.9
Ciprofloxacin	31.1/66.0	65.9/22.0	38.4/61.6	65.6/30.2	39.4/60.6	87.3/9.1
Polymyxin B	98.6/1.4	94.7/5.3	100.0/0.0	100.0/0.0	100.0/0.0	100.0/0.0
P. aeruginosa						
Pip/Tazo[c]	83.8/16.2	89.5/10.5	86.4/13.6	87.7/12.3	88.3/11.7	89.6/10.4
Ceftazidime	77.7/16.4	82.6/12.5	77.6/15.9	75.6/17.7	80.1/14.5	80.2/12.8
Cefepime	78.6/7.5	81.4/7.0	77.0/8.4	80.3/8.3	82.3/7.6	82.1/7.5
Imipenem	83.6/9.3	86.9/7.3	82.8/10.1	85.7/7.0	85.3/8.7	83.8/8.7
Meropenem	86.6/7.2	92.2/4.7	86.1/7.7	88.3/6.7	89.6/5.8	89.6/6.0
Amikacin	95.7/2.0	91.9/3.5	95.9/3.0	93.0/2.0	93.7/3.5	92.3/5.0
Tobramycin	88.0/10.8	94.8/4.1	91.2/7.3	88.1/10.8	93.1/4.6	90.1/7.2
Ciprofloxacin	65.8/25.0	68.9/21.2	72.6/20.0	76.0/20.2	78.1/17.1	73.3/14.4
Polymyxin B	98.9/1.1	100.0/0.0	99.1/0.9	100.0/0.0	98.3/1.7	96.8/3.2
S. maltophilia						
Trim/Sulfa[c]	96.5/3.5	100.0/0.0	93.7/6.3	100.0/0.0	96.5/3.5	97.1/2.9
Tic/Clav[c]	57.6/13.4	55.8/13.4	53.7/24.2	51.7/17.3	54.5/9.1	63.7/15.5
Ceftazidime	48.3/37.8	51.9/34.6	45.3/44.2	51.7/37.9	44.3/42.0	60.1/32.1
Ciprofloxacin	28.5/43.6	23.1/44.2	20.0/56.9	22.4/39.7	22.7/52.3	17.3/50.7
Gatifloxacin	79.7/5.2	76.9/9.6	74.7/7.4	87.9/6.9	81.8/14.8	77.4/10.1
Levofloxacin	80.8/7.0	78.8/11.5	77.9/12.6	84.5/8.6	78.4/13.6	79.2/13.1
Polymyxin B	70.0/30.0	66.7/33.3	65.7/34.3	78.9/21.1	62.2/37.8	59.6/40.4
S. aureus						
Oxacillin	39.8/60.2	49.6/50.4	57.7/42.3	55.1/44.9	55.7/44.3	94.0/6.0
Erythromycin	26.6/71.6	36.6/59.8	41.1/52.9	43.7/51.9	41.6/54.3	69.8/16.8
Clindamycin	45.4/54.4	61.7/38.4	60.8/38.8	65.9/33.3	59.8/39.5	92.2/7.4
Gentamicin	87.3/12.1	85.1/14.9	88.5/11.0	85.0/14.1	83.4/16.2	95.0/4.6
Tetracycline	92.0/7.3	92.1/7.2	91.5/7.8	85.7/13.3	95.7/3.7	95.6/4.1
Ciprofloxacin	36.7/62.5	47.1/51.4	55.2/43.5	62.6/35.5	55.6/43.7	89.0/7.7
Trim/Sulfa[c]	90.5/9.5	92.1/7.9	92.6/7.4	90.2/9.8	93.4/6.6	98.4/1.6
Chloramphenicol	77.0/1.2	78.2/3.2	80.9/2.0	81.3/0.4	86.4/0.9	91.5/0.7
Quin/Dalfo[c]	99.7/0.0	100.0/0.0	99.9/0.0	100.0/0.0	99.3/0.0	99.7/0.0
Rifampin	95.1/3.5	97.5/1.7	97.5/2.4	93.1/4.8	94.9/4.5	98.5/1.0
Linezolid	100.0/0.0	100.0/0.0	100.0/0.0	100.0/0.0	100.0/0.0	100.0/0.0
Vancomycin	100.0/0.0	100.0/0.0	100.0/0.0	100.0/0.0	100.0/0.0	100.0/0.0

	Region (% susceptible/resistant)[a]					
Organism/antimicrobial agent	Northeast	Southeast	Midwest	South	West	Canada
E. coli						
Ampicillin	59.6/37.7	56.9/43.1	56.8/39.8	48.2/49.4	52.1/46.9	61.7/35.3
Ceftazidime	95.1/3.1	98.6/0.0	96.6/2.5	97.6/1.2	93.8/5.2	98.8/1.2
Cefepime	100.0/0.0	100.0/0.0	98.3/0.8	100.0/0.0	99.0/0.0	100.0/0.0
Imipenem	100.0/0.0	100.0/0.0	100.0/0.0	100.0/0.0	100.0/0.0	100.0/0.0
Pip/Tazo[c]	93.8/4.9	90.3/5.8	95.8/2.5	95.2/1.2	95.8/2.1	98.2/1.2
Ciprofloxacin	88.9/9.9	97.2/2.8	92.4/6.8	95.2/4.8	90.6/9.4	95.8/3.0
Gentamicin	90.7/7.4	100.0/0.0	91.5/6.8	98.8/1.2	89.6/8.3	97.0/2.4
Tetracycline	74.7/24.1	79.2/18.1	69.5/29.7	73.5/24.1	69.8/29.2	82.6/16.2
Trim/Sulfa[c]	83.3/16.7	80.3/19.7	83.1/16.9	78.0/22.0	79.1/20.9	88.0/12.0
Klebsiella spp.						
Ceftazidime	82.7/16.8	97.5/1.7	95.6/4.0	95.7/4.3	96.8/3.2	96.8/2.7
Cefepime	97.8/1.1	99.2/0.0	100.0/0.0	98.8/0.6	99.5/0.5	99.5/0.0
Imipenem	99.5/0.5	100.0/0.0	100.0/0.0	100.0/0.0	98.9/0.5	100.0/0.0
Pip/Tazo[c]	84.6/11.9	95.0/4.2	91.9/5.0	93.8/3.7	94.6/3.8	93.7/3.2
Ciprofloxacin	91.1/5.1	97.5/2.5	94.3/5.3	95.1/4.9	94.1/3.8	94.6/3.7
Gentamicin	82.4/16.2	96.7/1.6	96.0/3.3	94.4/3.1	95.2/3.2	97.7/1.8
Tetracycline	82.2/9.7	85.0/10.0	86.2/8.7	81.5/13.6	81.2/8.6	83.8/11.3
Trim/Sulfa[c]	78.7/21.3	98.3/1.7	93.7/6.3	90.7/9.3	93.5/6.5	93.3/6.7
Enterobacter spp.						
Ceftazidime	74.9/23.0	75.4/21.1	74.0/18.8	77.2/19.3	74.4/21.8	81.5/15.4
Cefepime	97.1/1.3	100.0/0.0	99.1/0.0	99.3/0.0	98.1/0.6	100.0/0.0
Imipenem	100.0/0.0	100.0/0.0	100.0/0.0	100.0/0.0	100.0/0.0	100.0/0.0
Pip/Tazo[c]	80.8/11.3	76.1/4.9	75.8/9.4	81.4/8.3	76.9/10.3	83.6/7.7
Ciprofloxacin	91.2/5.8	93.0/3.5	94.2/4.0	94.5/3.5	94.9/1.9	96.4/1.5
Gentamicin	85.8/13.4	97.2/2.1	95.1/2.7	86.9/10.3	95.5/3.1	98.5/1.5
Tetracycline	88.3/7.9	88.7/7.7	84.8/8.5	81.4/15.9	88.5/9.0	87.2/6.7
Trim/Sulfa[c]	85.3/14.7	97.2/2.8	95.1/4.9	90.3/9.7	93.5/6.5	96.4/3.6
Serratia spp.						
Ceftazidime	96.7/3.3	96.3/2.5	95.5/4.5	97.3/1.3	96.2/1.9	96.4/2.7
Cefepime	99.3/0.7	100.0/0.0	97.0/0.7	98.7/0.0	100.0/0.0	100.0/0.0
Imipenem	98.7/0.7	100.0/0.0	100.0/0.0	100.0/0.0	100.0/0.0	100.0/0.0
Pip/Tazo[c]	92.7/2.0	92.6/0.0	91.0/3.7	98.7/1.3	89.5/2.9	96.4/0.9
Ciprofloxacin	90.7/5.2	95.1/2.5	95.5/3.7	96.0/4.0	91.4/4.8	84.5/7.2
Gentamicin	95.4/2.7	91.4/7.4	97.8/1.5	97.3/2.7	97.1/1.9	95.5/4.5
Tetracycline	9.4/70.2	8.6/70.4	16.4/53.0	5.3/62.7	13.3/64.8	11.8/57.3
Trim/Sulfa[c]	96.0/4.0	96.3/3.7	96.2/3.8	94.7/5.3	90.5/9.5	93.6/6.4

a. Percent susceptible/resistant was based upon CLSI recommended breakpoints (M100-S15).
b. NT = not tested.
c. Trim/Sulfa = Trimethoprim/sulfamethoxazole, Tic/Clav = Ticarcillin/clavulanate, Pip/Tazo = Piperacillin/tazobactam, Quin/Dalfo = Quinupristin/dalfopristin, Amp/Sul = Ampicillin/sulbactam

Table 3. Regional variability of the phenotypic resistance rates to MLS_B antimicrobial agents among *S. aureus* in North America (1997 - 2004).

	Region (no. strains resistant to erythromycin)					
Percentage of strains resistant due to:	Northeast (1,013)	Southeast (376)	Midwest (400)	South (250)	West (370)	Canada (115)
Erythromycin-resistant/clindamycin-susceptible[a]	23.7	35.9	26.5	36.0	27.0	55.7
Erythromycin-resistant/clindamycin-resistant	76.3	64.1	73.5	64.0	73.0	44.3

a. Inducible resistance to clindamycin was not determined.

Table 4. Regional variation of the frequency of ESBL phenotypes among *E. coli* and *Klebsiella* spp. in North America (1997 - 2004).[a]

	Region (% ESBL phenotype)					
Organism/antimicrobial agent	Northeast	Southeast	Midwest	South	West	Canada
E. coli (no. tested)	(162)	(72)	(118)	(83)	(96)	(167)
Aztreonam	5.6	5.6	8.5	6.0	7.3	1.8
Ceftazidime	5.6	2.8	5.9	6.0	6.3	3.0
Ceftriaxone	5.6	5.6	5.9	2.4	7.3	0.6
Klebsiella spp. (no. tested)	(370)	(120)	(298)	(162)	(186)	(222)
Aztreonam	20.3[b]	5.8	8.7	5.6	7.0	8.1
Ceftazidime	21.1[b]	4.2	5.4	4.9	5.4	5.4
Ceftriaxone	19.2[b]	4.2	6.4	6.2	6.5	5.0

a. ESBL rates were based upon CLSI recommendations (M100-S15) with MIC values for all three antimicrobial agents (≥ 2 µg/ml).
b. Higher rate compared to other regions was due to a clonal outbreak in one hospital.

CONCLUSIONS

- *S. aureus* and seven Gram-negative enteric and non-enteric pathogens were among the most common causes of pneumonia in hospitalized patients, and all of these species are known to have intrinsic resistances, or can acquire resistance mechanisms including the ability to become multidrug-resistant.
- Overall, the bacterial pathogens isolated from Canada showed lower rates of resistance to the antimicrobial agents presented, particularly *Acinetobacter* spp. and *S. aureus*. Conversely, the isolates from the Northeast region of the United States were generally more resistant.
- The frequency of *E. coli* and *Klebsiella* spp. with an ESBL phenotype remained low in North America compared to other regions of the world. Elevated rates can be due to epidemic or endemic clones that can persist in the hospital environment for extended periods of time.
- Continued surveillance of bacterial species that cause nosocomial pneumonia or patients hospitalized with community-acquired RTI remains an important objective due to the significant morbidity and mortality related to this illness.

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