Carbapenem-Resistance Mechanisms among *Acinetobacter* spp. Hospitalised Patients in the SENTRY Asia-Pacific Region

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Introduction

Resistance to carbapenems and *Acinetobacter* spp. (ACIN) species is being described with increasing frequency in many parts of the world. As carbapenems are commonly used in hospital practice in the Asia-Pacific region, we wished to determine whether resistance was emerging and in particular investigate the mechanisms involved

Methods

Isolates

As part of the SENTRY Asia-Pacific region we examined ACIN from infected hospitalized patients in 9 countries (17 laboratory centres) collected since 1998. Isolates came from blood, LRTI, skin/skin structure, urine and intensive care specimens. All strains were referred to the Women's and Children's Hospital, Adelaide, Australia for testing.

Susceptibility testing

Isolates were tested using custom made broth microdilution panels (Trek Diagnostic Systems) against a wide range of antimicrobials including imipenem (IMI) and meropenem (MER) according to CLSI standards.[1] Breakpoints for resistance were those recommended by the CLSI.[2]

Screening methods

All isolates with either IMI or MER MIC ≥ 8 mg/ L were screened for *bla*IMP, *bla*VIM, *bla*SIM metallo-ß-lactamases (MBL) and OXA-23 like; OXA-24; OXA-51, OXA-58 enzymes using a double disc synergy test.[3] Two reagents (sodium mercaptoacetic acid (SMA) and EDTA were used.

Metallo-ß-lactamases (MBL)

Multiplex PCR was used to detect *bla*IMP and *bla*VIM,[4] and *bla*OXA-type genes.[5] *bla*SIM-1 was detected as described by Lee et al.[6]

Table 1. Carbapenem resistance vs country

	AUS	HKK	CHI	PHL	SIN	TWN	KOR	JPN	SAF	Total
Acinetobacter spp.	97	112	61	76	134	237	28	104	115	964
Meropenem ≥ 8 mg/L	1	7	1	0	49	54	14	4	31	161
IMI ≥8 or MER ≥8 mg/L	1	8	2	1	49	55	15	4	32	167
% non-susceptible	*1.0%*	*7.1%*	*3.3%*	*1.3%*	*36.6%*	*23.2%*	*53.6%*	*3.8%*	*27.8%*	*17.3%*

Figure 1. Imipenem Resistance vs metallo-ß-lactamase Class and Type

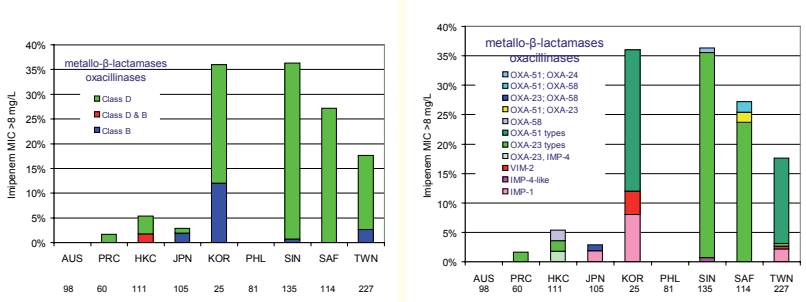


Figure 2. Carbapenem Resistance vs metallo-ß-lactamase Class and Type

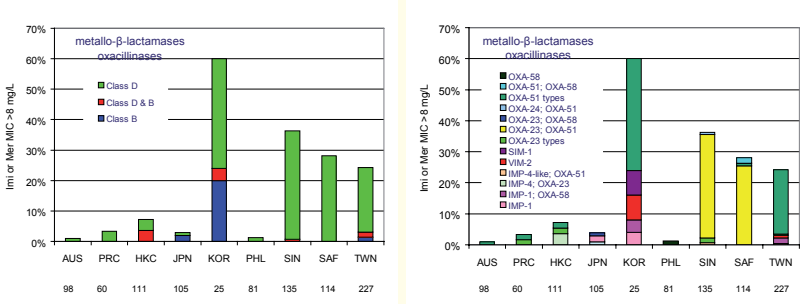
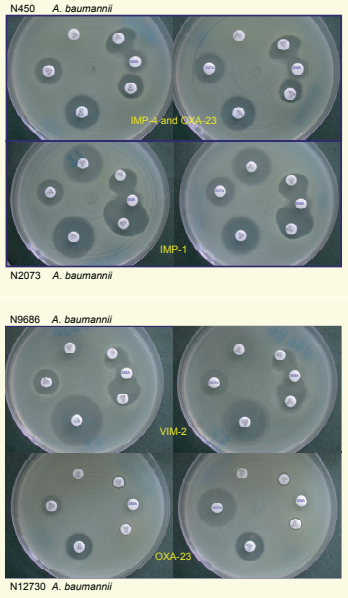


Figure 3.
Detection of metallo-ß-lactamases using double disc synergy tests



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2. CLSI. 2006. M100-S16
3. Yong D, K. Lee, J.H. Yum, B.H. Shin, G.M. Rossolini, and Y Chong. 2002. J. Clin. Microbiol. 40:3798-3801.
4. Pitout, J.D.D, D.B. Gregson, L. Poirel, J. McClure, P. Le, D.L. Church. 2005. J. Clin. Microbiol. 43:3129-3135
5. Woodford, N., Mj Ellington, J. Coelho, J. Turton, ME Ward, S. Brown, SGB Amyes, and DM Livermore. 2005.
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Results

- A total of 964 ACIN isolates were collected over the 7-year period
- Class D enzymes were common (88% of all carbapenem resistant ACIN), and were detected in all countries
- OXA-51 types were dominant in Korea and (24%) Taiwan (15%)
- Carbapenem resistant ACIN rapidly spread in Singapore (11% in 1998 to 84% in 2003) and South Africa (11% to 67% in 2000 - 2004). In both sites, the resistance was predominantly due to OXA-23-like enzymes
- ACIN with both Class D and Class B enzymes were found in Hong Kong, China, Korea and Taiwan. In Korea, 60% of ACIN were carbapenem resistant. Five different enzyme groups were found, with both class D enzymes (OXA-51 types; 36%) and class B (*bla*IMP-1 *bla*SIM-1, *bla*VIM 2; 20%), and 1 strain with both *bla*IMP-1 and OXA-58
- Five enzyme groups were also found in Taiwan
- Hong Kong, Japan, Singapore and South Africa all had three enzyme groups
- Carbapenem resistant ACIN were uncommon (1%) in Australia (OXA-51) and the Philippines (OXA-58).

Conclusions

- **Carbapenem resistance in *Acinetobacter* spp. is a rapidly emerging problem in sites in the Asia-Pacific region**
- **A wide diversity of enzymes from both molecular class D and B were involved**
- **Co-existance of enzymes from different classes were found**
- **All *A. baumannii* isolates contained the $bla_{OXA\text{-}51\text{-}like}$ carbapenemase gene**