Prevalence of Antimicrobial Resistances in Common Pathogenic Enterobacteriaceae in Australia, 2006: Report from the Australian Group on Antimicrobial Resistance

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Introduction

E. coli and *Klebsiella* species are common causes of both hospital and community-acquired infection. Both of these species have a tendency to accumulate resistances to different antibiotic classes, especially β-lactams which are considered the drugs of choice. Particularly problematic are strains with extended-spectrum β-lactamases (ESBLs), which hydrolyse third- and fourth generation cephalosporins, used for more serious infection requiring treatment in hospital. Such strains are frequently resistant to other useful antibiotics, including aminoglycosides, fluoroquinolones and co-trimoxazole. Recently it has become apparent that the genes encoding ESBLs can spread to other enteric Gram-negative species, especially *Enterobacter* species which are important hospital-associated pathogens, and act as an unrecognised reservoir for these genes. Last line antibiotics such as carbapenems are often required for treatment of infections caused by ESBL-producing strains.

Methods

Thirty-one laboratories around Australia collected up to 75 clinical isolates of pathogenic Gram-negative bacteria (25 *E. coli*, 25 *Klebsiella* species, 25 *Enterobacter* species) from hospital and community patients.

Identification: Isolates were identified to species level by one of the following methods: API 20NE, API 20E, Vitek or Vitek 2, Phoenix, agar replication, Microscan, chromogenic agar, or conventional biochemical tests.

Susceptibility testing: Antimicrobial susceptibility tests were performed using the Vitek 2 AST-N044 card. CLSI (2009) criteria were used for interpretations for all antimicrobials except tigecycline where FDA guidelines (2005) were used. An ESBL phenotype was defined as ceftazidime or ceftriaxone MIC >1mg/L for *E. coli* and *Klebsiella* species and cefepime MIC >1mg/L for *Enterobacter* species. A selection of isolates with ESBL, plasmid-borne AmpC and carbapenemase phenotypes were examined by molecular techniques for the presence of known resistance genes. TaqMan probes were used to determine CTX-M groups, and real-time PCR for all known metallo-β-lactamases, KPC, TEM, SHV and plasmid-borne AmpC groups.

To ensure institutional anonymity data from New South Wales (NSW) and the Australian Capital Territory (ACT); Tasmania (Tas) and Victoria (Vic); and Queensland (Qld) and the Northern Territory (NT) have been combined.

Results

Table 1 *Escherichia coli*

Antibiotic	Cat*	NSW/ACT (n=225)	QLD/NT (n=161)	SA (n=99)	VIC/TAS (n=196)	WA (n=100)	Australia (n=781)
Ampicillin	%R	52.0%	44.1%	39.4%	51.0%	49.0%	48.1%
Amoxycillin-clavulanate	%I	9.8%	12.4%	7.1%	14.3%	15.0%	11.8%
	%R	6.2%	3.7%	4.0%	5.1%	7.0%	5.2%
Piperacillin-tazobactam	%R	0.0%	0.6%	0.0%	0.0%	2.0%	0.4%
Cefazolin	%I	1.3%	3.1%	7.1%	3.1%	4.0%	3.2%
	%R	7.6%	6.2%	6.1%	6.6%	10.0%	7.2%
Ceftriaxone	%NS	3.6%	1.2%	2.0%	2.0%	1.0%	2.2%
Ceftazidime	%NS	1.8%	0.6%	0.0%	1.5%	2.0%	1.3%
Cefepime	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Meropenem	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Ciprofloxacin	%NS	6.7%	2.5%	6.1%	4.6%	4.0%	4.9%
Gentamicin	%R	6.7%	2.5%	7.1%	4.6%	1.0%	4.6%
Co-trimoxazole	%R	18.7%	13.0%	14.1%	14.8%	14.0%	15.4%
Tigecycline	%R	0.4%	0.0%	0.0%	0.0%	0.0%	0.1%

Table 2 *Klebsiella* species

Antibiotic	Cat*	NSW/ACT (n=218)	QLD/NT (n=155)	SA (n=82)	VIC/TAS (n=184)	WA (n=98)	Australia (737)
Amoxycillin-clavulanate	%I	1.8%	7.1%	1.2%	3.8%	2.0%	3.4%
	%R	6.0%	1.9%	2.4%	2.7%	3.1%	3.5%
Piperacillin-tazobactam	%R	3.2%	3.2%	1.2%	1.6%	2.0%	2.4%
Cefazolin	%I	2.3%	2.6%	6.1%	2.7%	9.2%	3.8%
	%R	13.8%	9.0%	8.5%	12.5%	13.3%	11.8%
Ceftriaxone	%NS	5.5%	2.6%	0.0%	3.8%	0.0%	3.1%
Ceftazidime	%NS	5.5%	1.3%	2.4%	2.7%	1.0%	3.0%
Cefepime	%NS	2.3%	0.0%	0.0%	1.1%	0.0%	0.9%
Meropenem	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Ciprofloxacin	%NS	4.1%	3.2%	2.4%	1.6%	1.0%	2.7%
Gentamicin	%R	3.2%	3.2%	1.2%	3.3%	1.0%	2.7%
Co-trimoxazole	%R	4.1%	7.1%	7.3%	2.7%	2.0%	4.5%
Tigecycline	%R	4.1%	3.2%	1.2%	1.1%	0.0%	2.3%

Table 3 *Enterobacter* species

Antibiotic		NSW/ACT (n=224)	QLD/NT (n=155)	SA (n=77)	VIC/TAS (n=201)	WA (n=99)	Australia (n=756)
Piperacillin-tazobactam	%R	3.1%	6.5%	6.5%	6.5%	1.0%	4.8%
Ceftriaxone	%NS	29.5%	18.1%	28.6%	30.3%	10.1%	24.7%
Ceftazidime	%NS	33.9%	20.6%	32.5%	32.3%	13.1%	27.9%
Cefepime	%NS	0.0%	0.0%	3.9%	1.0%	0.0%	0.7%
Meropenem	%NS	0.0%	0.6%	1.3%	0.0%	0.0%	0.3%
Ciprofloxacin	%NS	5.4%	1.3%	3.9%	2.5%	3.0%	3.3%
Gentamicin	%R	11.6%	6.5%	7.8%	3.0%	0.0%	6.3%
Co-trimoxazole	%R	15.6%	12.3%	10.4%	7.0%	1.0%	10.2%
Tigecycline	%R	1.3%	4.0%	2.6%	5.5%	1.0%	3.0%

*Category: R = resistant, I = intermediate, NS = not susceptible (intermediate + resistant)

Table 4 Multi-resistance

Species	Non-multi-resistant					Multi-resistant						
No. resistant	**0**	**1**	**2**	**3**	**%**	**4**	**5**	**6**	**7**	**8**	**9**	**%**
E. coli[1]	379	178	115	56	93.2	31	10	5	5	2		6.8
Klebsiella[2]	587	75	21	27	96.3	13	6	5	1	1	1	3.7
Enterobacter[3]	495	45	30	138	93.6	25	15	7	1			6.4

1. *Antibiotics included*: ampicillin, amoxycillin-clavulanate, piperacillin-tazobactam, cefazolin, ceftriaxone, ceftazidime, cefepime, meropenem, ciprofloxacin, gentamicin, co-trimoxazole, tigecycline
2. *Antibiotics include:* amoxycillin-clavulanate, piperacillin-tazobactam, cefazolin, ceftriaxone, ceftazidime, cefepime, meropenem, ciprofloxacin, gentamicin, co-trimoxazole, tigecycline
3. *Antibiotics included*: piperacillin-tazobactam, ceftriaxone, ceftazidime, cefepime, ciprofloxacin, gentamicin, co-trimoxazole, tigecycline

Results

Seven hundred and eighty one *E. coli*, 737 Klebsiella species (70% *K. pneumoniae*, 27% *K. oxytoca*, 3% other species or not speciated) and 756 *Enterobacter* species (66% *E. cloacae*, 31% *E. aerogenes* and 3% other species or not speciated) were collected.

E. coli: Acquired resistance to ampicillin was common (50%), and clinically significant percentages of intermediate susceptibility and resistance (>10%) were observed to amoxycillin-clavulanate, cefazolin, and co-trimoxazole (Table 1). 6.8% of *E. coli* were multi-resistant (Table 4).

***Klebsiella* spp:** Acquired resistance was seen to co-trimoxazole (4.5%). 3.7% of *Klebsiella* species were multi-resistant (Table 4).

***Enterobacter* species:** Acquired resistance was seen to ceftriaxone, ceftazidime, trimethoprim and co-trimoxazole. Carbapenem resistance was detected in two (0.3%) *Enterobacter* species. 6.4% of *Enterobacter* species were multi-resistant (Table 4).

ESBLs: 3% of *E. coli*, 6% of *Klebsiella* species and 9% of *Enterobacter* species had an ESBL phenotype. Co-resistance to ciprofloxacin, gentamicin and/or co-trimoxazole was common in isolates presumptively harbouring ESBLs.

CTX-M-1, -2 and -9 types were detected in several institutions around Australia as were plasmid-borne AmpC enzymes (CMY, DHA, EBC and FOX). TEM and SHV ESBLs were widespread.

Conclusions

Although resistance and multi-resistance is common amongst the organisms tested, resistance to third-generation cephalosporins remains uncommon in *E. coli* and *Klebsiella* species, and resistance to carbapenems is relatively rare. Australia may be controlling its resistance rates to third-generation cephalosporins by reducing reliance on them in hospital practice, but there is molecular evidence of increasing rates of strains harbouring CTX-M enzymes, which have become a problem in the community in other countries. Rates of resistance to fluoroquinolones appear to be slowly rising.

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