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Antimicrobial Susceptibility Patterns for Pathogens Isolated from Patients in Latin American Medical Centers with a Diagnosis of Pneumonia: Analysis from 5 Years of the SENTRY Antimicrobial Surveillance Program

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ABSTRACT

Background: Pneumonia is the most common fatal hospital-acquired infection and rapid initiation of optimal antimicrobial therapy is essential for obtaining treatment success. The results from the SENTRY Program 5-year experience were analyzed for the best agents.
Methods: A total of 3,346 strains from the lower respiratory tract of patients with pneumonia in 14 Latin American centers (7 nations) were susceptibility (S) tested by NCCLS reference broth microdilution methods.
Results: The five most frequently isolated pathogens were (n/%): *P. aeruginosa* (PSA - 862/25.8%), *S. aureus* (SA - 760/22.7%), *Klebsiella* spp. (KSP - 328/9.8%), *Acinetobacter* spp. (Acb - 298/8.9%), and *Enterobacter* spp. (165/4.9%). Amikacin, carbapenems, and piperacillin/tazobactam demonstrated the highest S rates (68.7 – 65.5%) against PSA. All other compounds inhibited less than 60% of isolates at NCCLS breakpoints. *S. aureus* showed 54.6% resistance to oxacillin and 100% S to vancomycin and linezolid. More than 40% of KSP and more than 20% of *E. coli* showed an ESBL-phenotype. Resistance (R) rates to quinolones, aminoglycosides, and cefoxitin were high among ESBL-producing strains. Only the carbapenems demonstrated reasonable activity against Acb (84.2-85.2% S). *Enterobacter* spp. showed high rates of R to third-generation cephalosporins, broad spectrum penicillins and monobactams (52.7-64.8% S); however, cefepime (90.3% S) and the carbapenems (>99% S) remain very active against this pathogen.
Conclusions: LA SENTRY results demonstrated a higher prevalence of Acb and higher R rates among Gram-negative bacilli when compared with similar controlled studies from North America, the Western Pacific region and Europe. The increasing R rates to carbapenems among PSA and Acb in the region is of great concern.

INTRODUCTION

Pneumonia is the most common fatal hospital-acquired infection, with attributable mortality rates ranging from 27% to as high as 60%. In the intensive care unit, pneumonia is the most frequent nosocomial infection in European medical centers, and the second most common nosocomial infection in the United States.

There has been a rapid increase in antimicrobial resistance among bacteria from both community- and nosocomial acquired infections, and resistance rates are markedly higher among isolates causing nosocomial pneumonia. Furthermore, rapid initiation of optimal antimicrobial therapy is essential for obtaining treatment success.

We report the antimicrobial susceptibilities of isolates collected from the lower respiratory tract in patients hospitalized with pneumonia in Latin American medical centers during the monitored period of 1997-2001, as part of SENTRY Antimicrobial Surveillance Program.

MATERIAL & METHODS

Bacterial strains. The bacterial strains were isolated from respiratory tract specimens of hospitalized patients with pneumonia (only one isolate per patient). Clinical specimens included only bronchoalveolar lavage, tracheal aspirate, and high-quality sputum samples. Ten Latin American centers participated in the study each year, and the majority of them were represented by tertiary-care hospitals. The participants were distributed throughout seven countries including Argentina (Buenos Aires and San Isidro), Brazil (São Paulo, Florianopolis, Rio de Janeiro [only 1997 and 1998], Porto Alegre [1999-2001], and Brasilia [2001], Chile (two sites in Santiago), Uruguay (Montevideo, only 1997), Colombia (Medellin, 1997-2000), Venezuela (Caracas, 1998-2001), and Mexico (Mexico City). Each participant laboratory contributed approximately 50 strains each year, consecutively collected in the respiratory disease season from July to December.

Susceptibility testing. The isolates were identified to the species level by the participant center and sent to the monitoring laboratory for identification confirmation and reference susceptibility testing. Antimicrobial susceptibility testing was performed and results interpreted using the broth microdilution method as described by the National Committee for Clinical Laboratory Standards (NCCLS). *Klebsiella pneumoniae* and *Escherichia coli* isolates with increased MIC values (≥ 2 μg/mL) for ceftazidime or ceftriaxone or aztreonam were considered as extended-spectrum ß-lactamase (ESBL)-producing phenotypes. Quality control was performed by testing *E. coli* ATCC 25922, *Staphylococcus aureus* ATCC 29213, *Pseudomonas aeruginosa* ATCC 27853, *Enterococcus faecalis* ATCC 29212, *Haemophilus influenzae* ATCC 49247 and *Streptococcus pneumoniae* ATCC 49619.

Table 1. Occurrence of the ten major pathogens isolated from patients hospitalized with lower respiratory tract infections in Latin American medical centers (SENTRY Program Latin America, 1997-2001).

		No. of isolates tested by country (%)							
Organism in rank order	Argentina	Brazil	Chile	Colombia	Mexico	Uruguay	Venezuela	Total
1. *Pseudomonas aeruginosa*	203	473	73	34	37	8	34	862 (25.8)
2. *Staphylococcus aureus*	179	346	184	15	10	15	11	760 (22.7)
3. *Klebsiella pneumoniae*	101	124	38	29	3	4	29	328 (9.8)
4. *Acinetobacter* spp.	88	139	26	10	4	13	19	299 (8.9)
5. *Enterobacter* spp.	25	76	21	11	6	1	25	165 (4.9)
6. *Streptococcus pneumoniae*	45	22	83	6	-	1	1	158 (4.7)
7. *Haemophilus influenzae*	35	7	98	2	-	1	-	143 (4.3)
8. *Escherichia coli*	31	46	17	7	9	2	16	128 (3.8)
9. *Serratia* spp.	18	40	10	6	2	3	10	89 (2.7)
10. *S. maltophilia*	17	23	3	3	4	-	10	60 (1.8)
Total	822	1435	602	143	112	52	180	3346 (100.0)
	(24.6)	(42.9)	(18.0)	(4.3)	(3.3)	(1.6)	(5.4)	

RESULTS

- *P. aeruginosa* (25.8%) was the most frequently isolated pathogen overall, followed by *S. aureus* (22.7%) > *K. pneumoniae* (9.8%) > *Acinetobacter* spp. (8.9%). These four pathogens accounted for almost 70% of the isolates and they were also the most frequently isolated pathogens in Argentina, Brazil and Uruguay. However, medical centers in Chile reported higher numbers of *H. influenzae* (16.3% of their isolates) and *S. pneumoniae* (13.8%), probably of community origin (Table 1).
- Amikacin (MIC_{50}, 8 μg/mL; 68.7% susceptibility [S]), meropenem (MIC_{50}, 1 μg/mL; 67.1% S) and piperacillin/tazobactam (MIC_{50}, 16 μg/mL; 67.1% S) were the most active compounds against *P. aeruginosa*; and the cephalosporins cefepime and ceftazidime presented very similar in vitro activity (MIC_{50}, 8 μg/mL; 58.5-58.7% S; Table 2).
- Only the carbapenems, imipenem (MIC_{50}, 1 μg/mL; 85.2% S) and meropenem, (MIC_{50}, 2 μg/mL; 84.2% S) showed reasonable activity against *Acinetobacter* spp. (Table 2).
- The prevalence of ESBL-producing strains was extremely high among *K. pneumoniae* (41.8%) and *E. coli* (23.6%). The carbapenems were highly active against these pathogens (>99% S) (Table 2).
- Fluoroquinolone resistance rates were high among *Enterobacteriaceae*, especially in *E. coli* (78.1% S to ciprofloxacin). The three commercially available fluoroquinolones tested (ciprofloxacin, gatifloxacin, and levofloxacin) showed very similar activity against the Gram-negative bacilli evaluated (Table 2).
- Cefepime was active against 90.3% of *Enterobacter* spp. strains (MIC_{90}, 8 μg/mL); however, resistance rates to "third-generation" cephalosporins (63.0% S to ceftazidime), piperacillin/tazobactam (64.8% S) and aztreonam (62.4% S) were high among this important pathogen.
- More than a half of *S. aureus* strains were resistant to oxacillin (and all other ß-lactams), clindamycin, erythromycin, gentamicin, ciprofloxacin and levofloxacin. On the other hand, gatifloxacin (MIC_{50}, 1 μg/mL) and the novel des-F(6)-quinolone garenoxacin (MIC_{50}, 0.06 μg/mL), were active against 85.7% and 95.4% of isolates, respectively (Table 3).
- Among *S. pneumoniae*, 72.2% of isolates were considered susceptible (MIC, ≤0.06 μg/mL) and 15.8% were considered resistant (MIC, ≥2 μg/mL) to penicillin (Table 3).
- Cefepime (MIC_{90}, 1 μg/mL) and amoxicillin/clavulanate (MIC_{90}, ≤2 μg/mL) were active against 98.7% of *S. pneumoniae* isolates at the NCCLS susceptible breakpoints, while the quinolones gatifloxacin (MIC_{90}, 0.5 μg/mL), levofloxacin (MIC_{90}, 1 μg/mL) and garenoxacin (MIC_{90}, 0.06 μg/mL) showed complete (100.0%) activity against this pathogen (Table 3).

Table 2. Antimicrobial activity and spectrum of drugs tested against the five most prevalent gram-negative pathogens isolated from patients hospitalized with pneumonia in Latin American hospitals (SENTRY Program Surveillance – Latin America, 1997-2001).

	Pathogen (prevalence rank/ nº tested)									
	P. aeruginosa (1/862)		*Klebsiella* spp. (2/328)		*Acinetobacter* spp. (3/298)		*Enterobacter* spp. (4/165)		*E. coli* (8/128)	
Antimicrobial class/agent	$MIC_{50/90}$	% Susc.[a]	$MIC_{50/90}$	% Susc.[a]	$MIC_{50/90}$	% Susc.[a]	$MIC_{50/90}$	% Susc.[a]	$MIC_{50/90}$	% Susc.[a]
Cephalosporins										
Cefazolin	>16/>16	-	4/>16	54.6	>16/>16	-	>16/>16	6.1	4/>16	56.3
Cefuroxime	>16/>16	-	4/>16	55.2	>16/>16	-	>16/>16	40.6	4/>16	68.0
Cefoxitin	>32/>32	-	2/16	84.9	>32/>32	-	>32/>32	6.5	4/16	85.7
Ceftriaxone	>32/>32	8.7	≤0.25/>32	62.9 (41.8)[b]	>32/>32	9.1	≤0.25/>32	61.2	≤0.25/>32	78.9 (21.1)[b]
Ceftazidime	8/>16	58.7	≤2/>16	67.4 (39.3)[b]	>16/>16	17.8	≤ 2/>16	63.0	0.5/16	89.1(21.9)[b]
Cefepime	8/>16	58.5	≤0.12/>16	77.4	>16/>16	25.8	≤0.12/8	90.3	≤0.12/>16	85.9
Other ß-lactams										
Ampicillin	>16/>16	-	>16/>16	1.5	>16/>16	-	>16/>16	6.7	>16/>16	28.9
Aztreonam	16/>16	42.1	≤0.12/>16	63.4 (40.2)[b]	>16/>16	4.4	0.25/>16	62.4	≤0.12/>16	78.7(23.6)[b]
Ticarcillin/Clavulanate	64/>128	52.8	8/>128	56.7	>128/>128	13.4	16/>128	52.7	32/>128	48.4
Piperacillin/Tazobactam	16/>64	67.1	4/>64	72.3	>64/>64	16.4	4/>64	64.8	2/>64	77.3
Imipenem	2/>8	65.5	0.25/0.5	99.7	1/>8	85.2	0.5/2	99.4	0.12/0.5	99.2
Meropenem	1/>8	68.3	≤0.06/0.12	99.4	2/>8	84.2	≤0.06/0.12	99.4	≤0.06/≤0.06	100.0
Aminoglycosides										
Amikacin	8/>32	68.7	2/32	85.7	>32/>32	22.8	2/32	86.7	2/16	92.2
Gentamicin	4/>16	56.3	≤1/16	71.6	>8/>16	23.2	≤1/>8	79.4	1/>16	77.3
Tobramycin	1/>16	57.7	1/>16	60.6	16/>16	32.8	1/>16	68.3	1/>16	72.0
Fluoroquinolones										
Ciprofloxacin	0.5/>2	55.7	≤0.25/>2	87.5	>2/>2	18.5	≤0.25/>2	81.2	≤0.25/>2	78.1
Levofloxacin	2/>4	54.4	0.25/4	88.4	>4/>4	23.8	≤0.5/>4	83.0	≤0.5/>4	78.1
Gatifloxacin	2/>4	50.9	0.06/2	89.9	>4/>4	25.1	0.06/4	83.6	≤0.03/>4	78.9
Garenoxacin	>4/>4	40.7	0.12/>4	88.5	>4/>4	24.5	0.12/>4	78.5	0.06/>4	73.2
Others										
Tetracycline	>8/>8	1.5	≤4/>8	71.6	8/>8	46.3	≤4/>8	73.3	≤4/>8	54.7
Trimethoprim/Sulfamethoxazole	>1/>2	5.2	≤0.5/>1	76.1	>1/>2	23.5	≤0.5/>1	77.9	≤0.5/>2	58.3

a. Interpreted by NCCLS 2003 criteria,
b. % of strain with MIC ≥ 2 μg/mL indicating possible ESBL production.

Table 3. Antimicrobial activity and susceptibilities of drugs tested against the most prevalent Gram-positive pathogens isolated from hospitalized patients with pneumonia (SENTRY Program – Latin America, 1997 - 2001.

	Pathogen (prevalence rank/ nº tested)			
	S. aureus (2/760)		*S. pneumoniae* (6/158)	
Antimicrobial class/agent	$MIC_{50/90}$	% Susc.	$MIC_{50/90}$	% Susc.
Cephalosporins				
Cefazolin	>16/>16	45.4 [a]	--	--
Ceftriaxone	>32/>32	45.4 [a]	0.25/1	94.9
Cefepime	>16/>16	45.4 [a]	0.12/1	98.7
Ceftazidime	>16/>16	37.0	--	--
Other ß-lactams				
Oxacillin	>8/>8	45.4	--	--
Ampicillin	>16/>16	5.0	--	--
Penicillin	32/>32	5.7	0.01/2	72.2 (15.8)[b]
Amoxicillin/Clavulanate	16/>16	45.4 [a]	≤2/≤2	98.7
Piperacillin/Tazobactam	4/>64	45.4 [a]	--	--
Imipenem	8/>8	45.4 [a]	0.06/0.25	83.8
MLS				
Clindamycin	>8/>8	46.3	0.06/0.06	94.9
Erythromycin	>8/>8	37.4	0.06/1	89.2
Quinnupristin/Dalfopristin	0.5/0.5	100.0	0.5/0.5	100.0

	Pathogen (prevalence rank/ nº tested)			
	S. aureus (2/760)		*S. pneumoniae* (6/158)	
Antimicrobial class/agent	$MIC_{50/90}$	% Susc.	$MIC_{50/90}$	% Susc.
Fluoroquinilones				
Ciprofloxacin	>2/>2	45.9	--	--
Levofloxacin	2/>4	48.4	1/1	100.0
Gatifloxacin	1/4	85.7	0.25/0.5	100.0
Garenoxacin	0.06/2	95.4	0.06/0.06	100.0
Others				
Gentamicin	>8/>16	45.8	--	--
Rifampin	≤0.25/>2	66.3	0.25/0.25	95.8
Chloramphenicol	8/>16	54.5	2/4	95.6
Tetracycline	≤4/>8	61.6	≤4/>8	84.2
Doxycycline	≤0.5/>4	75.7	--	--
Trimethoprim/Sulfametoxazole	---	64.8	≤0.5/>2	63.7
Vancomycin	1/1	100.0	0.25/0.5	100.0
Teicoplanin	1/2	99.9	--	--
Linezolid	2/2	100.0	1/1	100.0

a. Susceptibility is predicted by the oxacillin result.
b. Percentage of resistant isolates (MIC ≥2 μg/mL) in parenthesis

CONCLUSIONS

- Multi-drug resistant pathogens, including *P. aeruginosa* and *Acinetobacter* spp. resistant to most commercially available antimicrobials, oxacillin-resistant *S. aureus*, and ESBL-producing *K. pneumoniae* and *E. coli*, accounted for approximately 40% of the isolates examined from patients with pneumonia.
- Not one of the compounds evaluated showed excellent coverage against the Gram-negative bacilli. The carbapenems, meropenem and imipenem, were very active against *Enterobacteriaceae*; however, high emerging rates of resistance to these compounds were detected among *P. aeruginosa* and *Acinetobacter* spp.
- No resistance to vancomycin, quinupristin/dalfopristin or linezolid was detected among *S. aureus* or *S. pneumoniae*.
- In summary, resistance rates were extremely high among isolates from patients hospitalized with pneumonia in the Latin American medical centers participating in the SENTRY Program. Continued surveillance through longitudinal programs remains necessary to develop therapeutic and infection control strategies for these patients.

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