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Frequency of Occurrence and Antimicrobial Susceptibility of Bacterial Pathogens from Intensive Care Units in Latin American Medical Centers: Report from the SENTRY Antimicrobial Surveillance Program (2001)

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ABSTRACT

Objectives: Resistance rates are usually higher in intensive care units (ICUs) due to a more focused antimicrobial selective pressure. This study assesses the antimicrobial susceptibility of bacterial isolates collected in ICUs from Latin American (LA) countries.

Methods: The isolates were collected in 10 medical centers (4 countries) as part of the SENTRY Antimicrobial Surveillance Program. Beginning in January 2001, each participant center collected 50 consecutive and clinically relevant bacterial isolates from patients hospitalized in the ICU. The isolates were tested by reference broth microdilution methods (NCCLS) against a large number of antimicrobial agents.

Results: A total of 470 isolates were evaluated. The 10 most frequently isolated species were (n(%)): *S. aureus* (SA – 102/21.7%), *P. aeruginosa* (PSA – 85/18.1%), *E. coli* (55/11.7%), *Klebsiella* spp. (43/9.1%), *Acinetobacter* spp. (ACB - 39/8.3%), *Enterobacter* spp. (38/8.1%), *Enterococcus* spp. (29/6.2%), coagulase-negative staphylococci (CoNS – 16/3.4%), *Serratia* spp. (16/3.4%), and *S. maltophilia* (13/2.8%). Resistance to oxacillin was detected in 54.9% of SA. Carbapenem resistance was detected in 42.4% of PSA and 28.2% of ACB. Polymyxin B (98.8% susceptibility [S]), piperacillin/tazobactam (64.7% S) and amikacin (63.5% S) were the most active compounds against PSA. Polymyxin B resistance (MIC \geq 4 mg/L) was also detected among ACB (97.4% S). ESBL-producing phenotypes occurred in 12.7% of *E. coli* and 54.5% of *Klebsiella* spp. and 36.8% of *Enterobacter* spp. showed resistance to third-generation cephalosporins (Amp C hyperproduction). Only 82.8% of enterococci were vancomycin-S.

Conclusions: Resistance rates were extremely high among isolates from ICU patients in Latin American (LA) hospitals, especially among Gram-negative bacilli. The most alarming problems detected were imipenem and meropenem resistance among PSA and ACB, and ESBL mediated beta-lactam resistance and/or chromosomally-based beta-lactamase (Amp C) among Enterobacteriaceae. Vancomycin resistance has clearly emerged among enterococci as a serious ICU problem in the LA region.

Table 1. Occurrence of the ten major pathogens isolated in ICU, SENTRY Program Latin America, 2001 (470 strains).

Organisms in rank order	No. of isolates tested by country (%)				
	Argentina	Brazil	Chile	Venezuela	Total
1. <i>Staphylococcus aureus</i>	21 (21.6)	42 (18.3)	38 (34.2)	1 (3.0)	102 (21.7)
2. <i>Pseudomonas aeruginosa</i>	14 (14.4)	47 (20.5)	19 (17.1)	5 (15.2)	85 (18.1)
3. <i>Escherichia coli</i>	11 (11.3)	26 (11.4)	14 (12.6)	4 (12.1)	55 (11.7)
4. <i>Klebsiella pneumoniae</i>	11 (11.3)	25 (10.9)	6 (5.4)	1 (3.0)	43 (9.1)
5. <i>Acinetobacter</i> spp.	7 (7.2)	21 (9.2)	3 (2.7)	8 (24.2)	39 (8.3)
6. <i>Enterobacter</i> spp.	4 (4.1)	21 (9.2)	8 (7.2)	5 (15.2)	38 (8.1)
7. <i>Enterococcus</i> spp.	6 (6.2)	17 (7.4)	3 (2.7)	3 (9.1)	29 (6.2)
8. Coagulase-negative staphylococci	2 (2.1)	13 (5.7)	0 (0.0)	1 (3.0)	16 (3.4)
9. <i>Serratia</i> spp.	4 (4.1)	8 (3.5)	4 (3.6)	0 (0.0)	16 (3.4)
10. <i>Stenotrophomonas maltophilia</i>	5 (5.2)	3 (1.3)	3 (2.7)	2 (6.0)	13 (2.8)
Total	97 (20.6)	229 (48.7)	111 (23.6)	33 (7.0)	470 (100.0)

Table 2. Distribution of isolates according to the site of infection.

Site of infection	Number of isolates	Percentage
Respiratory tract ^a	173	36.8
Blood stream	85	18.1
Urine	72	15.3
Wound, skin and soft tissue	49	10.4
Catheter	23	4.9
Intra-abdominal	17	3.6
Others	51	10.9

a. Include specimens collected through bronchoscopy or other invasive procedure (78), sputum (70), tracheal aspirate (17), and pleural fluid (8).

INTRODUCTION

Antimicrobial use will always be an important component of medical practice in the intensive care unit. Prevalence of infections among patients in these units is usually higher as compared to patients in general hospital wards. In addition, the great majority of infections in ICU patients are of nosocomial origin and antimicrobial resistance rates are usually higher due to a more focused antimicrobial selective pressures.

MATERIALS AND METHODS

The microbial isolates were collected in 10 medical centers from 5 Latin American countries (Argentina [2 centers], Brazil [4 centers], Chile [2 centers], Mexico [1 center], and Venezuela [1 center]) as a study objective of the SENTRY Antimicrobial Surveillance Program. Beginning in January 2001, each participating center collected 50 consecutive and clinically relevant bacterial isolates from patients hospitalized in ICUs. Isolates from Mexico were excluded from the analysis due to extremely low number contributed.

The isolates were identified at the participating institutions by the routine methodology in use at each laboratory and forwarded to the monitoring center (The JONES Group / JMI Laboratories, North Liberty, IA, USA). Each strain was tested by the reference broth microdilution method against more than 30 antimicrobial agents; however, only agents with the greatest in vitro activity are reported here. Interpretation of quantitative MIC results was determined using NCCLS (2003) criteria.

Table 3. Antimicrobial activity and susceptibilities for drugs when tested against the three most common Gram-positive pathogens from ICU patients (SENTRY Program Latin America, 2001).

Antimicrobial class/agent	Pathogen (prevalence rank/no. tested)					
	<i>S. aureus</i> (1/102)		<i>Enterococcus</i> spp. (7/29)		CoNS (8/16)	
	MIC _{50/90}	% susc. ^a	MIC _{50/90}	% susc. ^a	MIC _{50/90}	% susc. ^a
Cephalosporins						
Ceftriaxone	>32/>32	45.1	>32/>32	0.0	16/>32	12.5
Cefepime	>16/>16	45.1	>16/>16	0.0	16/>16	12.5
Ceftazidime	>16/>16	45.1	>16/>16	0.0	>16/>16	12.5
Other β-Lactams						
Penicillin	32/>32	5.9	4/32	69.0	16/>32	0.0
Ampicillin	-	-	\leq 2/16	86.2	-	-
Amoxicillin/clavulanic acid	>16/>16	45.1	-	-	\leq 2/>16	12.5
Oxacillin	>8/>8	45.1	>8/>8	0.0	>8/>8	12.5
Piperacillin/Tazobactam	2/>64	45.1	16/>64	86.2	4/>64	12.5
Imipenem	>8/>8	45.1	4/>8	69.0	2/>8	12.5
MLS						
Clindamycin	0.12/>8	50.0	>8/>8	-	>8/>8	18.8
Erythromycin	>8/>8	43.1	>8/>8	3.4	>8/>8	6.3
Rifampin	>2/>2	73.5	>2/>2	13.8	>2/>2	43.8
Fluoroquinolones						
Ciprofloxacin	>2/>2	47.1	2/>2	48.3	>2/>2	25.0
Gatifloxacin	1/4	88.2	1/>4	55.2	2/2	100.0
Levofloxacin	2/>4	52.0	2/>4	51.7	>4/>4	37.5
Garenoxacin	0.5/1	-	2/4	-	1/2	-
Others						
Chloramphenicol	>16/>16	58.8	8/>16	55.2	>16/>16	43.8
Gentamicin	>8/>8	43.1	\leq 500/>1000	58.6 ^b	>8/>8	25.0
Doxycycline	\leq 0.5/>4	75.5	>4/>4	27.4	1/>4	87.5
Tetracycline	>8/>8	66.7	>8/>8	24.1	\leq 4/>8	81.3
Trimethoprim/Sulfamethoxazole	\leq 0.5/>2	65.7	\leq 0.5/>1	-	>2/>2	31.3
Quinupristin/dalfopristin	0.25/0.5	100.0	8/>8	6.9	0.25/1	93.8
Linezolid	2/2	100.0	2/2	100.0	1/2	100.0
Teicoplanin	1/2	100.0	0.25/>16	86.2	2/16	87.5
Vancomycin	1/1	100.0	1/>16	82.8	1/2	100.0

a. Categories of susceptibility interpreted by NCCLS criteria (2003).
b. Percent susceptible using high range dilutions (\leq 500 mg/L) for high-level aminoglycoside resistance.

RESULTS

Brazil contributed almost one-half of all strains (48.7%), followed by Chile (23.6%), Argentina (20.6%), and Venezuela (7.0%). The six most frequently isolated pathogens were *S. aureus* (21.7%), *P. aeruginosa* (18.1%), *E. coli* (11.7%), *K. pneumoniae* (9.1%), *Acinetobacter* spp. (8.3%), and *Enterobacter* spp. (8.1%). This rank order was similar for the three major countries participating in the SENTRY Program-Latin America (Argentina, Brazil and Chile; see *Table 1*).

The most frequent site of infection was the lower respiratory tract (36.8%), followed by the bloodstream (18.1%), urinary tract (15.3%) and wound, skin and soft tissue (10.4%; see *Table 2*).

More than a half of *S. aureus* strains (54.9%) were resistant to oxacillin and all other β -lactams. In addition, the vast majority of oxacillin-resistant *S. aureus* showed cross resistance to fluoroquinolones, clindamycin, erythromycin, and gentamicin. Gatifloxacin (MIC₅₀, 4 mg/L) was active against 88.2% of *S. aureus* isolates, and the novel des-F(6)-quinolone garenoxacin inhibited 98.0% of strains at the proposed breakpoint of \leq 2 mg/L.

Vancomycin resistance was detected in 17.8% of enterococcal isolates, while teicoplanin resistance was only found in 13.8% of enterococci. A total of 12.5% of coagulase-negative staphylococci were also resistant to teicoplanin. No resistance to linezolid was observed among the Gram-positive cocci isolated from the ICU patient cultures evaluated in this study (*Table 3*).

Resistance rates were generally very high among Gram-negative bacilli, especially for the non-fermentative species, *P. aeruginosa* and *Acinetobacter* spp. Only polymyxin B showed reasonable in vitro activity against these two important ICU pathogens (98.8% susceptibility for *P. aeruginosa* and 97.4% susceptibility for *Acinetobacter* spp.). Among the other compounds tested, piperacillin/tazobactam (MIC₅₀, 64 mg/L; 64.7% susceptible) and amikacin (MIC₅₀, 8 mg/L; 63.5%) were the most active drugs against *P. aeruginosa* isolates, and the carbapenems imipenem (MIC₅₀, 1 mg/L) and meropenem (MIC₅₀, 2 mg/L), both with 71.8% susceptibility, were the most active agents tested against *Acinetobacter* spp. (*Table 4*).

Isolates showing an ESBL-producing phenotype were detected among 10.9-12.7% of *E. coli* and 51.2-53.5% of *K. pneumoniae*. Resistance rates to fluoroquinolones and aminoglycosides were significantly high among Enterobacteriaceae, and 26.3% of *Enterobacter* spp. showed resistance to polymyxin B (*Table 4*).

Table 4. Antimicrobial activity and susceptibilities for drugs tested against the five most prevalent Gram-negative pathogens causing infections in ICU patients (SENTRY Program Latin America, 2001).

Antimicrobial class/agent	Pathogen (prevalence rank/no. tested)									
	<i>P. aeruginosa</i> (2/85)		<i>E. coli</i> (3/55)		<i>K. pneumoniae</i> (4/43)		<i>Acinetobacter</i> spp. (5/39)		<i>Enterobacter</i> spp. (6/38)	
	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	0.0	\leq 2/>16	78.2	>16/>16	39.5	>16/>16	0.0	>16/>16	5.3
Cefuroxime	>16/>16	0.0	8/16	83.6	>16/>16	44.2	>16/>16	2.6	>16/>16	39.5
Cefoxitin	>32/>32	0.0	0.12/2	89.1	4/32	76.7	>32/>32	0.0	>32/>32	0.0
Ceftriaxone	>32/>32	5.9	4/16	90.9 (10.9) ^b	2/32	53.5 (61.2) ^b	>32/>32	5.1	1/32	63.2
Ceftazidime	8/>16	52.9	0.25/8	92.7 (12.7) ^b	8/>16	55.8 (63.5) ^b	>16/>16	17.9	\leq 2/>16	63.2
Cefepime	8/>16	50.6	\leq 2/8	92.7	0.5/>16	60.5	>16/>16	25.9	0.25/>16	86.8
Other β-Lactams										
Ampicillin	>16/>16	0.0	>16/>16	36.4	>16/>16	0.0	>16/>16	0.0	>16/>16	0.0
Aztreonam	16/>16	36.5	0.12/>16	89.1 (10.9) ^b	16/>16	48.8 (61.2) ^b	>16/>16	0.0	0.5/>16	60.5
Piperacillin/Tazobactam	64/>64	64.7	1/16	90.9	4/>64	69.8	>64/>64	17.9	4/>64	63.2
Imipenem	2/>8	58.8	0.12/0.12	100.0	0.12/0.5	100.0	1/8	71.8	0.25/1	100.0
Meropenem	2/>8	57.6	0.06/0.06	100.0	0.06/0.25	95.3	2/>8	71.8	0.06/0.12	100.0
Aminoglycosides										
Amikacin	8/>32	63.5	2/4	100.0	8/>32	72.1	>32/>32	23.1	2/32	84.2
Gentamicin	>8/>8	45.9	\leq 1/>8	83.6	4/>8	51.2	>8/>8	17.9	\leq 1/>8	63.2
Tobramycin	>16/>16	45.9	1/16	85.5	16/>16	46.5	16/>16	35.9	0.5/>16	55.3
Fluoroquinolones										
Ciprofloxacin	1/>2	50.6	0.015/>2	83.6	0.03/>2	72.1	>2/>2	15.4	0.03/>2	86.8
Levofloxacin	2/>4	50.6	0.03/>4	83.6	0.06/>4	72.1	>4/>4	15.4	0.03/>4	84.2
Gatifloxacin	4/>4	48.2	0.03/>4	83.6	0.06/>4	72.1	>4/>4	17.9	0.03/>4	86.8
Garenoxacin	>4/>4	-	0.03/>4	-	0.12/>4	-	>4/>4	-	0.12/>4	-
Others										
Tetracycline	>8/>8	0.0	\leq 4/>8	56.4	\leq 4/>8	58.1	>8/>8	28.2	\leq 4/>8	73.7
Trimethoprim/Sulfamethoxazole	>2/>2	0.0	>2/>2	15.5	\leq 0.5/>2	55.8	\leq 0.5/>2	17.9	\leq 0.5/>2	68.4
Polymyxin B	\leq 1/2	98.8	\leq 1/2	100.0	\leq 1/2	90.7	\leq 1/2	97.4	\leq 1/>8	73.7

a. Categories of susceptibility interpreted by NCCLS criteria.
b. Percentage in parenthesis indicates the strains having an ESBL phenotype by NCCLS criteria for the three tested substrates (MICs, \geq 2 mg/L).

CONCLUSIONS

S. aureus (21.7%) and *P. aeruginosa* (18.1%) were the most frequently isolated pathogens.

Only linezolid was active against 100% of the Gram-positive isolates. Vancomycin was the second most active compound, but resistance (17.2%) to this glycopeptide was detected among enterococci.

Not one of the compounds evaluated showed excellent coverage against the Gram-negative bacilli. Polymyxin B was the most widely active agent for the non-fermenters; however, resistance to this compound was common among some Enterobacteriaceae, such as *Enterobacter* spp. (73.7% susceptible), *Serratia* spp. (0.0%) and *Proteus* spp. (0.0%).

The carbapenems (meropenem > imipenem) were very active against Enterobacteriaceae, but relatively high rates of resistance to these compounds was detected among *P. aeruginosa* (57.6-58.8% susceptible) and *Acinetobacter* spp. (71.8%).

High prevalences of ESBL-producing strains were detected among both *K. pneumoniae* (51.2-53.5%) and *E. coli* (10.9-12.7%).

In summary, resistance rates were extremely high among ICU patient isolates, from the ICUs evaluated by the SENTRY Program in Latin America. Continued surveillance through longitudinal programs remains necessary to allow the development of therapeutic and infection control strategies for patients hospitalized in the ICU.