Temporal and Geographical Prevalence of Carbapenem-Resistant *Pseudomonas aeruginosa* and the In Vitro Activity of Ceftolozane/Tazobactam and Comparators in Taiwan – SMART 2012-2020

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Introduction

Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) is listed as a critical pathogen by the World Health Organization (WHO)[1]. Using clinical isolates collected in Taiwan as part of the global SMART surveillance program, we evaluated the trend of CRPA prevalence in recent nine years (2012-2020) as well as in vitro susceptibility of ceftolozane/tazobactam (C/T) and comparators against CRPA collected from ICU vs non-ICU wards from 2016 to 2020.

Materials & Methods

Between 2012-2020, *Pseudomonas aeruginosa* (PA) isolates were collected from nine sites in Taiwan (2 in Northern, 3 in Central and 4 in Southern Taiwan). MICs were determined and interpreted based on CLSI broth microdilution guidelines and 2021 CLSI breakpoints[2,3]. CRPA was defined as PA isolates resistant to either imipenem or meropenem. PCR screening and β-lactamase gene sequencing were performed for isolates non-susceptible to imipenem or imipenem/relebactam or C/T.

Results

Figure 1. Trends of CRPA prevalence over the years, 2012-2020 (n=2639)

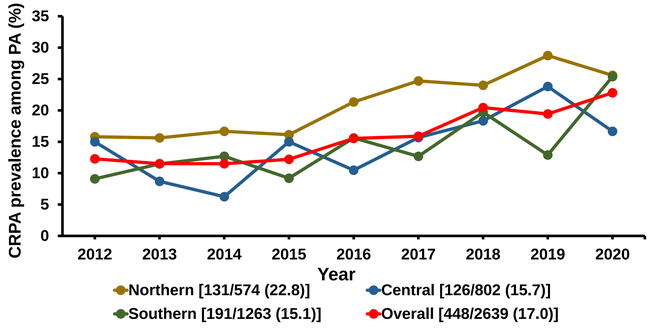
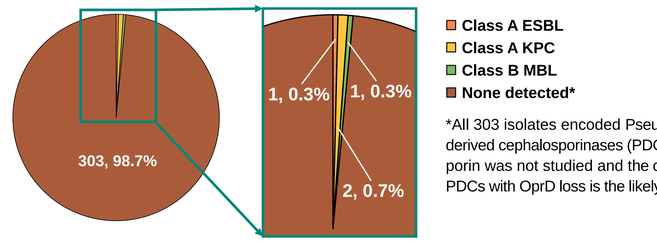


Figure 2. Acquired β-lactamases detected in CRPA, 2015-2019 (n=307)



*All 303 isolates encoded Pseudomonas-derived cephalosporinases (PDCs). OprD entry porin was not studied and the combination of PDCs with OprD loss is the likely mechanism.

Figure 3. Distribution of infection sources (A), and wards (B) among PA & CRPA, 2012-2020 (n=2639, 448)

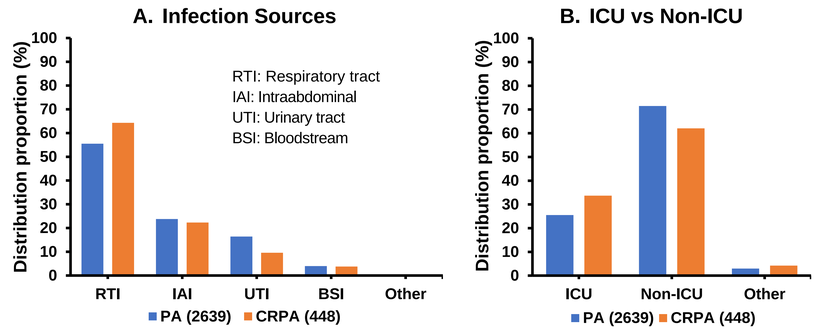


Figure 4. Susceptibility of antibiotics against CRPA in ICU & non-ICU patients, 2012-2020 (n=429)

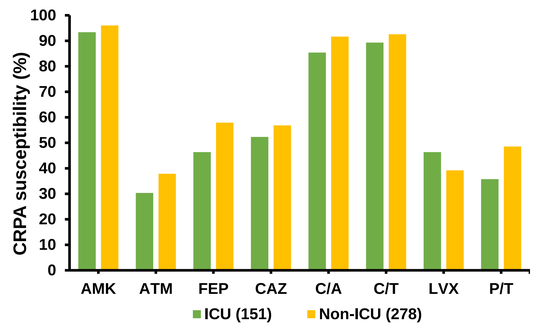


Table 1. Susceptibility trends of antibiotics against CRPA, 2012-2020 (n=448)

Antibiotics	2012 N/n (%)	2013 N/n (%)	2014 N/n (%)	2015 N/n (%)	2016 N/n (%)	2017 N/n (%)	2018 N/n (%)	2019 N/n (%)	2020 N/n (%)
AMK	12/14 (85.7)	15/16 (93.8)	11/13 (84.6)	40/41 (97.6)	53/57 (93)	66/68 (97.1)	71/73 (97.3)	71/75 (94.7)	87/91 (95.6)
ATM				22/41 (53.7)	19/57 (33.3)	17/68 (25.0)	22/73 (30.1)	25/75 (33.3)	33/91 (36.3)
FEP	8/14 (57.1)	9/16 (56.3)	8/13 (61.5)	26/41 (63.4)	28/57 (49.1)	33/68 (48.5)	40/73 (54.8)	32/75 (42.7)	52/91 (57.1)
CAZ	7/14 (50.0)	11/16 (68.8)	8/13 (61.5)	25/41 (61)	28/57 (49.1)	36/68 (52.9)	41/73 (56.2)	38/75 (50.7)	49/91 (53.9)
C/A							64/73 (87.7)	63/75 (84.0)	84/91 (92.3)
C/T					51/57 (89.5)	54/68 (79.4)	68/73 (93.2)	68/75 (90.7)	90/91 (98.9)
LVX	7/14 (50.0)	7/16 (43.8)	5/13 (38.5)	26/41 (63.4)	23/57 (40.4)	20/68 (29.4)	30/73 (41.1)	24/75 (32.0)	43/91 (47.3)
P/T	7/14 (50.0)	9/16 (56.3)	8/13 (61.5)	22/41 (53.7)	17/57 (29.8)	24/68 (35.3)	29/73 (39.7)	31/75 (41.3)	43/91 (47.3)

Susceptibility >90%; Susceptibility 80%-90%; No data; n: Total CRPA ; N: CRPA susceptible to antibiotics tested

AMK: Amikacin; ATM: Aztreonam; FEP: Cefepime; CAZ: Ceftazidime; C/A: Ceftazidime/Avibactam; C/T: Ceftolozane/Tazobactam; LVX: Levofloxacin; P/T: Piperacillin/Tazobactam

Table 2. Susceptibility trends of C/T against CRPA in ICU & non-ICU patients, 2016-2020 (n=347)

Taiwan Regions	Ward	2016 N/n (%)	2017 N/n (%)	2018 N/n (%)	2019 N/n (%)	2020 N/n (%)
Overall (347)	Non-ICU	20/24 (83.3)	14/18 (77.8)	25/27 (92.6)	27/31 (87.1)	31/31 (100.0)
	ICU	30/32 (93.8)	33/40 (82.5)	39/42 (92.9)	41/44 (93.2)	57/58 (98.3)
Northern (101)	Non-ICU	11/12 (91.7)	1/3 (33.3)*	7/9 (77.8)*	6/7 (85.7)*	6/6 (100.0)*
	ICU	6/7 (85.7)*	6/9 (66.7)*	12/14 (85.7)	17/18 (94.4)	16/16 (100.0)
Central (99)	Non-ICU	2/5 (40.0)*	7/8 (87.5)*	9/9 (100.0)*	13/14 (92.9)	9/9 (100.0)*
	ICU	6/6 (100.0)*	12/13 (92.3)	13/13 (100.0)	10/11 (90.9)	10/11 (90.9)
Southern (147)	Non-ICU	7/7 (100.0)*	6/7 (85.7)*	9/9 (100.0)*	8/10 (80.0)*	16/16 (100.0)
	ICU	18/19 (94.7)	15/18 (83.3)	14/15 (93.3)	14/15 (93.3)	31/31 (100.0)

Susceptibility >90%; n: Total CRPA ; N: CRPA susceptible to C/T

*Data should be interpreted with caution due to limited case number.

Results Summary

- During the study period, a total of 2639 PA isolates were collected. Among these, 448 isolates were resistant to either imipenem or meropenem (17.0%).
- Yearly prevalence rate of CRPA increased from 12.3% in 2012 to 22.8% in 2020: 12.3% in 2012 (14/114), 11.5% in 2013 (16/139), 11.5% in 2014 (13/113), 12.2% in 2015 (41/336), 15.5% in 2016 (57/367), 15.9% in 2017 (68/428), 20.4% in 2018 (73/357), 19.4% in 2019 (75/386), and 22.8% (91/399) in 2020.
- Overall (2012-2020), hospitals in Northern Taiwan had higher CRPA prevalence rate (22.8%, 131/574) compared to those in Central (15.7%, 126/802) and Southern Taiwan (15.1%, 191/1263).
- Among 307 CRPA isolates tested for molecular resistance mechanisms (2015-2019), two CRPA isolates were carrying class A carbapenemases (0.7%, 1 KPC-2, 1 KPC-3), one isolate was carrying a class A extended-spectrum β-lactamase (0.3%, 1 SHV-31), and one was carrying a class B metallo-β-lactamase (0.3%, 1 IMP-1).
- The most common infection source for both PA and CRPA was respiratory tract (55.5%, 1465/2639; 64.3%, 288/448). 25.5% (674/2639) of PA isolates were collected from ICU, while 33.7% (151/448) of CRPA isolates were collected from ICU. The ward source of 4.2% (19/448) CRPA isolates were not recorded.
- Percentage susceptibility of CRPA isolates to C/T from 2016 to 2020 showed 89.5% (51/57) in 2016, 79.4% (54/68) in 2017, 93.2% (68/73) in 2018, 90.7% (68/75) in 2019 and 98.9% (90/91) in 2020. For ICU vs. Non-ICU CRPA isolates, the susceptibility to C/T were 83.3% vs.93.8%, 77.8% vs. 82.5%, 92.6 % vs. 92.9%, 87.1% vs.93.2%, and 100% vs. 98.3%, in 2016, 2017, 2018, 2019, and 2020, respectively.

Conclusions

During the period of 2012-2020, the yearly prevalence of CRPA in Taiwan hospitals increased from 12.3% to 22.8%. The susceptibility trends of C/T against CRPA remained higher than 90% during recent years (2018-2020). Regarding CRPA isolates, the majority of them do not have clear resistance mechanisms identified via the molecular screening algorithm by PCR. The high prevalence and increasing trend of CRPA warrant continuous monitoring of evolving antibiotic resistance in Taiwan.

References & Acknowledgments

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2. Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing. 31st ed. CLSI supplement M100. 2021.
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