G-933

ICAAC 2005
JMI Laboratories
North Liberty, IA, USA
www.jmilabs.com
319.665.3370
fax 319.665.3371
ronald-jones@jmilabs.com

Assessment of Pathogen Frequency and Resistance Patterns Among Pediatric Patients: Report from the SENTRY Antimicrobial Surveillance Program (2004) on Three Continents

KA FEDLER, JT KIRBY, TR FRITSCHE, HS SADER, RN JONES

JMI Laboratories, North Liberty, IA, USA

SENTRY ANTIMICROBIAL SURVEILLANCE

ABSTRACT

Background: Selecting empiric or directed therapy for pathogens isolated from pediatric patients (PP) can be problematic. Many antimicrobial agents are not indicated for use in PP and regional variations of R mechanisms have been reported. The purpose of this study was to monitor antimicrobial R patterns (especially fluoroquinolones [FQ]) and pathogen occurrence in PP infections in SENTRY Program sites.

Methods: 3,537 clinical isolates were collected from 47 sites worldwide. 80 consecutive isolates (94.1% compliance) from children ≤ 18 years of age from infection sites were sent to a central laboratory. Isolates were tested for susceptibility (S) against >25 antimicrobial agents by reference broth microdilution methods and current CLSI breakpoint criteria were applied. Clonality of selected MDR isolates was determined using ribotyping (RT) and PFGE, when necessary.

Results: The ten most frequently observed pathogens accounted for 83.8% of the isolates. *S. aureus* (SA) was the most common pathogen isolated in NA (27.4%) and EU (19.0%), but *E. coli* (EC) was most common in LA (19.3%). All *S. pneumoniae* (SPN) strains from NA and LA were S to gatifloxacin (GATI) and levofloxacin (LEVO). Two SPN strains from Italy were R to GATI, LEVO, and ciprofloxacin (≥ 4 µg/ml). RT (105.333.3) and PFGE pattern showed these SPN isolates were clonal. 22.5, 4.5, and 4.9% of *Klebsiella* spp., EC, and *P. mirabilis* exhibited phenotypic ESBL patterns, respectively. Four *P. aeruginosa* (PSA) strains (3 from LA; 1 from EU) were multi-drug R. Two PSA from Turkey were polymyxin B-R (≥ 4 µg/ml). 8.7% (LA) and 0.0% (NA and EU) of *S. maltophilia* (XM) were R to trimethoprim/sulfamethoxazole.

Conclusions: There were regional differences in R rates among SPN, PSA, and XM isolates. Clonal FQ-R SPN was detected in PP in Italy, FQR SPN remain rare. Continued surveillance will be necessary to monitor emerging antimicrobial R in the PP population as FQs are utilized in this group.

INTRODUCTION

Regional variations in pathogen frequency and resistance patterns have been previously reported and are particularly evident in the pediatric patient population worldwide. Increased resistance to current antimicrobial agents indicated for use in this patient population has become problematic. As these antimicrobial agents become less effective, empiric or directed antimicrobial therapies may need to focus on novel drug classes for this population.

The necessity of newer antimicrobials in pediatric patient therapy is in part due to the rapid escalation of penicillin- and erythromycin-resistant *Streptococcus pneumoniae* and increased rates of resistance among coagulase-negative staphylococci to methicillin in infants. Likewise, other trends previously reported are the occurrence of high rates of extended-spectrum ß-lactamase (ESBL)-producing Enterobacteriaceae in children < one year of age and the emergence of multidrug-resistant (MDR) *Pseudomonas aeruginosa* in pediatric patients in general.

The SENTRY Antimicrobial Surveillance Program has monitored susceptibility rates and trends of pathogens worldwide since 1997. The purpose of this study was to analyze antimicrobial resistance patterns (especially of fluoroquinolones) and pathogen occurrence in pediatric patient infections monitored by the SENTRY Program (2004) and to compare the data by geographic regions and specific patient age.

MATERIALS AND METHODS

A total of 3,537 clinical isolates were collected from 47 medical centers worldwide by the SENTRY Program in 2004. These organisms included *S. aureus* (752 isolates), *E. coli* (663 isolates), *P. aeruginosa* (296 isolates), *Klebsiella* spp. (271 isolates), coagulase-negative staphylococci (CoNS; 185 isolates), ß-haemolytic streptococci (181 isolates), *Enterobacter* spp. (180 isolates), *S. pneumoniae* (156 isolates), *Enterococcus* spp. (146 isolates), *H. influenzae* (134 isolates) and several other species (Table 1). The study protocol mandated that 80 consecutive infection site isolates from children (≤ 18 years of age) be sent to a central laboratory for susceptibility testing and confirmation of organism identification.

Susceptibility tests were performed at the Jones Microbiology Institute (North Liberty, IA, USA) by reference broth microdilution methods of the Clinical and Laboratory Standards Institute (CLSI; formerly the National Committee for Clinical Laboratory Standards [NCCLS]) against more than 25 antimicrobial agents that included: ciprofloxacin, levofloxacin, and gatifloxacin representing the fluoroquinolones and 22 other agents. Data was analyzed using current CLSI category breakpoint criteria, where available.

Clonality of selected multi-drug resistant (MDR) isolates was determined utilizing a ribotype pattern and pulsed field gel electrophoresis (PFGE) analyses, when necessary. Quality Control (QC) tests and colony counts were routinely performed with *S. aureus* ATCC 29213, *E. faecalis* ATCC 29212, *S. pneumoniae* ATCC 49619, *H. influenzae* ATCC 49247, *E. coli* ATCC 25922 and 35218, and *P. aeruginosa* ATCC 27853; all results were within CLSI published QC ranges.

RESULTS

- Table 1 illustrates the rank order of pathogens in pediatric patients on three continents. The ten most frequently observed pathogens accounted for 83.8% of the organisms isolated in this study.
- *S. aureus* was the most common pediatric patient pathogen isolated in North America (27.4%) and Europe (19.0%). However, in Latin America, *S. aureus* (15.2%) was replaced by *E. coli* (19.3%) as the most commonly isolated organism. The most stark contrasts were the high ranking of pathogenic streptococci (ß-haemolytic and *S. pneumoniae*) and *H. influenzae* in Europe compared to the Americas (rank order 8-15).
- *S. aureus* and *E. coli* isolation rates increased as the patient age increased with *E. coli* predominating (20.6%) in patients less than 1 year of age. Enterobacteriaceae (*Klebsiella* spp. and *Enterobacter* spp.), enterococci and CoNS decrease in prevalence (two-fold) after age 1 year. ß-haemolytic streptococci and pneumococci (6.4 - 9.4%) were most often found between ages 1 and 11, while *H. influenzae* occurred most frequently between birth and 5 years (Table 2).
- Table 3 lists the in vitro activity of selected antimicrobial agents tested against the 15 most frequently isolated pediatric patient pathogens worldwide.
  - MRSA rates were only 27.9%.
  - Gatifloxacin and ciprofloxacin exhibited high levels of susceptibility among the tested pathogens indicating the fluoroquinolone-naïve nature of pediatric pathogens.
  - ESBL-phenotype rates among *E. coli* and *Klebsiella* spp. ranged from 4.2 - 4.5% and 20.3 - 22.5%, respectively.
  - High level penicillin-resistant pneumococci were frequent (18.6%).
  - VRE were uncommonly (4.1%) isolated.
- Tables 4 and 5 illustrate the in vitro activity of selected antimicrobial agents tested against the top five Gram-positive and -negative pediatric patient pathogens analyzed by continent.
  - All *S. pneumoniae* strains from North America and Latin America were susceptible to gatifloxacin (MIC_{50}, 0.25 µg/ml and MIC_{90}, 0.5 µg/ml) and levofloxacin (MIC_{50} and MIC_{90}, 1 µg/ml). However, two *S. pneumoniae* strains from Italy were resistant to gatifloxacin, levofloxacin, moxifloxacin and ciprofloxacin with MIC values of ≥ 4 µg/ml. Ribotyping and PFGE patterns showed these *S. pneumoniae* were clonal (see Poster #C2-242).
  - No resistant strains of staphylococci were detected for linezolid, quinupristin/dalfopristin, teicoplanin and vancomycin (Table 4).
  - Pneumococcal susceptibility was greatest in North America, but macrolides were most active against Latin American isolates (Table 4).
  - ESBL-phenotype rates in *E. coli* were greatest in Latin America (7.7 - 9.0%; Table 5). The rank order of ESBL-phenotypes in *Klebsiella* spp. by continent was: Latin America (34.4 - 39.8%) > Europe (21.2 - 24.7%) > North America (1.1 - 3.2%).
  - *P. aeruginosa* were quite susceptible to fluoroquinolones (4.5% resistance) in North American isolates.
  - ß-lactamase-mediated resistance in *H. influenzae* was highest in North America and Latin America (41.2 - 45.5%) in contrast to Europe (18.0%).

Table 1. Frequency of pathogen occurrence (rank order) for pediatric-age patients (top 15) in regions (North America, Europe, and Latin America) participating in the SENTRY Program (2004).

Organism (no. tested)	Rank order by region: All regions combined	North America	Latin America	Europe
S. aureus (752)	1	1	2	1
E. coli (663)	2	2	1	2
P. aeruginosa (296)	3	3	4	4
Klebsiella spp. (271)	4	4	3	7
CoNS (185)	5	6	6	9
ß-haemolytic streptococci (181)	6	8	12	3
Enterobacter spp. (180)	7	5	5	10
S. pneumoniae (156)	8	10	8/9	5
Enterococcus spp. (146)	9	7	11	8
H. influenzae (134)	10	11	15	6
P. mirabilis (82)	11	12	8/9	12
Serratia spp. (76)	12	9	13	13
Salmonella spp. (73)	13	15	14	11
Acinetobacter spp. (64)	14	14	7	14
S. maltophilia (53)	15	13	10	-

Table 2. Percentage of occurrences for each organism by patient age (% of pathogens in age group) for all regions combined.

Organism	% with age group: < 1 year	1 - 5 years	6 - 11 years	12 - 18 years
S. aureus	19.0	24.7	32.4	34.8
E. coli	20.6	18.3	22.3	25.9
P. aeruginosa	8.4	11.6	9.7	10.7
Klebsiella spp.	13.2	6.8	6.4	7.7
CoNS	9.8	4.3	3.7	6.6
ß-haemolytic streptococci	3.2	8.1	9.3	4.3
Enterobacter spp.	8.7	6.1	4.1	3.4
S. pneumoniae	5.1	7.5	6.8	1.5
Enterococcus spp.	6.2	5.3	3.3	3.4
H. influenzae	5.8	7.3	2.1	1.7
Total	865	880	516	468

Table 3. Antimicrobial activity of selected agents against the top 15 pathogens isolated from pediatric patients world wide (three regions), listed in rank order.

Organism/antimicrobial agent (no. tested)	MIC (µg/ml) 50%	MIC (µg/ml) 90%	% susceptible[a]	% resistant
S. aureus (752)				
Gatifloxacin	0.06	2	85.6	13.8
Ciprofloxacin	0.25	>4	84.2	14.6
Levofloxacin	0.12	4	85.5	13.8
Oxacillin	0.5	>2	72.1	27.9
Erythromycin	0.25	>8	59.7	38.8
Clindamycin	0.12	1	89.8	9.8
Quinupristin/dalfopristin	0.5	0.5	99.9	0.0
Vancomycin	1	1	100.0	0.0
Teicoplanin	0.5	1	100.0	0.0
Linezolid	2	2	100.0	-
Trim/sulfa[d]	≤0.5	≤0.5	97.3	2.7
E. coli (663)				
Gatifloxacin	≤0.03	0.12	94.9	3.9
Ciprofloxacin	≤0.03	0.12	94.7	5.3
Ceftazidime	≤1	≤1	97.3	1.5(4.5)[b]
Ceftriaxone	≤0.25	≤0.25	96.8	2.3(4.2)
Cefepime	≤0.12	≤0.12	98.0	1.7
Aztreonam	≤0.12	≤0.12	97.3	1.7(4.4)
Piperacillin/tazobactam	2	4	96.1	1.7
Imipenem	≤0.12	≤0.12	100.0	0.0
Gentamicin	≤2	≤2	96.5	3.2
Trim/sulfa[d]	≤0.5	>2	69.0	31.0
P. aeruginosa (296)				
Gatifloxacin	0.5	>4	84.8	10.1
Ciprofloxacin	0.12	2	88.9	9.5
Ceftazidime	2	>16	85.1	12.8
Cefepime	2	16	86.5	7.4
Aztreonam	4	>16	80.7	12.8
Amikacin	2	32	88.9	7.4
Gentamicin	≤2	>8	83.1	13.2
Piperacillin/tazobactam	8	64	91.6	8.4
Tobramycin	0.5	>16	88.2	11.1
Imipenem	1	8	88.2	6.4
Meropenem	0.5	4	92.2	6.1
Polymyxin B	0.5	1	99.3	0.7
Klebsiella spp. (271)				
Gatifloxacin	0.06	0.25	98.2	1.8
Ciprofloxacin	≤0.03	0.12	97.0	2.2
Ceftazidime	≤1	>16	84.1	13.3(20.3)
Ceftriaxone	≤0.25	>32	84.1	11.4(22.5)
Cefepime	≤0.12	8	90.0	8.9
Aztreonam	≤0.12	>16	82.3	15.5(20.7)
Piperacillin/tazobactam	4	64	85.2	8.9
Imipenem	≤0.12	0.25	99.6	0.0
Gentamicin	≤2	>8	80.1	18.8
Trim/sulfa[d]	≤0.5	>2	81.5	18.5
CoNS (185)				
Gatifloxacin	0.12	2	71.4	22.7
Ciprofloxacin	0.25	>4	70.8	28.1
Levofloxacin	0.25	>4	71.4	25.4
Oxacillin	>2	>2	15.1	84.9
Erythromycin	>8	>8	34.1	65.4
Clindamycin	≤0.06	>8	63.8	35.1
Quinupristin/dalfopristin	≤0.25	0.5	100.0	0.0
Vancomycin	1	2	100.0	0.0
Teicoplanin	2	4	98.9	0.0
Linezolid	1	1	100.0	-
Trim/sulfa[d]	≤0.5	>2	66.5	33.5
ß-haemolytic streptococci (181)				
Gatifloxacin	0.25	0.25	100.0	0.0
Levofloxacin	0.5	1	100.0	0.0
Penicillin	≤0.016	0.03	100.0	-
Ceftriaxone	≤0.25	≤0.25	100.0	-
Erythromycin	≤0.06	4	84.5	15.5
Clindamycin	≤0.25	≤0.25	95.6	4.4
Quinupristin/dalfopristin	≤0.5	≤0.5	100.0	0.0
Vancomycin	0.25	0.5	100.0	-
Linezolid	1	1	100.0	-
Enterobacter spp. (180)				
Gatifloxacin	≤0.03	0.12	100.0	0.0
Ciprofloxacin	≤0.03	≤0.03	99.4	0.6
Ceftazidime	≤1	>16	73.2	18.4
Ceftriaxone	≤0.25	>32	79.4	11.1
Cefepime	≤0.12	2	96.7	2.8
Aztreonam	≤0.12	>16	78.9	15.6
Piperacillin/tazobactam	2	64	78.9	7.8
Imipenem	0.5	1	99.4	0.0
Gentamicin	≤2	≤2	92.2	5.6
Trim/sulfa[d]	≤0.5	1	91.1	8.9
S. pneumoniae (156)				
Gatifloxacin	0.25	0.5	98.7	1.3
Ciprofloxacin	1	2	-	1.3[c]
Levofloxacin	1	1	98.7	1.3
Penicillin	≤0.03	2	67.3	18.6
Amoxicillin/clavulanate	≤1	2	94.9	3.2
Ceftriaxone	≤0.25	1	97.4	0.0
Cefepime	≤0.12	1	93.6	0.0
Erythromycin	≤0.25	>32	59.0	40.4
Clindamycin	≤0.25	>8	75.0	24.4
Quinupristin/dalfopristin	≤0.5	≤0.5	100.0	0.0
Tetracycline	≤2	>8	72.6	26.0
Trim/sulfa[d]	≤0.5	4	62.2	28.8
Vancomycin	0.25	0.5	100.0	-
Enterococcus spp. (146)				
Gatifloxacin	0.5	>4	87.0	11.6
Ciprofloxacin	1	>4	76.0	15.8
Levofloxacin	1	>4	86.3	12.3
Ampicillin	2	4	91.1	8.9
Chloramphenicol	8	>16	76.0	21.2
Gentamicin (HL)	≤500	>1000	80.8	19.2
Quinupristin/dalfopristin	>2	>2	6.8	80.8
Vancomycin	1	2	94.5	4.1
Teicoplanin	0.25	0.5	96.6	2.7
Linezolid	2	2	100.0	0.0
H. influenzae (134)				
Gatifloxacin	≤0.03	≤0.03	100.0	-
Ciprofloxacin	≤0.03	≤0.03	100.0	-
Levofloxacin	≤0.03	≤0.03	100.0	-
Ampicillin	≤1	>4	71.6	26.1
Amoxicillin/clavulanate	0.5	2	100.0	0.0
Ceftriaxone	≤0.25	≤0.25	100.0	-
Imipenem	0.5	1	100.0	-
Tetracycline	≤2	≤2	96.0	4.0
Trim/sulfa[d]	≤0.5	>4	70.9	24.6
P. mirabilis (82)				
Gatifloxacin	0.12	0.25	95.1	3.7
Ciprofloxacin	≤0.03	0.06	93.9	4.9
Ceftazidime	≤1	≤1	96.3	2.4(3.7)
Ceftriaxone	≤0.25	≤0.25	96.3	1.2(4.9)
Cefepime	≤0.12	≤0.12	100.0	0.0
Aztreonam	≤0.12	≤0.12	100.0	0.0(3.7)
Piperacillin/tazobactam	≤0.5	1	100.0	0.0
Imipenem	0.5	2	100.0	0.0
Gentamicin	≤2	≤2	93.9	4.9
Trim/sulfa[d]	≤0.5	>2	76.8	23.2
Serratia spp. (76)				
Gatifloxacin	0.25	0.5	100.0	0.0
Ciprofloxacin	0.06	0.12	100.0	0.0
Ceftazidime	≤1	≤1	100.0	0.0
Ceftriaxone	≤0.25	8	94.7	2.6
Cefepime	≤0.12	0.5	97.4	2.6
Aztreonam	≤0.12	1	97.4	2.6
Piperacillin/tazobactam	2	16	90.8	2.6
Imipenem	0.5	1	100.0	0.0
Gentamicin	≤2	≤2	92.1	5.3
Trim/sulfa[d]	≤0.5	1	94.7	5.3
Salmonella spp. (73)				
Gatifloxacin	0.06	0.25	100.0	0.0
Ciprofloxacin	≤0.03	0.12	100.0	0.0
Ceftazidime	≤1	≤1	100.0	0.0
Ceftriaxone	≤0.25	≤0.25	100.0	0.0
Cefepime	≤0.12	≤0.12	100.0	0.0
Aztreonam	≤0.12	≤0.12	100.0	0.0
Piperacillin/tazobactam	4	8	98.6	0.0
Imipenem	0.25	0.25	100.0	0.0
Gentamicin	≤2	≤2	97.3	2.7
Trim/sulfa[d]	≤0.5	≤0.5	90.4	9.6
Acinetobacter spp. (64)				
Gatifloxacin	0.06	>4	76.6	15.6
Ciprofloxacin	0.25	>4	73.4	26.6
Ceftazidime	4	>16	65.6	28.1
Cefepime	4	>16	64.1	23.4
Aztreonam	>16	>16	18.8	67.2
Amikacin	2	>32	78.1	17.2
Gentamicin	≤2	>8	70.3	25.0
Ampicillin/sulbactam	4	32	75.0	21.9
Piperacillin/tazobactam	16	>64	53.1	32.8
Tobramycin	0.5	>16	79.7	18.8
Imipenem	0.25	2	92.2	6.3
Meropenem	0.5	4	90.6	7.8
Polymyxin B	0.5	0.5	100.0	0.0
S. maltophilia (53)				
Gatifloxacin	0.5	2	94.3	0.0
Ciprofloxacin	2	4	28.3	32.1
Ceftazidime	16	>16	45.3	41.5
Cefepime	>16	>16	9.4	54.7
Ticarcillin/clavulanate	32	>128	37.7	17.0
Imipenem	>8	>8	1.9	98.1
Trim/sulfa[d]	≤0.5	≤0.5	96.2	3.8

a. CLSI breakpoints were used, where available.
b. Rate of ESBL phenotypes (MIC, ≥ 2 µg/ml) for that substrate and species per CLSI criteria (2005).
c. A break point of ≥ 4 µg/ml was used for ciprofloxacin against *S. pneumoniae*.
d. Trimethoprim/sulfamethoxazole

Table 4. Antimicrobial activity of selected agents against the top five Gram-positive pathogens isolated from pediatric patients in North America, Latin America and Europe.

Organism/antimicrobial agent (no. tested)	North America % susceptible[a]	North America % resistant	Latin America % susceptible[a]	Latin America % resistant	Europe % susceptible[a]	Europe % resistant
S. aureus (752)						
Gatifloxacin	82.8	16.9	72.4	25.2	95.5	4.5
Ciprofloxacin	80.8	17.2	72.4	27.6	94.1	5.2
Levofloxacin	82.8	16.4	72.4	26.8	95.2	4.5
Oxacillin	58.1	41.9	69.9	30.1	91.8	8.2
Erythromycin	43.6	54.7	53.7	45.5	84.0	14.5
Clindamycin	92.5	6.9	70.7	29.3	94.8	4.8
Quinupristin/dalfopristin	99.7	0.0	100.0	0.0	100.0	0.0
Vancomycin	100.0	0.0	100.0	0.0	100.0	0.0
Teicoplanin	100.0	0.0	100.0	0.0	100.0	0.0
Linezolid	100.0	-	100.0	-	100.0	-
Trimethoprim/sulfamethoxazole	99.4	0.6	86.2	13.8	99.6	0.4
CoNS (185)						
Gatifloxacin	82.8	17.2	64.7	23.5	65.7	27.1
Ciprofloxacin	82.8	17.2	62.7	33.3	65.7	34.3
Levofloxacin	82.8	17.2	64.7	29.4	65.7	30.0
Oxacillin	10.9	89.1	13.7	86.3	20.0	80.0
Erythromycin	20.3	78.1	41.2	58.8	41.4	58.6
Clindamycin	54.7	43.8	66.7	33.3	70.0	28.6
Quinupristin/dalfopristin	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
Teicoplanin	98.4	0.0	100.0	0.0	98.6	0.0
Linezolid	100.0	-	100.0	-	100.0	-
Trimethoprim/sulfamethoxazole	75.0	25.0	58.8	41.2	64.3	35.7
ß-haemolytic streptococci (181)						
Gatifloxacin	100.0	0.0	100.0	0.0	100.0	0.0
Levofloxacin	100.0	0.0	100.0	0.0	100.0	0.0
Penicillin	100.0	-	100.0	-	100.0	-
Ceftriaxone	100.0	-	100.0	-	100.0	-
Erythromycin	82.4	17.6	94.1	5.9	84.1	15.9
Clindamycin	90.2	9.8	100.0	0.0	97.3	2.7
Quinupristin/dalfopristin	100.0	0.0	100.0	0.0	100.0	0.0
Vancomycin	100.0	-	100.0	-	100.0	-
Linezolid	100.0	-	100.0	-	100.0	-
Enterococcus spp. (146)						
Gatifloxacin	92.9	7.1	73.7	21.1	85.9	12.7
Ciprofloxacin	78.6	10.7	57.9	26.3	78.9	16.9
Levofloxacin	91.1	7.1	73.7	26.3	85.9	12.7
Ampicillin	94.6	5.4	89.5	10.5	88.7	11.3
Chloramphenicol	91.1	8.9	63.2	26.3	67.6	29.6
Gentamicin (HL)	83.9	16.1	73.7	26.3	80.3	19.7
Quinupristin/dalfopristin	5.4	87.5	10.5	78.9	7.0	76.1
Vancomycin	91.1	5.4	94.7	5.3	97.2	2.8
Teicoplanin	96.4	1.8	94.7	5.3	97.2	2.8
Linezolid	100.0	0.0	100.0	0.0	100.0	0.0
S. pneumoniae (156)						
Gatifloxacin	100.0	0.0	100.0	0.0	97.9	2.1[b]
Ciprofloxacin	-	2.6	-	4.2	-	5.3[b]
Levofloxacin	100.0	0.0	100.0	0.0	97.9	2.1[b]
Penicillin	71.1	13.2	62.5	20.8	67.0	20.2
Amoxicillin/clavulanate	86.8	10.5	95.8	4.2	97.9	0.0
Ceftriaxone	97.4	0.0	100.0	0.0	96.8	0.0
Cefepime	92.1	0.0	95.8	0.0	93.6	0.0
Erythromycin	63.2	36.8	87.5	12.5	50.0	48.9
Clindamycin	89.5	10.5	95.8	4.2	63.8	35.1
Quinupristin/dalfopristin	100.0	0.0	100.0	0.0	100.0	0.0
Tetracycline	100.0	0.0	80.0	20.0	69.4	29.0
Trimethoprim/Sulfamethoxazole	60.5	34.2	58.3	33.3	63.8	25.5
Vancomycin	100.0	-	100.0	-	100.0	-

a. Current CLSI interpretive criteria and those recommended by Chen et al. (1999) for ciprofloxacin resistance in *S. pneumoniae*.
b. Rates driven by clonal epidemic in Italy.

Table 5. Antimicrobial activity of selected agents against the top five Gram-negative pathogens isolated from pediatric patients in North America, Latin America and Europe.

Organism/antimicrobial agent (no. tested)	North America % susceptible[a]	North America % resistant	Latin America % susceptible[a]	Latin America % resistant	Europe % susceptible[a]	Europe % resistant
E. coli (663)						
Gatifloxacin	95.5	3.0	92.9	5.8	95.5	3.7
Ciprofloxacin	95.5	4.5	92.9	7.1	95.0	5.0
Ceftazidime	98.5	0.4(1.5)[b]	94.8	3.2(8.3)	97.5	1.7(5.4)
Ceftriaxone	98.5	0.8(1.5)	94.2	3.8(9.0)	96.7	2.9(4.1)
Cefepime	99.2	0.4	96.2	3.2	97.9	2.1
Aztreonam	99.2	0.8(1.9)	94.2	3.2(7.7)	97.1	1.7(5.0)
Piperacillin/tazobactam	97.0	1.5	94.9	1.9	95.9	1.7
Imipenem	100.0	0.0	100.0	0.0	100.0	0.0
Gentamicin	97.4	2.6	93.6	5.8	97.5	2.1
Trimethoprim/sulfamethoxazole	75.8	24.2	52.3	47.7	72.3	27.7
P. aeruginosa (296)						
Gatifloxacin	89.1	4.5	80.0	14.7	83.8	12.6
Ciprofloxacin	93.6	4.5	84.0	14.7	87.4	10.8
Ceftazidime	92.7	5.5	84.0	14.7	78.4	18.9
Cefepime	92.7	1.8	81.3	12.0	83.8	9.9
Aztreonam	88.2	5.5	80.0	12.0	73.9	20.7
Piperacillin/tazobactam	94.5	5.5	90.7	9.3	89.2	10.8
Amikacin	94.5	2.7	84.0	12.0	86.5	9.0
Gentamicin	90.0	3.6	72.0	22.7	83.8	16.2
Tobramycin	94.5	3.6	80.0	20.0	87.4	12.6
Imipenem	96.4	1.8	84.0	10.7	82.9	8.1
Meropenem	100.0	0.0	90.7	8.0	85.6	10.8
Polymyxin B	100.0	0.0	100.0	0.0	98.2	1.8
Klebsiella spp. (271)						
Gatifloxacin	100.0	0.0	96.8	3.2	97.6	2.4
Ciprofloxacin	100.0	0.0	94.6	3.2	96.5	3.5
Ceftazidime	98.9	1.1(1.1)	67.7	29.0(38.7)	85.7	9.5(21.2)
Ceftriaxone	98.9	0.0(3.2)	72.0	17.2(39.8)	81.2	17.6(24.7)
Cefepime	98.9	1.1	84.9	12.9	85.9	12.9
Aztreonam	98.9	1.1(3.2)	65.6	29.0(34.4)	82.4	16.5(24.7)
Piperacillin/tazobactam	97.8	1.1	74.2	15.1	83.5	10.6
Imipenem	98.9	0.0	100.0	0.0	100.0	0.0
Gentamicin	96.8	1.1	62.4	37.6	81.2	17.6
Trimethoprim/sulfamethoxazole	91.4	8.6	73.1	26.9	80.0	20.0
Enterobacter spp. (180)						
Gatifloxacin	100.0	0.0	100.0	0.0	100.0	0.0
Ciprofloxacin	100.0	0.0	100.0	0.0	98.1	1.9
Ceftazidime	83.1	15.4	71.7	18.3	63.0	22.2
Ceftriaxone	86.2	9.2	80.3	8.2	70.4	16.7
Cefepime	100.0	0.0	100.0	0.0	88.9	9.3
Aztreonam	84.6	10.8	80.3	18.0	70.4	18.5
Piperacillin/Tazobactam	81.5	3.1	82.0	11.5	72.2	9.3
Imipenem	100.0	0.0	100.0	0.0	98.1	0.0
Gentamicin	96.9	1.5	91.8	8.2	87.0	7.4
Trimethoprim/sulfamethoxazole	95.4	4.6	91.7	8.3	85.2	14.8
H. influenzae (134)						
Gatifloxacin	100.0	-	100.0	-	100.0	-
Ciprofloxacin	100.0	-	100.0	-	100.0	-
Levofloxacin	100.0	-	100.0	-	100.0	-
Ampicillin	52.9	41.2	54.5	45.5	80.9	18.0
Amoxicillin/clavulanate	100.0	0.0	100.0	0.0	100.0	0.0
Ceftriaxone	100.0	-	100.0	-	100.0	-
Imipenem	100.0	-	100.0	-	100.0	-
Tetracycline	66.7	33.3	100.0	0.0	100.0	0.0
Trimethoprim/Sulfamethoxazole	70.6	23.5	54.5	45.5	73.0	22.5

a. CLSI breakpoints (2005) were used, where available.
b. A breakpoint of ≥ 2 µg/ml was used to screen for ESBL rates. Percentage of ESBL phenotype strains is found in parenthesis.

CONCLUSIONS

- Regional differences in resistance rates among some pediatric patient pathogens such as *S. pneumoniae*, *P. aeruginosa*, and *S. maltophilia* isolates were demonstrated.
- Clonal fluoroquinolone-resistant *S. pneumoniae* were detected (Italy), however, fluoroquinolone-resistant *S. pneumoniae* and other pediatric pathogens remain at lower occurrence rates in pediatric patients worldwide.
- There appears to be a direct correlation between increased patient population age and the frequency of occurrence among many cited pathogens.
- This study in 2004 has demonstrated that continued resistance surveillance will be necessary to monitor emerging therapeutic problems in the pediatric age group as fluoroquinolones and other drug classes are more widely utilized in these patients.