Antibiogram data from private hospitals in Hong Kong: 6-year retrospective study

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ABSTRACT

Introduction: The surveillance of antibiotic resistance is critical for the establishment of effective control strategies. The antibiotic resistance situations in private hospitals in Hong Kong have not been systematically described. The objective of the study was to analyse antibiogram data from private hospitals and describe the temporal trends of non-susceptibility percentages in this setting.

Methods: This retrospective descriptive study used antibiogram data from all private hospitals in Hong Kong that had been collected annually for 6 years (2014-2019). Data on six targeted bacteria and their corresponding multidrug-resistant organisms were included.

Results: The non-susceptibility percentages of isolates remained stable or decreased during the study period: methicillin-resistant *Staphylococcus aureus* had a stable prevalence of approximately 20%; extended-spectrum beta-lactamase-producing *Escherichia coli* and *Klebsiella* species had stable prevalences of 20% to 30% and 10% to 20%, respectively; multidrug-resistant *Acinetobacter* species had prevalences of approximately 2% to 8%, which decreased over time; multidrug-resistant *Pseudomonas aeruginosa* had prevalences of 0.0% to 0.3%; *Streptococcus pneumoniae* penicillin and macrolide non-susceptibility percentages were 2% to 9% and 71% to 79%, respectively. These values generally were comparable with findings from public hospitals and Residential Care Homes for the Elderly in Hong Kong. However, the prevalences of carbapenem-resistant Enterobacteriaceae, which are increasing in Hong Kong and other nations, were also increasing in our dataset despite their currently low values (<1% for *Escherichia coli* and <2% for *Klebsiella* species).

Conclusion: The antibiotic resistance landscape among private hospitals in Hong Kong is satisfactory overall; there remains a need for surveillance, antibiotic stewardship, and other infection control measures.

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New knowledge added by this study
• This report of antibiotic resistance prevalence includes 6 years of data from all private hospitals in Hong Kong.
• The prevalences of methicillin-resistant *Staphylococcus aureus* and extended-spectrum beta-lactamase-producing *Escherichia coli* and *Klebsiella* species were moderate but stable (approximately 20%).
• The prevalences of multidrug-resistant *Acinetobacter* species (approximately 2%-8%) and multidrug-resistant *Pseudomonas aeruginosa* (0%-0.3%) were low.

Implications for clinical practice or policy
• Antibiogram data can be used to monitor antibiotic resistance trends, which may help to guide empirical treatment and assess the effectiveness of infection control measures.
• The lower prevalences of multidrug-resistant organisms (MDROs) in private hospitals (compared with public hospitals) may be related to the presence of additional staff members and the use of a strict MDRO carrier isolation policy.

Introduction

Surveillance is a critical aspect of antibiotic resistance control. Susceptibility data periodically collected from patients can be used to construct antibiograms for monitoring of resistance trends and guidance of empirical treatment.[1]

The Working Group of Collaboration between the Centre for Health Protection (CHP) and Private Hospitals on Safe Use of Antibiotics and Infection Control (the "Working Group") was established to exchange information regarding infection prevention and to promote safe antibiotic use. Members

included the Infection Control Branch of the CHP and the Hong Kong Private Hospitals Association. Each year, the Infection Control Branch collected from and shared the susceptibility data with private hospitals. The resulting antibiograms were uploaded to the CHP website.[2]

Hong Kong runs a dual-track healthcare system, in which the private sector complements the public system with a range of general and specialist services. In accordance with the market-set price principle, private hospitals and out-patient clinics establish their charges based on the costs of services provided. Although private sector expenses can be severalfold higher than the expenses of their public counterparts, services provided by the private sector are often considered more flexible and personalised; thus, they are more appealing to individuals with the ability and interest in payment for such services. In 2018, private hospitals provided approximately 5000 beds for >370 000 in-patients, which constituted approximately 17% of all in-patients in Hong Kong.[3,4]

The objective of this study was to analyse the antibiogram data collected from private hospitals in Hong Kong by describing the temporal trends of non-susceptibility percentages in this setting. The results may provide insights regarding the current level of antibiotic resistance in private hospitals, in comparison with other settings; they may guide the establishment of future surveillance methods.

Methods

Private hospitals included

The surveillance data submitted by all 12 private hospitals during the period from 2014 to 2019 were included in this study. Please refer to the Acknowledgement for the membership of the Working Group and their affiliated hospitals/institutions.

Targeted bacteria

Considering the antibiotic resistance situations in Hong Kong and other countries, as well as the health effects of various bacterial species, members of the Working Group agreed upon six targeted bacteria for the annual submission of antibiotic susceptibility testing (AST) results, including: *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella* spp, *Pseudomonas aeruginosa*, *Acinetobacter* spp, and *Streptococcus pneumoniae* (since 2015).

Multidrug-resistant organisms

Resistant strains of the targeted bacteria can cause increased morbidity and mortality because of limited treatment options. International health authorities have set clear priorities in their efforts to control multidrug-resistant organisms (MDROs).[5,6]

香港私家醫院的抗菌譜數據：6年回顧研究

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引言：抗生素耐藥性的監測對制訂有效的控制策略至為重要，而香港私家醫院的抗生素耐藥性狀況一直未被有系統地描述。本研究旨在分析私家醫院的抗菌譜數據，並闡述細菌對抗菌素呈現耐藥性的比率的時間趨勢。

方法：本描述性回顧研究使用過去6年（2014-2019）從香港所有私家醫院收集的年度抗菌譜數據，數據包括六種指定細菌及其相應的多重耐藥性細菌。

結果：研究期內，分離株呈現耐藥性的比率維持穩定或有所下降：耐藥性金黃葡萄球菌的患病率保持在20%；超廣譜乙內酰胺酶大腸桿菌及克雷伯氏菌屬的患病率分別保持在約20%至30%及10%至20%；耐多藥鮑氏不動桿菌的患病率有所下降，約2%至8%；耐多藥綠膿假單胞菌的患病率介乎0.0%至0.3%；對青黴素及大環內酯類抗生素呈現耐藥性的肺炎鏈球菌比率分別為2%至9%及71%至79%。這些數值與香港公立醫院和安老院舍的調查結果相若。然而，在香港及外地患病率正在增加的耐碳青霉烯腸道桿菌，在這研究也顯示其患病率有所上升，惟仍處於低水平（大腸桿菌<1%，克雷伯氏菌屬<2%）。

結論：整體而言，香港私家醫院的抗生素耐藥性情況令人滿意，而監測、抗生素導向以及其他感染控制措施仍須持續進行。

The definitions for MDROs used in this study were as follows: methicillin-resistant *S aureus* (MRSA) demonstrated resistance to methicillin, oxacillin, cefoxitin, or cloxacillin; extended-spectrum beta-lactamase-producing (ESBL+) *E coli* or *Klebsiella* spp were defined as *E coli* or *Klebsiella* spp isolates with positive ESBL test results; carbapenem-resistant Enterobacteriaceae (CRE) were defined as *E coli* or *Klebsiella* spp with resistance to a carbapenem (ertapenem, imipenem, or meropenem); multidrug-resistant *P aeruginosa* (MRPA) demonstrated simultaneous resistance to 11 drugs under four classes of antibiotics (beta-lactams, carbapenems, aminoglycosides, and fluoroquinolones); multidrug-resistant *Acinetobacter* spp (MDRA) demonstrated simultaneous resistance to 12 drugs under five classes of antibiotics (cephalosporins, fluoroquinolones, aminoglycosides, beta-lactams [± beta-lactamase inhibitor], and carbapenems). Tests to identify MRPA and MDRA were performed in accordance with Hospital Authority guidelines, although piperacillin assessment was omitted. Multidrug-resistant strains of *S pneumoniae* have not been defined.

Data collection

The following data (concerning the previous calendar year) were annually collected from the Infection Control Teams of individual private hospitals: identification number and date for admission or attendance; location of specimen collection (in- or

out-patient); specimen type (eg, sputum or mid-stream urine) and specimen date (collection, request, or laboratory registration); identification number of isolates within the same specimen; and AST results of each targeted bacterium. Only isolates from clinical specimens (rather than screening specimens) were submitted.

Antibiotic susceptibility testing results

The AST results were divided into three categories: "susceptible", "intermediate", and "resistant". "Intermediate" and "resistant" were collectively regarded as "non-susceptible" (NS). Interpretations by private hospital microbiology laboratories were based on Clinical Laboratory Standards Institute definitions.

Data analysis

Repeated isolates were de-duplicated for each calendar year using the first isolate in each admission, location, specimen group, and targeted bacterium. Importantly, some isolates may not have been tested for susceptibility to all antibiotics listed. The NS percentages for each antibiotic were calculated based on the proportion of isolates tested for that antibiotic. The Cochran–Armitage trend test was used for temporal trends. P values <0.05 were considered statistically significant. All analyses were performed using Stata 14.2 (Stata Corp, College Station [TX], US).

Ethical approval and reporting standards

Patient consent was not obtained because aggregated patient data were used without identifying information.[2] Ethics approval was obtained. This manuscript adheres to the STROBE statement checklist of cross-sectional studies for items to be included.

Results

The total number of isolates per year, NS percentages, and MDRO percentages for isolates from both in- and out-patients were calculated for *S aureus* (Table 1), *E coli* (Table 2), *Klebsiella* spp (Table 3), *P aeruginosa* (Table 4), *Acinetobacter* spp (Table 5), and *S pneumoniae* (Table 6). Key in-patient results are highlighted below.

Staphylococcus aureus

There were approximately 4100 to 5800 *S aureus* isolates per year (Table 1); respiratory specimens comprised 50% and wound/pus swab specimens comprised approximately 35% (online Supplementary Table). The NS percentage for clindamycin ranged from 24% to 31%. The NS percentages for co-trimoxazole and fusidic acid were low (1%-2% and 3%-5%, respectively). *Staphylococcus aureus* showed full susceptibility to both vancomycin and linezolid (ie, NS percentages of 0%). The overall prevalence of MRSA was 19% to 22%. For analysis of blood

TABLE 1. Non-susceptibility in *Staphylococcus aureus* isolates from in- and out-patients, 2014-2019*

	In-patients							Out-patients						
	2014	2015	2016	2017	2018	2019	P value‡	2014	2015	2016	2017	2018	2019	P value‡
No. of isolates†	2817	2992	2901	3056	3602	3730		1233	1309	1297	1568	1864	2062	
Clindamycin	31%§	26%§	26%§	27%§	24%§	26%§	⬇ 0.0047	27%§	26%§	25%§	28%	24%	25%	0.3643
Erythromycin	33%	31%	32%	31%	29%	31%	⬇ 0.0250	32%	32%	29%	33%	28%	29%	⬇ 0.0178
Fusidic acid	3%§	3%§	3%§	5%§	3%§	5%§	0.1034	4%§	4%§	5%§	5%§	4%§	5%§	0.7214
Gentamicin	11%	12%	9%	8%	8%	7%	⬇ <0.0001	8%	8%	5%	8%	6%	6%	⬇ 0.0337
Linezolid	0%§	0%§	0%§	0%§	0%§	0%§	-	0%§	0%§	0%§	0%§	0%§	0%§	0.1124
Penicillin	87%	84%§	87%	86%	84%	84%	⬇ 0.0010	91%	86%§	88%	89%	90%	88%	0.7615
Trimethoprim + sulfamethoxazole	2%	2%	1%	2%	2%	2%	0.6228	2%	3%§	2%	1%	1%	2%	0.0573
Vancomycin	0%	0%§	0%§	0%	0%	0%	-	0%	0%§	0%	0%	0%	0%	-
MRSA‖	22%	20%	19%	21%	19%	21%	0.2103	18%	20%	16%	18%	19%	16%	0.0866

Abbreviation: MRSA = methicillin-resistant *Staphylococcus aureus*

* Data are shown as non-susceptibility percentages towards specific antimicrobials during antibiotic susceptibility testing of *Staphylococcus aureus* isolates, unless otherwise specified. All percentages are rounded to the nearest full percentage point

† No. of isolates refers to annual number of isolates of a particular bacterium

‡ Cochran–Armitage test to identify a temporal trend; arrows show the direction of statistically significant trends

§ Results of susceptibility testing performed for <70% of isolates

‖ Resistance (%) to methicillin, oxacillin, cefoxitin, or cloxacillin among all *Staphylococcus aureus* isolates; percentages are rounded to the nearest full percentage point

TABLE 2. Non-susceptibility in *Escherichia coli* isolates from in- and out-patients, 2014-2019[*]

	In-patients							Out-patients						
	2014	2015	2016	2017	2018	2019	P value[‡]	2014	2015	2016	2017	2018	2019	P value[‡]
No. of isolates[†]	4575	4732	4409	4298	5374	5090		3803	3756	3801	3580	4312	4124	
Amikacin	3%	2%	1%[§]	1%[§]	2%[§]	2%[§]	↓ 0.0012	3%	1%	1%[§]	1%[§]	1%[§]	1%[§]	↓ <0.0001
Amoxicillin + clavulanate	31%	33%	27%	25%	28%	31%	↓ 0.0028	24%	28%	26%	23%	24%	26%	0.4402
Ampicillin	72%	73%	74%	72%	74%	74%	0.1387	68%	72%	74%	72%	73%	71%	↑ 0.0199
Cefotaxime	31%[§]	30%[§]	29%[§]	29%[§]	29%[§]	28%[§]	↓ 0.0035	21%[§]	21%[§]	19%[§]	21%[§]	25%[§]	24%[§]	↑ 0.0035
Ceftazidime	30%[§]	29%[§]	28%	27%	24%[§]	20%[§]	↓ <0.0001	21%[§]	20%[§]	19%	19%[§]	21%[§]	18%[§]	0.1089
Ceftriaxone	30%	29%	28%	27%	28%	26%	↓ 0.0004	20%	21%	20%	20%	22%	21%	0.5242
Cefuroxime	37%	37%	36%	36%	38%	37%	0.9669	24%	25%	25%	24%	28%	27%	↑ <0.0001
Ciprofloxacin	38%	36%	36%	35%	37%[§]	38%[§]	0.4396	30%	29%	30%	29%	34%	33%	↑ <0.0001
Ertapenem	0%[§]	0%	0%	1%[§]	1%	1%[§]	↑ <0.0001	0%[§]	0%	0%	1%[§]	0%[§]	0%	↑ 0.0042
Gentamicin	30%	29%	28%	28%	28%	26%	↓ <0.0001	28%	26%	25%	24%	24%	23%	↓ <0.0001
Imipenem	0%[§]	0%[§]	0%	0%	1%	0%	↑ 0.0018	0%[§]	0%[§]	0%	1%[§]	0%	0%	0.3998
Levofloxacin	37%	35%	33%	31%	33%	36%	↓ 0.0201	28%	27%	26%	26%	29%	32%	↑ <0.0001
Meropenem	0%	0%[§]	0%[§]	0%[§]	1%[§]	1%[§]	↑ <0.0001	0%[§]	0%[§]	0%[§]	1%[§]	0%[§]	0%[§]	0.0622
Nitrofurantoin	7%[§]	8%[§]	6%[§]	4%[§]	6%[§]	4%[§]	↓ <0.0001	8%	6%	6%	4%	4%	3%	↓ <0.0001
Piperacillin + tazobactam	6%[§]	6%[§]	6%[§]	5%[§]	6%[§]	6%[§]	0.2864	4%[§]	3%[§]	4%[§]	4%[§]	4%[§]	5%[§]	0.0747
Trimethoprim + sulfamethoxazole	46%[§]	46%[§]	45%[§]	45%[§]	46%[§]	43%[§]	↓ 0.0412	42%	40%	41%	40%	40%	35%	↓ <0.0001
ESBL[ǁ]	28%	28%	27%	26%	27%	25%	↓ 0.0012	20%	20%	18%	18%	21%	20%	0.6201
CRE[¶]	0.2%	0.2%	0.1%	0.4%	0.7%	0.6%	↑ <0.0001	0.1%	0.0%	0.1%	0.4%	0.1%	0.3%	↑ 0.0158

Abbreviations: CRE = carbapenem-resistant Enterobacteriaceae; ESBL = extended-spectrum beta-lactamase

[*] Data are shown as non-susceptibility percentages towards specific antimicrobials during antibiotic susceptibility testing of *Escherichia coli* isolates, unless otherwise specified. All percentages are rounded to the nearest full percentage point

[†] No. of isolates refers to annual number of isolates of a particular bacterium

[‡] Cochran–Armitage test to identify a temporal trend; arrows show the direction of statistically significant trends

[§] Results of susceptibility testing performed for <70% of isolates

[ǁ] Positive (%) for ESBL isolates among all *Escherichia coli* isolates; percentages are rounded to the nearest full percentage point

[¶] Resistance (%) to carbapenems among all *Escherichia coli* isolates; percentages are rounded to one decimal place

specimens, 29 to 73 isolates were obtained from in-patients each year; of these, 10% to 18% were MRSA.

Escherichia coli

There were approximately 7900 to 9700 *E coli* isolates per year (Table 2); nearly 70% were from urine and approximately 10% were from wound/pus swabs. The NS percentages for amoxicillin-clavulanate and cefuroxime (parenteral) were moderately high (25%-33% and 36%-38%, respectively). The NS percentages for fluoroquinolones were also moderately high (eg, 31%-37% for levofloxacin). The NS percentages for nitrofurantoin and carbapenems were low (4%-8% and 0%-1%, respectively). In terms of MDROs, ESBL+ *E coli* demonstrated moderate prevalence (25%-28%), while carbapenem-resistant *E coli* was uncommon (0.1%-0.7%) among all isolates.

Klebsiella spp

There were approximately 2400 to 3400 *Klebsiella* isolates per year (Table 3); >30% were from urine and >30% were from respiratory specimens. The NS percentages were somewhat high: 16% to 24% for amoxicillin-clavulanate, 25% to 30% for cefuroxime (parenteral), 12% to 18% for levofloxacin, and 18% to 26% for ciprofloxacin. The NS percentage for carbapenems ranged from 0% to 2%, with an increasing trend during the study period. In terms of MDROs, ESBL+ *Klebsiella* demonstrated low prevalence (13%-17%), while carbapenem-resistant *Klebsiella* was uncommon (0.2%-1.3%) among all isolates.

Pseudomonas aeruginosa

There were approximately 1300 to 1800 *P aeruginosa* isolates per year (Table 4); approximately 60% were from respiratory specimens and 15% were

TABLE 3. Non-susceptibility in *Klebsiella* isolates from in- and out-patients, 2014-2019[*]

	In-patients							Out-patients						
	2014	2015	2016	2017	2018	2019	P value[‡]	2014	2015	2016	2017	2018	2019	P value[‡]
No. of isolates[†]	1772	1967	1982	1890	2432	2483		662	728	675	714	789	911	
Amikacin	1%	1%	1%[§]	2%[§]	2%[§]	2%[§]	↑ 0.0111	1%	0%	1%[§]	3%[§]	0%[§]	0%[§]	0.8407
Amoxicillin + clavulanate	20%	19%	16%	18%	19%	24%	↑ 0.0006	21%	21%	23%	21%	20%	25%	0.0954
Ampicillin	99%	99%	99%	99%	99%	100%	↑ 0.0362	99%	100%	100%	100%	100%	100%	↑ 0.0007
Cefotaxime	19%[§]	17%[§]	16%[§]	19%[§]	20%[§]	19%[§]	0.1805	21%[§]	20%[§]	20%[§]	23%[§]	14%[§]	21%[§]	0.2312
Ceftazidime	19%	16%	15%	19%	16%	15%	0.0973	20%	17%	19%	22%	14%[§]	15%[§]	↓ 0.0145
Ceftriaxone	18%	16%	14%	18%	17%	17%	0.7831	19%	18%	16%	21%	15%	17%	0.2005
Cefuroxime	30%	27%	25%	27%	25%	29%	0.5822	23%	25%	26%	28%	24%	28%	0.1698
Ciprofloxacin	22%	20%	18%	21%	22%[§]	26%[§]	↑ 0.0005	22%	18%	21%	22%	20%	23%[§]	0.3458
Ertapenem	0%[§]	1%	1%	1%[§]	2%[§]	1%[§]	↑ 0.0031	1%[§]	1%	1%	1%[§]	1%[§]	0%[§]	0.1090
Gentamicin	9%	9%	7%	9%	9%	8%	0.4476	11%	12%	10%	11%	9%	6%	↓ 0.0002
Imipenem	0%[§]	0%[§]	1%	1%	2%	1%	↑ 0.0018	0%	0%	0%	0%	1%	1%[§]	0.1414
Levofloxacin	17%	15%	12%	16%	16%	18%	↑ 0.0101	17%	15%	16%	17%	15%	16%	0.9409
Meropenem	0%	0%	1%[§]	1%[§]	2%[§]	1%[§]	↑ 0.0003	0%	0%	0%[§]	0%[§]	0%[§]	0%[§]	0.3738
Nitrofurantoin	61%[§]	65%[§]	65%[§]	63%[§]	61%[§]	67%[§]	0.4242	65%[§]	73%[§]	70%[§]	71%[§]	72%[§]	73%[§]	0.0636
Piperacillin + tazobactam	9%[§]	9%[§]	8%[§]	10%[§]	11%[§]	12%[§]	↑ 0.0008	12%[§]	9%[§]	12%[§]	12%[§]	8%[§]	10%[§]	0.3801
Trimethoprim + sulfamethoxazole	24%[§]	25%[§]	23%[§]	26%[§]	24%[§]	21%[§]	↓ 0.0447	26%	23%	25%	23%	22%	22%	0.0883
ESBL[‖]	17%	14%	13%	16%	15%	14%	0.2815	14%	15%	16%	18%	13%	13%	0.2645
CRE[¶]	0.2%	0.7%	0.6%	1.0%	1.3%	0.9%	↑ 0.0005	0.3%	0.7%	0.4%	0.4%	0.4%	0.3%	0.6321

Abbreviations: CRE = carbapenem-resistant Enterobacteriaceae; ESBL = extended-spectrum beta-lactamase
* Data are shown as non-susceptibility percentages towards specific antimicrobials during antibiotic susceptibility testing of *Klebsiella* isolates, unless otherwise specified. All percentages are rounded to the nearest full percentage point
† No. of isolates refers to annual number of isolates of a particular bacterium
‡ Cochran–Armitage test to identify a temporal trend; arrows show the direction of statistically significant trends
§ Results of susceptibility testing performed for <70% of isolates
‖ Positive (%) for ESBL isolates among all *Klebsiella* isolates; percentages are rounded to the nearest full percentage point
¶ Resistance (%) to carbapenems among all *Klebsiella* isolates; percentages are rounded to one decimal place

from wound/pus swabs. The NS percentage for the antipseudomonal beta-lactams piperacillin-tazobactam was generally low (6%-11%), whereas it was very high for ticarcillin-clavulanate (63%-74%). The NS percentages for aminoglycosides were also generally low (3%-11% for gentamicin and 1%-5% for amikacin). The NS percentage for ciprofloxacin remained consistent throughout the study period (14%-15%). The prevalence of MRPA was very low (0.0%-0.3%).

Acinetobacter spp

There were approximately 400 to 500 *Acinetobacter* isolates per year (Table 5); they were mostly from respiratory specimens, wound/pus swabs, and urine (70%, 12%, and 10%, respectively). The NS percentages for sulbactam-containing antibiotics were 7% to 17% (ampicillin-sulbactam) and 8% to 15% (cefoperazone-sulbactam). The NS percentages for fluoroquinolones (eg, ciprofloxacin) ranged from 13% to 25%. The NS percentages for carbapenems were somewhat high values (8%-20% for imipenem and 8%-19% for meropenem). The overall prevalence of MDRA ranged from 2.2% to 7.8%.

Streptococcus pneumoniae

There were approximately 300 to 600 *S pneumoniae* isolates per year (Table 6); approximately 90% were from respiratory specimens. The NS percentages for beta-lactams were low (2%-9% for penicillin, 2%-10% for cefotaxime, and 1%-7% for ceftriaxone). The NS percentages for fluoroquinolones (eg, levofloxacin) were low (0%-3%); the NS percentages for macrolides (eg, erythromycin) were very high (71%-79%). *Streptococcus pneumoniae* showed full susceptibility to vancomycin (ie, NS percentage of 0%).

TABLE 4. Non-susceptibility in *Pseudomonas aeruginosa* isolates from in- and out-patients, 2014-2019[*]

	In-patients							Out-patients						
	2014	2015	2016	2017	2018	2019	P value[‡]	2014	2015	2016	2017	2018	2019	P value[‡]
No. of isolates[†]	1170	1082	1009	1147	1229	1359		301	263	276	326	335	393	
Amikacin	5%	2%	1%	2%	3%	2%	↓ 0.0077	4%	0%	1%	2%	3%	5%	0.1274
Cefepime	9%	5%	3%	5%[§]	5%[§]	11%[§]	0.0694	5%[§]	2%	3%	3%[§]	1%[§]	2%	0.0706
Cefoperazone + sulbactam	15%[§]	14%[§]	14%	16%[§]	16%[§]	16%[§]	0.3291	9%[§]	11%	14%	7%[§]	6%[§]	12%[§]	0.6807
Ceftazidime	7%	5%	5%	6%	6%	10%	↑ 0.0008	2%	2%	2%	6%	3%	3%	0.1759
Ciprofloxacin	15%	14%	14%	14%	14%	15%	0.7532	15%	8%	10%	12%	10%	10%	0.3180
Gentamicin	11%	5%	3%	5%	10%	8%	0.2206	10%	2%	2%	8%	10%	8%	0.1042
Imipenem	19%	17%	15%	17%	17%	19%	0.6445	10%	8%	12%	11%	10%	9%	0.7571
Levofloxacin	22%	17%	17%	19%	19%[§]	23%	0.2834	21%	9%	16%	16%[§]	12%	17%	0.8565
Meropenem	14%	15%	12%	15%	14%	14%[§]	0.9832	5%	7%	14%	7%	6%	6%	0.5237
Piperacillin + tazobactam	8%	6%	6%	7%	8%	11%	↑ 0.0001	5%	2%	4%	4%	2%	4%	0.6871
Ticarcillin + clavulanate	63%[§]	72%[§]	71%[§]	74%[§]	74%[§]	70%[§]	↑ 0.0183	59%[§]	70%[§]	49%[§]	74%[§]	66%[§]	60%[§]	0.7088
MRPA[ǁ]	0.3%	0.0%	0.1%	0.0%	0.1%	0.2%	0.6367	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	-

Abbreviation: MRPA = multidrug-resistant *Pseudomonas aeruginosa*

[*] Data are shown as non-susceptibility percentages towards specific antimicrobials during antibiotic susceptibility testing of *Pseudomonas aeruginosa* isolates, unless otherwise specified. All percentages are rounded to the nearest full percentage point

[†] No. of isolates refers to annual number of isolates of a particular bacterium

[‡] Cochran–Armitage test to identify a temporal trend; arrows show the direction of statistically significant trends

[§] Results of susceptibility testing performed for <70% of isolates

[ǁ] Resistance (%) to multiple antimicrobials among all *Pseudomonas aeruginosa* isolates; percentages are rounded to one decimal place

Discussion

To our knowledge, this is the first analysis of susceptibility data among private hospitals in Hong Kong. Such information provides important guidance for clinical management and infection control measures in the private sector. Here, we consider our findings within local and international contexts.

Staphylococcus aureus

Staphylococcus aureus infections are usually treated by amoxicillin-clavulanate, cloxacillin, or cefazolin unless contra-indicated (eg, in cases of drug allergy) or MRSA is suspected. For mild and superficial infections, oral agents such as clindamycin and co-trimoxazole can be considered, particularly when such treatment is supported by AST results. Routine combination treatment with aminoglycosides for serious infections is no longer recommended because this carries a risk of nephrotoxicity.[7]

Methicillin-resistant *S aureus* bacteraemia is a serious condition with substantial mortality (>30%).[8] Methicillin-resistant *S aureus* is prevalent in Hong Kong; in 2020, it comprised 43.1% of *S aureus* isolates among all clinical specimens in public hospitals, as well as 46.6% of isolates from

blood cultures.[9] Residential Care Home for the Elderly (RCHE) resident carriage rates reportedly range from 30.1% to 37.9%.[10,11] In Australia, MRSA is present in 17% to 22% of blood and other specimens.[12] In the UK, MRSA was present in 6.0% of invasive isolates in 2019[13]; this low rate could be related to the extensive surveillance and infection control efforts that resulted in a remarkable 86% decrease in bloodstream infections (from 7700 to 1114 per year) from 2003 to 2012.[14] Moreover, the prevalence of MRSA among *S aureus* isolates from human specimens decreased from 14% in 2013 to 7% in 2017.[15] The prevalence of methicillin resistance should be considered when selecting empirical therapy for patients with *S aureus* infections.

Vancomycin is a key component of therapy for serious MRSA infections. Consistent with the low prevalence of vancomycin resistance worldwide,[16] vancomycin-resistant *S aureus* was absent from our dataset. *Staphylococcus aureus* rarely demonstrates resistance to linezolid[17]; as expected, *S aureus* isolates in this study showed full susceptibility to linezolid. However, although the NS percentages for co-trimoxazole and fusidic acid were low, these agents should serve as adjuncts only instead of monotherapy in serious infections.

TABLE 5. Non-susceptibility in *Acinetobacter* isolates from in- and out-patients, 2014-2019*

	In-patients							Out-patients						
	2014	2015	2016	2017	2018	2019	P value[‡]	2014	2015	2016	2017	2018	2019	P value[‡]
No. of isolates[†]	372	443	444	358	332	344		44	63	50	89	56	70	
Amikacin	13%	7%	6%	6%	4%	7%	↓ 0.0006	15%	5%	4%	1%	2%	4%	↓ 0.0106
Ampicillin + sulbactam	17%[§]	9%	7%	7%	8%[§]	10%	↓ 0.0282	10%[§]	2%	5%	3%	0%	11%	0.6174
Cefepime	24%	13%	9%	12%	12%[§]	12%	↓ 0.0008	13%	4%	8%	4%	3%[§]	6%	0.3169
Cefoperazone + sulbactam	15%[§]	9%	8%[§]	10%[§]	11%[§]	9%[§]	0.1456	10%[§]	2%	5%	3%[§]	0%[§]	12%[§]	0.7813
Ceftazidime	21%	16%	12%	15%	13%	14%	↓ 0.0120	13%	11%	10%	7%	9%	10%	0.5754
Ciprofloxacin	25%	13%	13%	13%	16%	13%[§]	↓ 0.0023	12%	14%[§]	19%[§]	11%	16%[§]	8%[§]	0.5778
Gentamicin	18%	8%	8%	9%	8%	8%	↓ <0.0001	15%	8%	4%	1%	4%	4%	↓ 0.0164
Imipenem	20%	12%	8%	12%	12%	10%	↓ 0.0018	11%	11%	5%	3%	8%[§]	6%	0.2060
Levofloxacin	21%	12%	11%	12%	11%	13%	↓ 0.0103	12%	4%	13%	9%	10%	10%	0.7847
Meropenem	19%	12%	8%	10%	11%	10%	↓ 0.0070	14%[§]	9%	4%	4%	2%	7%	0.1457
Piperacillin + tazobactam	22%	17%	12%	14%	14%	16%	↓ 0.0246	16%	13%	15%	8%	5%	16%	0.5517
Ticarcillin + clavulanate	42%[§]	32%[§]	26%[§]	22%[§]	16%[§]	32%[§]	↓ 0.0093	25%[§]	4%[§]	19%[§]	11%[§]	0%[§]	17%[§]	0.5695
MDRA[‖]	7.8%	5.2%	2.9%	2.2%	2.7%	3.5%	↓ 0.0006	4.5%	0.0%	2.0%	0.0%	0.0%	0.0%	↓ 0.0311

Abbreviation: MDRA = multidrug-resistant *Acinetobacter* species
* Data are shown as non-susceptibility percentages towards specific antimicrobials during antibiotic susceptibility testing of *Acinetobacter* isolates, unless otherwise specified. All percentages are rounded to the nearest full percentage point
[†] No. of isolates refers to annual number of isolates of a particular bacterium
[‡] Cochran–Armitage test to identify a temporal trend; arrows show the direction of statistically significant trends
[§] Results of susceptibility testing performed for <70% of isolates
[‖] Resistance (%) to multiple antimicrobials among all *Acinetobacter* isolates; percentages are rounded to one decimal place

TABLE 6. Non-susceptibility in *Streptococcus pneumoniae* isolates from in- and out-patients, 2014-2019*

	In-patients							Out-patients						
	2014	2015	2016	2017	2018	2019	P value[‡]	2014	2015	2016	2017	2018	2019	P value[‡]
No. of isolates[†]	N/A	222	242	342	423	365		N/A	46	93	128	142	90	
Cefotaxime	N/A	10%	6%	3%	2%[§]	2%[§]	↓ 0.0001	N/A	3%[§]	4%	1%[§]	0%[§]	2%[§]	0.1861
Ceftriaxone	N/A	7%	4%	2%	1%	2%	↓ 0.0002	N/A	2%	3%	1%	0%[§]	0%	0.0631
Clindamycin	N/A	66%[§]	70%[§]	66%[§]	64%[§]	60%[§]	0.1648	N/A	54%[§]	47%[§]	68%	51%[§]	52%	0.7313
Erythromycin	N/A	79%	77%	78%	71%	72%	↓ 0.0101	N/A	58%	60%	71%	63%	67%	0.3788
Levofloxacin	N/A	1%[§]	3%	0%[§]	3%[§]	1%[§]	0.5823	N/A	3%	1%	4%[§]	0%[§]	0%[§]	0.2218
Penicillin	N/A	9%[§]	3%	2%	2%	3%	↓ 0.0016	N/A	3%	4%	0%	0%	0%	↓ 0.0044
Trimethoprim + sulfamethoxazole	N/A	59%	64%	52%	48%	45%	↓ <0.0001	N/A	36%	44%	50%[§]	27%	34%	0.0838
Vancomycin	N/A	0%	0%	0%	0%	0%	-	N/A	0%	0%	0%	0%	0%	-

Abbreviation: N/A = not applicable
* Data are shown as non-susceptibility percentages towards specific antimicrobials during antibiotic susceptibility testing of *Streptococcus pneumoniae* isolates, unless otherwise specified. All percentages are rounded to the nearest full percentage point
[†] No. of isolates refers to annual number of isolates of a particular bacterium
[‡] Cochran–Armitage test to identify a temporal trend; arrows show the direction of statistically significant trends
[§] Results of susceptibility testing performed for <70% of isolates

Escherichia coli and *Klebsiella* spp

Non-extended-spectrum beta-lactamase-producing isolates

Susceptible strains of *E coli* and *Klebsiella* spp are usually treatable by amoxicillin-clavulanate or cefuroxime.[18] However, ESBL-producing strains should be suspected in cases of serious infection because of Enterobacteriaceae prevalence in Hong Kong, where ESBL-producing *E coli* is regarded as a critical MDRO.[18]

Extended-spectrum beta-lactamase-producing isolates

Community spread is an important source of ESBL-related infections; food animals are presumed to serve as a major reservoir.[19] For instance, the isolation rate from pig offal is 52.4%.[20] Among public hospitals, the percentage of resistance to third-generation cephalosporins ("3GC") as a surrogate marker for ESBL production among *E coli* is approximately 26%[9]; this value is similar to our findings. Furthermore, 17.0% to 18.6% of *E coli* isolates from community urinary specimens demonstrate ESBL-producing activity.[9] Among RCHE residents, 55.9% were reported to be carriers of ESBL-producing bacteria.[9] In the UK, 12% of *E coli* isolates from blood specimens showed ESBL-producing activity[15]; Singaporean public hospitals identified ESBL-producing activity in 25.2% of *E coli* isolates and 28.2% of *Klebsiella* isolates in 2017.[21] From 2014 to 2019, the percentages of ESBL-producing isolates among *Klebsiella* isolates at public hospitals in Hong Kong were 19% to 22%.[9]

Surveillance data regarding ESBL prevalence can be affected by changes in laboratory practice over time. Specifically, the Clinical and Laboratory Standards Institute revised the cephalosporin breakpoints in 2014, thus eliminating the need to perform ESBL testing for clinical management—testing remains necessary for some infection control purposes and epidemiological investigations.[22] However, not all laboratories have adopted the revised approach and the change remains controversial.[23] The clinical specimen data in this study indicate that all participating private hospitals have continued to perform ESBL testing for Enterobacteriaceae isolates.

For serious infections caused by ESBL-producing organisms, carbapenems are the most effective treatments.[18]

Carbapenem resistance

Our findings indicate that carbapenem resistance remains uncommon but is increasing. Among the known carbapenem resistance mechanisms, carbapenemase production is the most important from an infection control perspective, considering its propensity to spread to other organisms.[24] Carbapenem-resistant Enterobacteriaceae is often resistant to multiple classes of antibiotics, which hinders treatment.[25] The prevalence of this high-priority MDRO is increasing worldwide,[5,6] presumably in relation to heightened awareness, modified screening practices, and increased transmission.[26]

Public hospitals in Hong Kong reported increasing NS to carbapenem among *E coli* isolates from 0.2% in 2016 to 0.4% in 2020 (NS percentage of 1.1%-1.8% for *Klebsiella*).[9] Carbapenem-resistant *E coli* has become a major target of infection control efforts in public hospitals.[27] In contrast, CRE was not found among RCHE residents in a 2018 study.[10]

The limited treatment choices for CRE infection include beta-lactam agents such as ceftazidime-avibactam (inactive against metallo-beta-lactamases), aztreonam (active against metallo-beta-lactamases alone), and cefiderocol (active against all major classes of beta-lactamases); the choices also include non-beta-lactam agents such as intravenous colistin or tigecycline (if no alternative is available). A single dose of oral fosfomycin may be used for uncomplicated cystitis. Generally, these agents are either less readily available in Hong Kong (beta-lactams)[28] or may cause severe adverse effects (eg, nephrotoxicity for colistin and increased all-cause mortality for tigecycline).[29]

Pseudomonas aeruginosa

Piperacillin ± tazobactam and ticarcillin-clavulanate are commonly recommended for the treatment of *P aeruginosa* infections. Our data indicated susceptibility to piperacillin-tazobactam and a lack of susceptibility to ticarcillin-clavulanate. Thus, the use of ticarcillin-clavulanate should be supported by AST results. For serious infections, combination treatment (eg, beta-lactam and aminoglycoside) may be required to achieve synergistic effects.[18]

The prevalence of MRPA in our study was consistently low (0.0%-0.3%), consistent with data from public hospitals (0.02%-0.06% for 2014-2018).[27] Data from other sources indicate higher prevalences of MRPA (eg, 12%-14% among blood isolates, according to the European Centre for Disease Prevention and Control).[30] However, the definition of MRPA can vary among sources.[31] For instance, the European Centre for Disease Prevention and Control uses combined resistance to three or more antibiotic groups. The strict definition of simultaneous resistance to four antibiotic classes used in Hong Kong may at least partially contribute to the overall low prevalence.

Acinetobacter spp

Acinetobacter can survive for prolonged periods in dry environments, which facilitates nosocomial

transmission.[32] Sulbactam-containing beta lactams are highly effective against *Acinetobacter*.[18]

Similar to MRPA, definitions of MDRA vary. In the UK, multi-resistant *Acinetobacter* spp or multi-resistant *Acinetobacter baumannii* (MRAB) demonstrate co-resistance to aminoglycosides and 3GC; the term MRAB-C refers to MRAB with carbapenem resistance.[33] Using an MDRA definition identical to ours, public hospitals reported a decreasing MDRA prevalence (from 24% to 9% in 2014 to 2018[27]); another study indicated that 0.6% of 1028 RCHE residents were carriers of MDRA.[10] In analyses of carbapenem-resistant *Acinetobacter* alone, the prevalence in public hospitals ranged from 44% in 2014 to 53% in 2019[11]; 9.1% of RCHE residents were carriers.[11]

Antibiotic-resistant *Acinetobacter* is classified as a 'critical threat' by the World Health Organization and an 'urgent threat' by the US Centers for Disease Control and Prevention. Thus, although its prevalence is decreasing, MDRA should be closely monitored for any rebound.

Streptococcus pneumoniae

The primary treatments for invasive pneumococcal infection are beta-lactams (penicillin G or 3GC) for susceptible strains and vancomycin for penicillin-resistant strains (plus 3GC for meningitis).

In Europe, the prevalence of penicillin resistance among *S pneumoniae* isolates is approximately 12% to 14% (2015-2019, invasive isolates)[30]; the prevalence of macrolide resistance is approximately 14% to 16%. In Australia, these values are 3% to 6% and >20% to 25%, respectively.[12] Our findings indicated a low NS percentage for penicillin but a very high NS percentage for macrolides; these findings are compatible with the recommendation that macrolides should not be used as monotherapy during empirical treatment of infections in Hong Kong.[18] Fluoroquinolone resistance was previously reported to be high[34] (>13.3% for levofloxacin), although recent data from laboratory surveillance by the CHP in the community setting indicate lower resistance (0.0%-4.4% in 2014-2019).[9] Our data are similar to the community values, as expected for an organism that most commonly causes community-acquired pneumonia.[18]

Since the introduction of pneumococcal vaccination, the disease burden caused by penicillin- and erythromycin-resistant strains has decreased in the US.[5] In Hong Kong, approximately 180 invasive pneumococcal infections are reported each year.[35] Similar to other countries, Hong Kong has gradually made pneumococcal vaccination available to children, older adults, and high-risk individuals for >10 years.[35] As vaccine coverage increases, it would be prudent to assess the changes in disease burden caused by resistant strains of pneumococcus.

Implications

Compared with public hospitals, private hospitals tend to have lower MDRO prevalences, particularly for MRSA and MDRA, while following an overall similar prevalence pattern (ie, increasing CRE, stable ESBL, decreasing MDRA, and negligible MRPA). Nonetheless, further MDRO monitoring (particularly for CRE and MDRA) is warranted.

There may be multiple reasons for the lower overall NS percentages, which could not be assessed using the data collected in this study (eg, case composition, antibiotic consumption, and diagnostic practices). However, the physical environment and isolation policy within private hospitals may contribute to a generally lower NS percentage. A key private hospital prescribes single-room isolation for all MDRO carriers with strict contact precautions.[36] A more spacious environment with fewer beds per cubicle could theoretically lead to a lower cross-contamination rate through indirect contact (eg, by shared toilets), which is a main route for MDRO spread. With respect to staffing, the infection-control-nurse-to-bed ratio may be more likely to meet (personal communication) the level recommended by the CHP (1:150 for acute hospitals).[37] Sufficient single-patient rooms and staffing (eg, nursing) are regarded as crucial components of efforts to reduce healthcare-associated colonisations and infections.[38,39]

Notably, the NS percentage was generally lower among out-patient isolates than among in-patient isolates, consistent with the reported literature.[40]

Strengths

First, the AST data were stratified by both location (in- and out-patient) and specimen groups. The stratification of antibiogram data can facilitate antibiotic stewardship programmes by exposing important differences in susceptibility.[41] Second, the collected data spanned a 6-year period with a large number of isolates, enabling the application of a consistent methodology that can enhance trend analysis accuracy. Third, MDRO prevalences were collected; such data are not required by the World Health Organization[42] but are frequently regarded as key information in international surveillance reports.[5,12,15,30]

Limitations

Cautious interpretation of the findings is necessary. First, a subset of the antibiotic-bacterium combinations were tested in a smaller proportion of isolates (<70%), which could have led to biased assessment. Second, because member hospital laboratories had different levels and types of accreditation, inter-laboratory practice variations could have influenced the AST results. Third, the

specimen group classification was arbitrary. Fourth, differences in case composition among hospitals may lead to misleading conclusions if direct head-to-head comparison is performed. Finally, CRE was defined by susceptibility results, rather than specific tests for carbapenemase detection.

Conclusion

Our findings provide important insights concerning antibiotic resistance at private hospitals in Hong Kong. Although the overall situation in private hospitals is considered satisfactory, there remains a need for sustained efforts in resistance surveillance, infection control, and antibiotic stewardship.

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