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Abstract (poster session)

AmpC and MexAB-OprM hyperexpression are most common mechanisms among ceftazidime- and imipenem-resistant Pseudomonas aeruginosa from Chinese hospitals

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Objective: To evaluate evaluated beta-lactam resistance mechanisms among ceftazidime (CAZ)- and imipenem (IMI)-resistant P. aeruginosa (PSA) strains collected during 2011 in Chinese hospitals. CAZ- and IMI-resistance rates among PSA from China (30.3 and 26.5%, respectively) were remarkably greater than rates noted in the United States (16.9 and 19.8%, respectively). Methods: 212 PSA clinical isolates collected in 2011 from 11 Chinese hospitals were susceptibility tested. Isolates were further evaluated if CAZ and IMI MICs were >=16 and 1 mg/L, respectively. MICs for CAZ, IMI, other carbapenems, aztreonam and cefepime were determined ± of PABetaN (efflux inhibitor) and/or cloxacillin (AmpC inhibitor). Screening for beta-lactamases was performed by PCR/sequencing. Expression of chromosomal (c) ampC, mexA, mexC, mexE and mexX and oprD was determined using high quality RNA in triplicate reactions by qRT-PCR using an endogenous control and values compared to P. aeruginosa PAO1. Clonality was evaluated by PFGE and MLST. Results: 12 isolates collected in 7 hospitals were analyzed showing variable resistance rates against beta-lactams. Lower MICs were noted with PABetaN, but smaller differences were observed using cloxacillin. Five isolates exhibited lower MICs when efflux and AmpC inhibitors were tested together. Four isolates possessed metallo-beta-lactamases (MBLs; 1 IMP-9, 3 VIM-2; Table) and 2 VIM-producers hyperexpressed cAmpC ± mexA. One PSA had high levels of mexC transcripts and another of mexX + cAmpC, but the majority (8) had elevated cAmpC ± mexA transcription. No isolates had significant differences in oprD and mexE. ESBLs PER, PSE, and OXA-30 were detected among 3 PSA. Ten sequence types (STs) were identified among 12 isolates displaying 11 unique PFGE types. Two PSA from one hospital had the same PFGE and ST profile and two PSA from different hospitals had same ST profile despite the distinct PFGE patterns. Conclusions: AmpC ± MexAB-OprM hyperexpression were the most prevalent resistance mechanisms among genetically diverse PSA from Chinese hospitals, but other resistance determinants such as MBLs and increased MexCD-OprJ or MexXY-OprM were also observed. These results emphasize the prevalence of intrinsic resistance mechanisms among Chinese PSA, but also highlights that multiple factor might contribute to elevated PSA resistance rates in this country.

PFGE	ST	β-lactamase	Pump effect[a]	AmpC effect[b]	Relative expression (compared to PAO1)[c]					
					ampC	*mexA*	*mexC*	*mexE*	*mexX*	*oprD*
F	1335		+++	-	2.5	7.4	37.6	0.1	1.7	0.0
A	1336		++	+	94.9	42.4	0.8	0.1	1.5	0.0
D	257		++	+	240.8	91.5	8.0	0.2	2.4	0.0
C	1026	IMP-9, OXA-30	-	-	1.0	1.1	1.3	0.0	0.6	0.0
A	1336	VIM-2	+[d,e]	+[d,e]	1098.4	16.0	0.4	0.0	6.9	0.0
G	1338	VIM-2, PER-1/-5, PSE-1	++	-	1.8	7.7	0.2	0.1	8.4	0.1
K	1339		+[d,e]	+[d,e]	2800.6	7.7	0.5	0.3	12.5	2.1
H	1212		++	+[f]	45.8	3.5	NT[g]	0.1	7.5	0.4
J	697		++[d,e]	+[d,e]	168.4	46.0	0.6	0.2	0.6	0.1
B	1337		++[e]	+[e]	36.1	14.8	1.6	0.1	1.5	1.2
E	360		++[d,e]	++[d,e]	114.6	17.4	0.1	0.0	6.5	0.8
I	697	VIM-2, PER-1/-5	+	+	16.3	3.2	0.2	0.0	2.1	0.0

a. Difference between MIC ± PAβN.

b. Difference between MIC ± cloxacillin.

c. Values highlighted are >10-fold and considered significant.

d. Cephalosporins and aztreonam only.

e. Combined effect.

f. Carbapenems only.

g. NT = not tested.