

Frequency and Antimicrobial Susceptibility of Bacterial Pathogens Isolated from Bloodstream Infections in Hematology-Oncology Patients: Results from the Latin America SENTRY Antimicrobial Surveillance Program (1997-2002)

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ABSTRACT

Objective: To determine the frequency and susceptibility patterns of bacterial pathogens isolated from bloodstream infections (BSI) of hematology-oncology patients hospitalized at Latin American medical centers.
Material and Methods: As part of the SENTRY Antimicrobial Surveillance Program, a total of 1,587 BSI isolates were recovered from hematology-oncology patients from 1997 to 2002. The isolates were susceptibility tested to >20 antimicrobial agents in a central laboratory using NCCLS broth microdilution method.
Results: The most frequently isolated pathogen was coagulase-negative staphylococci (CoNS; 17.7%), followed by *Escherichia coli* (17.5%), *Staphylococcus aureus* (15.8%), *Klebsiella pneumoniae* (10.3%), *Pseudomonas aeruginosa* (8.9%), *Enterobacter* spp. (6.7%), *Acinetobacter* spp. (4.5%), and *Enterococcus* spp. (3.1%). Oxacillin-resistance rates were 33.9% and 74.4% among *S. aureus* and CoNS, respectively. The prevalence of ESBL-producing strains ranged from 9.4% for *E. coli* to 41.1% for *K. pneumoniae*. For *Enterobacter* spp., susceptibility rates were 54.7% and 86.9% to ceftazidime and cefepime, respectively. All *Enterobacteriaceae* isolates tested were susceptible to carbapenems. The susceptibility of *P. aeruginosa* to imipenem and meropenem was 83.7% and 86.5%, respectively. 82.2% and 92.8% of the Gram-negative bacilli were susceptible to cefepime and meropenem, respectively. Only 4.1% of the *Enterococcus* spp. isolates were resistant to vancomycin.
Conclusions: In contrast to American and European reports, Gram-negative bacilli represented the major cause of BSI among hematology-oncology patients in the Latin American hospitals evaluated. The antimicrobial agents with the best coverage against such pathogens were the carbapenems and cefepime. However, none of the evaluated antimicrobial agents inhibited the growth of 100.0% of the Gram-negative bacilli. Thus, continued monitoring by surveillance programs is necessary to determine if the observed trends would continue to be recorded.

MATERIAL AND METHODS (Cont.)

Staphylococcus aureus ATCC 29213, *Pseudomonas aeruginosa* ATCC 27853, *Enterococcus faecalis* ATCC 29212, *Haemophilus influenzae* ATCC 49247 and 49766, and *Streptococcus pneumoniae* ATCC 49619.
Isolates of *E. coli* and *Klebsiella pneumoniae* with increased MIC (≥ 2 mg/L) for ceftazidime and/or ceftriaxone and/or aztreonam were considered as possible extended-spectrum β -lactamase (ESBL)-producing phenotypes according to NCCLS criteria.
Statistical analysis. It was performed using SPSS Version 9.0 and values of $p < 0.05$ were considered statistically significant.

RESULTS

- The Brazilian medical centers contributed the majority of BSI isolates from hematology-oncology (HO) patients (51.3%), followed by Argentinean (23.3%), Chilean (14.5%), and Mexican (7.8%) medical centers (Table 1).
- Overall, CoNS was the most frequently isolated pathogen (17.7%) from HO patients, followed by *E. coli* (17.5%), *S. aureus* (15.8%), *K. pneumoniae* (10.3%), *P. aeruginosa* (8.9%), *Enterobacter* spp. (6.7%), *Acinetobacter* spp. (4.5%), and *Enterococcus* spp. (3.1%).
- E. coli* was the most frequent BSI pathogen recovered from 2001 and 2002 from HO patients (Table 2). This finding differs from American and European reports, where Gram-positive cocci represent the major cause of BSI among hematology-oncology patients.
- Overall, among non-hematology-oncology (NOH) patients, *S. aureus* (22.0%) was the predominant BSI pathogen, followed by *E. coli* (18.5%) and CoNS (12.7%; data not shown).
- In this study, linezolid and vancomycin were active against all *S. aureus* and CoNS from HO and NOH patients (Table 3).
- Against *E. coli* and *Enterobacter* spp., imipenem and meropenem provided complete coverage. Among *P. aeruginosa* isolates from HO patients, only meropenem, imipenem and piperacillin/tazobactam provided $\geq 80\%$ coverage (Table 4).

INTRODUCTION

Bloodstream infections (BSI) represent a major cause of morbidity and mortality among hematology-oncology patients. Several factors, including long-term intravascular devices and chemotherapy-induced mucositis, are associated with increased risk of infections in this patient population. In the United States and Europe, an increasing frequency of Gram-positive infections and drug-resistance phenotypes has been noticed, but limited data are available from Latin American countries. Antimicrobial therapy of these patients should be based on local epidemiology information and susceptibility results of predominant pathogens.

This study evaluates the frequency and susceptibility patterns of bacterial pathogens isolated from BSI of hematology-oncology patients hospitalized at Latin American medical centers, as part of the SENTRY Antimicrobial Surveillance Study.

MATERIAL AND METHODS

Bacterial strains. A total of 1,587 BSI bacterial isolates were collected from hematology-oncology patients hospitalized at Latin American medical centers between 1997 and 2002. All isolates were identified at the participating institution by the routine methodology in use at each laboratory. Upon receipt at the monitoring laboratory, isolates were subcultured onto blood agar to ensure viability and purity. Confirmation of species identification was performed with the Vitek (bioMérieux Vitek, St Louis, MO) or conventional methods as required.

Medical centers. The participant medical centers were located in eleven cities (seven countries): São Paulo (1997 - 2002), Rio de Janeiro (1997 - 98), Florianópolis (1997 - 2002), Brasília (2001 - 2002), and Porto Alegre (1999 - 2002) in Brazil; Buenos Aires and San Isidro in Argentina (1997 - 2002); Santiago in Chile (two sites; 1997 - 2002); Montevideo in Uruguay (1997); Medellín in Colombia (1997 - 2001); Mexico City in Mexico (three different sites; 1997 - 2002); and Caracas in Venezuela (1998 - 2002).

Susceptibility testing. Antimicrobial susceptibility testing was performed and interpreted following the guidelines for reference broth microdilution method described by the NCCLS. The antimicrobial agents were obtained from the respective manufacturers or purchased from Sigma (St. Louis, MO). Validated dry-form microdilution panels and broth for inoculation were manufactured by Trek Inc. (Westlake, OH, USA). Quality control of test procedures and reagents was monitored throughout routine testing of the following ATCC strains: *Escherichia coli* ATCC 25922 and 35218,

Table 1. Distribution of 1,587 BSI isolates from hematology-oncology patients hospitalized in Latin American medical centers by year of isolation (SENTRY Program, 1997-2002).

Nation/medical center (no. tested)	1997	1998	1999	2000	2001	2002
Argentina						
39 (244)	49	35	42	51	31	36
40 (126)	32	28	7	23	7	29
Brazil						
41 (61)	36	25	0	0	0	0
46 (417)	32	62	65	71	93	94
48 (248)	34	38	59	31	25	61
57 (16)	-	-	6	8	0	2
101 (73)	-	-	-	-	24	49
Chile						
42 (89)	11	25	24	12	11	6
43 (142)	57	49	18	0	8	10
Colombia						
44 (37)	4	7	11	15	-	-
Mexico						
45 (90)	34	11	-	-	-	45
92 (34)	-	-	-	28	6	-
Uruguay						
47 (7)	7	-	-	-	-	-
Venezuela						
49 (3)	-	3	0	0	0	0

a. The medical center did not participate in the Program that year.

Table 2. Occurrence of the top five BSI pathogens isolated from hematology-oncology patients hospitalized in Latin American medical centers listed by age category (SENTRY Program, 1997 - 2002).

Rank order	Occurrences (%)					
	1997	1998	1999	2000	2001	2002
Hematology-oncology						
1	CoNS ^a (17.9)	CoNS (18.4)	CoNS (25.2)	<i>S. aureus</i> (17.2)	<i>E. coli</i> (19.5)	<i>E. coli</i> (22.3)
2	<i>S. aureus</i> (15.9)	<i>E. coli</i> (17.3)	<i>E. coli</i> (16.4)	CoNS (15.2)	<i>S. aureus</i> (14.6)	<i>S. aureus</i> (17.2)
3	<i>E. coli</i> (14.5)	<i>S. aureus</i> (15.9)	<i>S. aureus</i> (13.4)	<i>E. coli</i> (14.2)	CoNS (13.7)	CoNS (16.0)
4	<i>K. pneumoniae</i> (11.5)	<i>P. aeruginosa</i> (11.0)	<i>K. pneumoniae</i> (10.3)	<i>K. pneumoniae</i> (14.2)	<i>K. pneumoniae</i> (12.7)	<i>P. aeruginosa</i> (8.1)
5	<i>P. aeruginosa</i> (8.8)	<i>K. pneumoniae</i> (7.1)	<i>P. aeruginosa</i> (7.3)	<i>P. aeruginosa</i> (8.4)	<i>P. aeruginosa</i> (9.8)	<i>Enterobacter</i> spp. (7.8)
Non-hematology-oncology						
1	<i>S. aureus</i> (21.6)	<i>S. aureus</i> (20.0)	<i>S. aureus</i> (23.3)	<i>S. aureus</i> (24.4)	<i>S. aureus</i> (21.8)	<i>S. aureus</i> (21.5)
2	<i>E. coli</i> (17.4)	<i>E. coli</i> (17.2)	<i>E. coli</i> (17.9)	<i>E. coli</i> (17.4)	<i>E. coli</i> (20.7)	<i>E. coli</i> (19.9)
3	CoNS (14.5)	CoNS (13.3)	CoNS (12.0)	CoNS (12.5)	CoNS (11.6)	CoNS (12.8)
4	<i>K. pneumoniae</i> (8.8)	<i>K. pneumoniae</i> (8.9)	<i>K. pneumoniae</i> (8.4)	<i>K. pneumoniae</i> (9.9)	<i>K. pneumoniae</i> (9.1)	<i>K. pneumoniae</i> (7.2)
5	<i>Acinetobacter</i> spp. (5.8)	<i>P. aeruginosa</i> (7.2)	<i>S. pneumoniae</i> (6.9)	<i>Enterobacter</i> spp. (6.4)	<i>P. aeruginosa</i> (6.0)	<i>P. aeruginosa</i> (6.7)

a. CoNS = coagulase-negative staphylococci.

Table 3. Antimicrobial susceptibility of Gram-positive cocci isolated from hematology-oncology patients with BSI (SENTRY Program, 1997 - 2002).

Organism/ antimicrobial agent	Hematology-oncology			Non-hematology-oncology		
	MIC (mg/L)			MIC (mg/L)		
	50%	90%	% susceptible ^a	50%	90%	% susceptible
Oxacillin-susceptible <i>S. aureus</i> n=116						
Ciprofloxacin	0.25	0.5	97.6	0.25	0.5	96.5
Gatifloxacin	0.06	0.12	98.8	0.06	0.12	99.7
Clindamycin	0.12	0.25	98.2	0.12	0.25	98.0
Erythromycin	0.5	>8	77.1	0.5	>8	77.7
Gentamicin	1	2	96.4	1	2	95.0
Rifampin	0.25	0.25	99.4	0.25	0.25	97.7
Linezolid	2	2	100.0	2	4	100.0
Quinupristin/ Dalfopristin	0.25	0.5	99.4	0.25	0.5	99.8
Teicoplanin	0.5	1	100.0	0.5	1	99.9
Vancomycin	1	1	100.0	1	1	100.0
Oxacillin-resistant <i>S. aureus</i> n=85						
Ciprofloxacin	>2	>2	15.3	4	>4	12.5
Gatifloxacin	2	4	71.8	2	4	72.2
Clindamycin	>8	>8	14.1	>8	>8	15.9
Erythromycin	>8	>8	8.2	>8	>8	9.5
Gentamicin	>8	>8	11.8	>8	>8	7.9
Rifampin	2	>2	28.2	2	>2	45.3
Linezolid	2	2	100.0	2	2	100.0
Quinupristin/ Dalfopristin	0.5	1	98.8	0.5	1	99.4
Teicoplanin	1	2	97.6	1	2	99.1
Vancomycin	1	1	100.0	1	1	100.0
Oxacillin-susceptible CoNS n=72						
Ciprofloxacin	0.25	0.5	98.6	0.25	0.5	95.8
Gatifloxacin	0.12	0.12	100.0	0.12	0.12	99.0
Clindamycin	0.12	0.25	95.8	0.12	0.25	93.4
Erythromycin	0.25	>8	77.8	0.25	>8	70.6
Gentamicin	<1	8	88.9	<1	2	92.3
Rifampin	0.25	0.25	95.8	0.25	0.25	97.5
Linezolid	1	2	100.0	1	2	100.0
Quinupristin/ Dalfopristin	0.12	0.25	100.0	0.25	0.5	100.0
Teicoplanin	2	8	97.2	1	4	96.9
Vancomycin	1	2	100.0	1	2	100.0
Oxacillin-resistant CoNS n=209						
Ciprofloxacin	>2	>2	42.1	>2	>2	44.8
Gatifloxacin	1	2	93.3	1	2	91.6
Clindamycin	>8	>8	47.4	>8	>8	43.5
Erythromycin	>8	>8	28.7	>8	>8	24.7
Gentamicin	>8	>8	32.5	>8	>8	31.4
Rifampin	0.25	>2	67.2	0.25	>2	65.7
Linezolid	1	2	100.0	1	2	100.0
Quinupristin/ Dalfopristin	0.25	0.5	99.5	0.25	0.5	100.0
Teicoplanin	2	8	90.0	2	8	99.8
Vancomycin	2	2	100.0	2	2	100.0

a. Interpreted according to the NCCLS guidelines (2004).

RESULTS

Table 4. Antimicrobial susceptibility of Gram-negative bacilli isolated from hematology-oncology patients with BSI (SENTRY Program, 1997 - 2002).

Organism/ antimicrobial agent	Hematology-oncology			Non-hematology-oncology		
	MIC (mg/L)			MIC (mg/L)		
	50%	90%	% susceptible ^a	50%	90%	% susceptible
<i>E. coli</i> n=278						
Aztreonam	<0.12	4	90.3	<0.12	0.25	95.2
Cefoxitin	4	16	89.9	4	16	84.3
Ceftriaxone	<0.25	8	90.6	<0.25	0.25	94.6
Ceftazidime	<1	4	92.1	<1	2	95.7
Cefepime	<0.12	2	93.5	<0.12	0.25	97.0
Imipenem	0.12	0.25	100.0	0.12	0.25	100.0
Meropenem	<0.06	0.06	100.0	<0.06	0.06	100.0
Piperacillin/ Tazobactam	2	16	90.3	2	8	92.5
Amikacin	2	8	96.0	2	8	97.3
Gentamicin	2	8	89.9	1	8	89.5
Ciprofloxacin	0.03	>2	80.6	0.03	>2	84.1
Gatifloxacin	<0.03	>4	81.7	<0.03	>4	84.7
Levofloxacin	<0.03	>4	81.3	<0.03	>4	84.6
<i>K. pneumoniae</i> n=163						
Aztreonam	<0.12	>16	63.8	0.25	>16	61.2
Cefoxitin	4	16	89.0	4	16	84.3
Ceftriaxone	<0.25	32	66.9	<0.25	>32	60.4
Ceftazidime	2	>16	65.6	2	>16	66.8
Cefepime	<0.12	>16	79.8	0.25	>16	75.2
Imipenem	0.12	0.5	99.4	0.12	0.5	100.0
Meropenem	<0.06	<0.06	99.4	<0.06	0.12	99.9
Piperacillin/ Tazobactam	4	>64	63.8	4	>64	66.8
Amikacin	2	32	81.0	2	>32	79.0
Gentamicin	1	16	79.1	2	>8	60.7
Ciprofloxacin	0.06	0.5	93.3	0.25	2	97.5
Gatifloxacin	0.06	0.5	95.1	0.06	2	90.7
Levofloxacin	0.06	0.5	95.1	0.12	4	89.8
<i>P. aeruginosa</i> n=141						
Aztreonam	8	>16	56.7	8	>16	51.6
Ceftriaxone	>32	>32	7.1	>32	>32	4.1
Ceftazidime	4	>16	73.8	4	>16	67.7
Cefepime	4	>16	75.2	4	>16	70.3
Imipenem	1	>8	83.7	1	>8	82.3
Meropenem	0.5	>8	86.5	1	>8	82.8
Piperacillin/ Tazobactam	8	>64	67.1	8	>64	76.2
Amikacin	4	>32	76.6	4	>32	75.5
Gentamicin	2	>16	72.3	2	>8	64.7
Ciprofloxacin	0.25	>2	67.4	0.25	>2	64.8
Gatifloxacin	1	>4	63.8	1	>4	63.0
Levofloxacin	1	>4	67.4	1	>4	6