Emergence of Multidrug- and Pandrug- Resistant *Pseudomonas aeruginosa* from Five Hospitals in Qatar

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SUMMARY

Background: A global rise in multidrug-resistant (MDR) nosocomial infections has led to a significant increase in morbidity and mortality. MDR Gram-negative bacteria (GNB) are recognised for rapidly developing drug resistance. Despite *Pseudomonas aeruginosa* being the second most common GNB isolated from healthcare associated infections, the magnitude of MDR *P. aeruginosa* (MDR-PA) has not been evaluated in Qatar.

Aim: To assess the prevalence and antimicrobial susceptibility patterns of MDR-PA from 5 major hospitals in Qatar.

Methods: A total of 2533 *P. aeruginosa* clinical isolates were collected over a one-year period. MDR-PA was defined as resistance to at least one agent of ≥ 3 antibiotic classes. Clinical and demographic data were collected prospectively.

Findings: The overall prevalence of MDR-PA isolates was 8.1% (205/2533); the majority of isolates were from patients exposed to antibiotics during 90 days prior to isolation (85.4%, 177/205), and the infections were mainly hospital-acquired (95.1%, 195/205) with only 4.9% from the community. The majority of MDR-PA isolates were resistant to cefepime (96.6%, 198/205), ciprofloxacin, piperacillin/tazobactam (91%, 186/205), and meropenem (90%, 184/205). Patient comorbidities with MDR-PA were diabetes mellitus (47.3%, n=97), malignancy (17.1%, n=35), end-stage renal disease (13.7%, n=28) and heart failure (10.7%, n=22).

Conclusion: There was a significant prevalence of MDR-PA in Qatar, primarily from healthcare facilities and associated with prior antibiotic treatment. There was an alarming

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level of antimicrobial resistance to carbapenems. Our results are part of a national surveillance of MDR to establish effective containment plans.

Introduction

Nosocomial infections are a major cause of morbidity and mortality in hospitals worldwide. Gram-negative bacteria (GNB) including *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and extended-spectrum β-lactamase (ESBL) producing-Enterobacteriaceae have increasingly been associated with healthcare-associated infections (HAIs) [1,2]. Amongst multidrug-resistant (MDR) microorganisms, GNB warrant distinct attention due to their potential to develop extensive resistance [2—4]. The National Nosocomial Infections Surveillance System in the United States reported during 1986—2003 that *P. aeruginosa* was the cause of 18% of cases of pneumonia, 16% urinary tract infections and 3% of blood stream infections [5]. In Europe, isolates of *P. aeruginosa* have become increasingly resistant to standard antipseudomonal therapy, with carbapenem resistance exceeding 10% [6]. To highlight the extent of the problem, the World Health Organization (WHO) published its foremost list of antimicrobial resistant "priority pathogens" including resistant *A. baumannii*, *P. aeruginosa*, and Enterobacteriaceae [7]. Several similar studies emphasized the alarming increase in MDR amongst GNB including *P. aeruginosa* [6,8—10].

P. aeruginosa is naturally resistant to many antibiotics with multiple mechanisms including the production of β-lactamases, presence of efflux pumps, formation of permeability barriers and modification of the outer membrane [11]. Antimicrobial resistance (AMR) in *P. aeruginosa* is often a consequence of a combination of intrinsic and acquired mechanisms obtained through transfer of mobile genetic elements [12]. These multiple factors have led to the emergence of MDR- *P. aeruginosa* (MDR-PA) as a serious global healthcare challenge with significant morbidity and mortality [6,13,14]. The burden of MDR infections has also impacted healthcare with significant economic costs [15].

To monitor the spread of MDR organisms, it has been advocated to adopt surveillance mechanisms across healthcare facilities to examine the trends and unforeseen outcomes associated with MDR infections [15,16]. Based on local microbiological reporting, there was a high prevalence of GNB isolated from patients at Hamad Medical Corporation (HMC) in Qatar, with *P. aeruginosa* being second most prevalent. From 2009 - 2014 there was a noticeable increase in resistance to both colistin and meropenem [17]. The present study aimed to evaluate the prevalence and antimicrobial susceptibility patterns of MDR-PA, together with clinical characteristics from five different hospitals between 2014 and 2015.

Methods

Ethical considerations, study population and sample collection

Ethical approval was obtained from the Institutional Review Board at the Medical Research Council, HMC, which complies with international ethical standards (Committee Protocol number IRGC-01-51-033).

The study was conducted on routine outpatient and inpatient specimens received at the Microbiology section at the Department of Laboratory Medicine and Pathology at HMC, Qatar from five separate hospitals. The HMC is a non-profit healthcare corporation that manages five specialized hospitals: Hamad General Hospital (HGH) with a capacity of 603 beds dealing with acute care including intensive care beds; Rumailah Hospital (RH) with 602 beds comprising specialized surgical units as well long-term care facilities; the Women's Hospital (WH) with 319 beds for maternal and gynaecological health; National Centre for Cancer Care and Research (NCCCR) with 46 beds for cancer management including a haemato-oncology unit; and the Heart Hospital (HH) with 116 beds primarily for cardiac and cardiothoracic surgery. Infection control and prevention is managed through a corporate infection control committee overseeing all specialised facilities.

Patient demographic data were collected from electronic medical record using data collection forms with no direct communication between data collector and patients, primary teams or infectious disease team following the patients. The clinical data were collected by an infectious disease physician.

Clinical isolate identification and antimicrobial susceptibility test (ID/AST)

A total of 2533 *P. aeruginosa* isolates were collected between October 2014 and September 2015 from various clinical specimens as part of the routine care. The bacterial isolates were analysed using the BD Phoenix™ Automated Microbiology System in compliance with the Clinical and Laboratory Standards Institute (CLSI). Species identification was confirmed, when necessary by Matrix-Assisted Laser Desorption Ionization—Time of Flight Mass Spectrometry (MALDI-TOF MS) using the Bruker Daltonics MALDI Biotyper (Billerica, MA, USA), according to the manufacturer's instructions. All MDR-PA isolates were preserved at -70°C for the further analysis.

The antimicrobial susceptibility analysis was performed using the Phoenix analyzer, as described previously [18,19]. When AST analyses terminated due to the lack of emulsification of mucoid strains, the antimicrobial susceptibility of mucoid *P. aeruginosa* strains was tested manually using MIC test strips (Liofilchem®, Diagnosticis, Italy) according to the manufacturer's instructions. The results were interpreted using the CLSI reference breakpoints. Isolates classified as intermediate or resistant were defined as non-susceptible. The standard reference strains, *Escherichia coli* ATCC 25922, *E. coli* ATCC 35218, and *P. aeruginosa* ATCC 27853, were used for quality control according to the CLSI guidelines. Using a standardized data collection tool, clinical and microbiological characteristics of MDR-PA were obtained and analysed.

Table I
Demographic profile of patients with MDR-PA infections at participating Qatar hospitals.

Characteristics	Hospital[a,b]				Total (%)	p-value
	HGH	RH	NCCCR	HH		
	Frequency (%)					
Age group						
Paediatric <14 years	12 (7.2)	0	0	0	12 (5.9)	0.535
Adult 14—65 years	107 (64.5)	19 (67.9)	4 (66.7)	2 (40)	132 (64.4)	
Geriatric >65 years	47 (28.3)	9 (32.1)	2 (33.3)	3 (60)	61 (29.8)	
Nationality						
Qatari	56 (33.7)	7 (25)	0	2 (40)	65 (31.7)	0.279
Non-Qatari[c]	110 (66.3)	21 (75)	6 (100)	3 (60)	140 (68.3)	
Gender						
Male	126 (75.9)	23 (82.1)	4 (66.7)	1 (20)	154 (75.1)	0.027
Female	40 (24.1)	5 (17.9)	2 (33.3)	4 (80)	51 (24.9)	
Location						
Outpatient	44 (26.5)	3 (10.7)	0	1 (20)	48 (23.4)	
Inpatient	72 (43.4)	24 (85.7)	6 (100)	2 (40)	104 (50.7)	0.001
Inpatient ICU	50 (30.1)	1 (3.6)	0	2 (40)	53 (25.9)	
Stay in ICU >5 days	47 (28.3)	1 (3.6)	0	2 (40)	50 (24.4)	0.853
Clinical diagnosis[d]						
Infection	74 (44.6)	6 (21.4)	3 (50)	1 (20)	84 (41)	0.072
Colonization	92 (55.4)	22 (78.6)	3 (50)	4 (80)	121 (59)	
Acquisition						
Hospital	156 (94)	28 (100)	6 (100)	5 (100)	195 (95.1)	0.481
Community	10 (6)	0	0	0	10 (4.9)	
Total	166 (100)	28 (100)	6 (100)	5 (100)	205 (100)	

[a] HGH, Hamad General Hospital; RH, Rumailah Hospital; NCCCR, National Centre for Cancer Care and Research; HH, Heart Hospital.

[b] WH, No MDR-PA isolates were recovered from the Women's hospital.

[c] Non-Qatari; Algerian, Bahraini, Bangladeshi, British, Egyptian, Indian, Iranian, Iraqi, Jordanian, Lebanese, Nepalese, Omani, Pakistani, Palestinian, Saudi, Sudanese, Syrian, Tunisian and Yemeni.

[d] Infection - when a patient received antibiotics based on the primary team's decision. Colonization - if patient results were conveyed but no treatment was initiated.

Exclusion criteria

Bacterial isolates of the same species and same antimicrobial susceptibility pattern in a patient isolated within 30 days regardless of the site of isolation (except blood culture and sterile body fluid isolates) were excluded. Isolates with major differences in susceptibility patterns were considered as new even if isolated within 30 days.

Statistical analysis

Categorical data such as patients' demographic, clinical characteristics and outcome, in addition to susceptibility patterns and prevalence of MDR-PA were presented as frequency and percentages. Continuous data such as age were expressed as median and interquartile range. Results with $p<0.05$ were considered statistically significant. All statistical analyses were done using Statistical Packages for Social Sciences (SPSS) v. 21.0 (Inc. Chicago, IL).

Results

Demographic profile of study population

The demographic profile of the study population (205 patients) from four of the five hospitals is summarized in Table I. Since there was no MDR-PA isolated from the WH, this hospital was excluded from the demographic profile. The majority of patients were male (74.6%, n=153), with a median age of 56 years (interquartile range 42.0—69.0). According to the age group, 64.4% (n=132) of the patients were 14—65 years, followed by 29.8% were >65 years (n=61), and 5.9% were <14 years (n=12). The majority of patients were non-Qatari nationals 68.3% (n=140) in line with the country demographics, including patients from the Middle East (31.2%), Indian Subcontinent (30.2%), Western countries (3.4%), North Africa (2.9%) and others (0.5%). Most of the MDR-PA infections were from inpatients (76.6%, n=157) and only 23.4% (n=48) were outpatients. Among the infected patients, 59% (n=121) were colonized, while 41% (n=84) were infected and the majority were hospital acquired (95.1%, n=195), while only 4.9% (n=10) were community acquired (Table I).

Prevalence and distribution of MDR-PA isolates

The overall prevalence of MDR-PA was 8.1% (n=205/2533). The MDR-PA organisms were isolated from different clinical samples including respiratory (44.9%, n=92) of which 6.9% (n=12) were from cystic fibrosis patients, skin and soft tissue (26.3%, n=54), urine (23.4%, n=48), blood (2.4%, n=5), and others (2.9%, n=6) (Table II). Among the MDR-PA isolates, 92.7% (n=190) were non-mucoid and only 7.3% were mucoid (n=15).

Table II
Distribution and prevalence of MDR *P. aeruginosa* from five participating hospitals in Qatar.

| Infection site | Hospital[a] | | | | | PA (n)[b] | MDR-PA (n)[b] | MDR-PA[b] (%) |
| | HGH | HH | NCCCR | RH | WH | | | |
	Frequency							
Respiratory	707	74	51	163	3	998	92	9.2%
SSI[c]	603	16	43	169	59	890	54	6.1%
Urine	421	22	18	30	13	504	48	9.5%
Blood	49	3	8	0	2	62	5	8.1%
Bone	12	0	1	0	0	13	0	0
Other[d]	52	1	1	4	8	66	6	9.1%
PA (n)	1844	116	122	366	85	2533	205	8.1%
MDR-PA (n)	166	5	6	28	0	205	205	
MDR-PA (%)	9%	4.3%	4.9%	7.7%	0	8.1%		

[a] HGH: Hamad General Hospital, RH: Rumailah Hospital, NCCCR: National Center for Cancer Care and Research, HH: Heart Hospital.
[b] PA, *Pseudomonas aeruginosa*; n, number of isolates; MDR, multidrug resistant.
[c] SSI, skin & soft tissue: abscess, biopsy, ear, swab, tissue and wound.
[d] Other: eye, sterile body fluid, non-sterile body fluid and catheter tip.

Of the mucoid *P. aeruginosa*, 11 were isolated from adult and 4 from paediatric patients and these were isolated from the respiratory tract (73.3%, n=11), urine (13.3%, n=2), and one each (6.6%) from wound and sterile body fluid samples, respectively. In addition, 2.4% (n=5) of the MDR-PA isolates were PDR-PA and these were isolated from urine (n=4) and respiratory (n=1) samples, with 3 PDR-PA infections from inpatients and 2 from outpatients. Majority of the isolates were from HGH (81%, n=166), followed by RH (13.7%, n=28), NCCCR (2.9%, n=6) and HH (2%, n=4). None of the MDR-PA samples were collected from WH during the study period (Table II).

Co-morbidity factors associated with MDR-PA infection

The most common co-morbidity factors for infected patients (Figure 1) were extensive health care contact 92.7% (n=190), followed by history of exposure to antibiotics 90 days prior to isolation at 85.4% (n=175) (Figure 2). Other co-morbidity included invasive devices 69.3% (n=142), isolation of prior susceptible strain of *P. aeruginosa* 62.0% (n=127), history of a MDR infection or colonization 60.5% (n=124), diabetes mellitus 47.3% (n=97), co-infection with another microorganisms 25.4% (n=52), malignancy 17.1% (n=35), chronic pulmonary disease 29.0% (n=14.1), end-stage renal disease 13.7% (n=28), heart failure 10.7% (n=22), renal stone 9.8% (n=20), cystic fibrosis 5.9% (n=12), post-transplantation 3.4% (n=7), and chronic liver disease 2.0% (n=4).

Antimicrobial susceptibility

The majority of the clinical isolates (96.6%, 90.7%, and 90.2%) were resistant to cephalosporins (cefepime), β-lactam/β-lactamase inhibitor combination (piperacillin/tazobactam) and carbapenem (meropenem), respectively (Figure 3). In addition, the clinical isolates showed high resistance (91.2%) to ciprofloxacin but relatively less resistance to aminoglycosides such as gentamicin, amikacin and tobramycin (73.2%, 58% and 54.6%, respectively) and to colistin (3.4%).

Clinical diagnosis and outcome of MDR-PA infection

The majority of patients were colonized (59%, n=121) rather than infected; sepsis was noted in 21.5% (n=44) and septic shock in 19.5% (n=40) (Table III). The antibiotic treatment of patients having MDR-PA was primarily with meropenem (30.2%, n=62), followed by colistin (25.9%, n=53), amikacin (6.3%, n=13), piperacillin/tazobactam (5.9%, n=12), ciprofloxacin (2.9%, n=6), gentamicin (2.9%, n=6), and finally, cefepime (2%, n=4). In some cases, a combination of 1, 2, 3 or 4 antibiotics were used in 11.2% (n=23), 24.9% (n=51) and 3.4% (n=7) 1.5% (n=3) cases, respectively, in comparison to 59% (n=121) where no antibiotics were used (Table III). Furthermore, the clinical outcome of MDR-PA infected patients showed that the majority improved (60%, n=123) after treatment, where 26.3% (n=54) were cured and 14.2% (n=29) died, amongst these 4.9% (n=10) died within 30 days after infection, and 2.4% (n=5) relapsed (Table III).

Discussion

In the coming decades, it is estimated that the morbidity and mortality from AMR will exceed any other acute or chronic illness by 2050 with a projected annual global mortality of nearly 10 million people if no action is taken to curtail the problem [20]. At the local hospital level, the potential presence or development of AMR is an important factor when dealing with patients with confirmed or suspected bacterial infections, since it will have direct impact on the success of initial management as well future development of resistance.

The present study is the first national evaluation of the prevalence of MDR-PA in Qatar assessing both clinical and microbiological aspects. The overall prevalence of MDR-PA was 8.1%, similar to other reports from Western countries [21,22]. However, the findings are in contrast with reports from the region, including Saudi Arabia (3% in 2004 and 2% in 2005) and Pakistan (2.7%), demonstrating lower levels of MDR-PA [23,24]. Most of the MDR-PA cases in the present study were hospital acquired and the patients had prior history of infection or colonization by susceptible *P. aeruginosa* strains. These
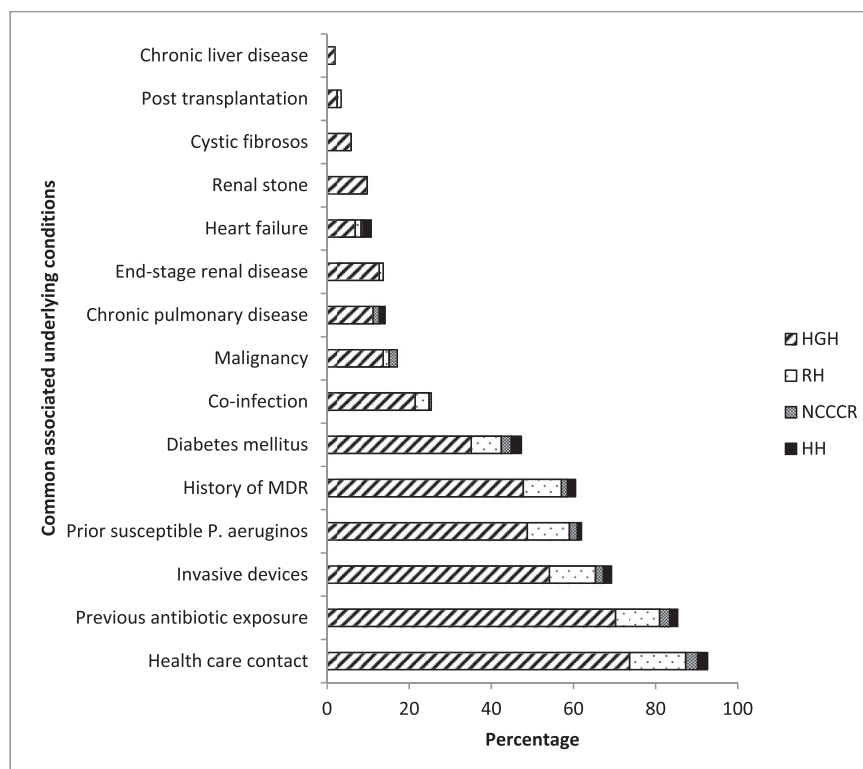
Figure 1. Common associated underlying conditions of patients with MDR-PA infections from 4 hospitals in Qatar. HGH, Hamad General Hospital; RH, Rumailah Hospital; NCCCR, National Center for Cancer Care and Research; HH, Heart Hospital. Co-infection are associated with the following organisms: *Achromoba xylosoxidans, Bacteroid fragilis, Bacteroid vugatus, E. coli, Entrococcus fecalis, Candida glaberata, Candida spp., Candida tropicalis, Citrobacter froundi, Enterobacter cloacae, K. pneumonia, Klebsiella oxytoca, Proteus mirabilis, Meticillin-resistant Staphylococcus aureus, Meticillin-sensitive Staphylococcus aureus, Serratia marcescenes, Steno-trophomonas maltophilia, Streptococcus group C.* Invasive devices involves exposure to breast implant, central line, colostomy bag, cardiac resynchronization therapy implantable cardioverter defibrillator, double J stent (ureteral stent), external ventricular drain, external fixation of the pelvis, Foley's catheter, internal drain, inferior vena cava filter, mechanical ventilator, nephrostomy, nasogastric tube, peritoneal dialysis catheter, permanent pacemaker, right upper abdomen drain, suprapubic catheter, surgical drain, tibial artery stent, tracheotomy tube and ventriculo-peritoneal shunt. Extensive health care contact involves the respiratory tract, urinary system, skin and soft tissue and blood.

findings suggest that the MDR-PA could be endemically circulating in the hospitals or may be related to a novel emergence of resistance in previously susceptible isolates. Although these are plausible explanations, genetic epidemiological investigation was beyond the scope of the study. We found that MDR-PA was isolated from different clinical specimens and, often from different locations in the same patient. We observed that the distribution and rank order of *P. aeruginosa* isolates by body site was generally in agreement with isolates obtained in the Global SENTRY Antimicrobial Surveillance Program, 1997–1999 [21]. The respiratory tract was found to be the most frequent source of *P. aeruginosa* isolates, followed by skin and soft tissue, urine, and blood. Conversely, it is worth highlighting that 41% of the patients were identified as being infected at the time of first isolation, while the majority of cases were colonized (59%). This finding is important for physicians, as they must be vigilant to distinguish between these entities and avoid excessive initial treatment.

A noticeable feature in this study is the associative characteristic co-morbidities with MDR-PA acquisition (primarily diabetes mellitus, end-stage renal disease, malignancy, heart failure and chronic lung diseases), although this is an observational correlation probably stemming from association of comorbidities with prolonged hospital stay and infection acquisition. Such associations have been observed in other AMR morbidity and mortality studies [25,26]. Additional observed risk factors included: history of preceding healthcare contact, insertion of invasive devices and prior infection with susceptible strains, which are in agreement with similar findings of case-control studies conducted in other institutions (Figure 1) [26–28].

Examining the associated outcome with MDR-PA bacteraemia; the overall mortality rate was 40%, which correlates with other studies, however, the risk significantly escalates with serious co-morbidities reaching 67%, and this implicates pre-existing conditions as major contributing factors to the high mortality rate [25,26,28]. There was also a clear difference in the incidence of MDR-PA between the different hospitals. The majority of the MDR-PA isolates were from HGH at 81% (n=166), the busiest acute hospital with the highest number of critical care beds, whereas no MDR-PA were recovered from WH, the maternal hospital. This is likely due to the younger age of the patients, absence of chronic medical conditions, a shorter hospital stay, fewer procedures and lower antibiotic exposure.
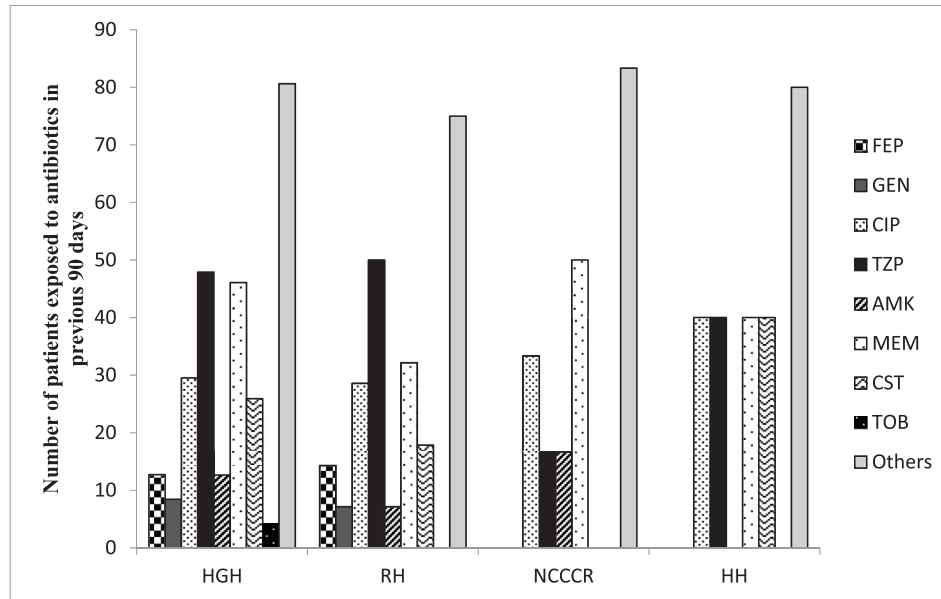
Figure 2. Patient history of antibiotic exposure during the 90 days prior to MDR-PA isolation. Hospitals; HGH, Hamad General Hospital; RH, Rumailah Hospital; NCCCR, National Center for Cancer Care and Research; HH, Heart Hospital. Antibiotics; AMK, amikacin; CIP, ciprofloxacin; CST, colistin; FEP, cefepime; GEN, gentamicin; MEM, meropenem; TZP, piperacillin/tazobactam; TOB, tobramycin. Others include the following antibiotics: azithromycin, ceftazidime, ceftriaxone, cefuroxime, cefixime, clarithromycin, clindamycin, cloxacillin, doxycyclin, ertapenem, erythromycin, fluroquinolone, levofloxacin, linezolid, meropenem, metronidazole, minocycline, moxifloxacin, nitrofurantoin, rifampcin, septrin, teicoplanin, tigecycline and vancomycin.

It was alarming to find five PDR-PA isolates from different patients that were also resistant to colistin. These patients had a typical history of multiple comorbidities necessitating encounter with different healthcare facilities with different invasive procedures, exposure to multiple broad-spectrum antibiotics and subsequently acquiring the serious infections.

Two patients with complicated urinary tract infections received initial empirical antibiotic treatment with subsequent improvement despite the isolates exhibiting PDR resistance patterns, which raises the question of *in vivo* behaviour of phenotypically resistant strains. The isolates from the remaining three cases were considered as colonized and did
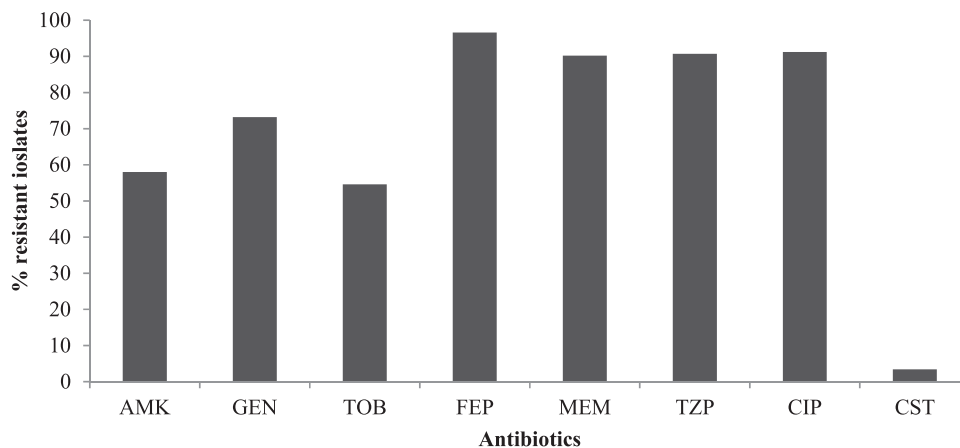
	AMK	GEN	TOB	FEP	MEM	TZP	CIP	CST
Resistance no. (%)	119 (58.0)	150 (73.2)	112 (54.6)	198 (96.6)	185 (90.2)	186 (90.7)	187 (91.2)	7 (3.4)
Range	0.75-256	0.25-256	0.38-256	1.5-256	0.125-32	1-256	0.125-32	0.19-8
MIC$_{50}$	32	48	24	64	32	256	32	1.5
MIC$_{90}$	256	256	256	256	32	256	32	2

Figure 3. Susceptibility patterns of MDR-PA isolates. AMK, amikacin; GEN, gentamicin; TOB, tobramycin; FEP, cefepime; MEM, meropenem; TZP, piperacillin-tazobactam; CIP, ciprofloxacin; CST, Colistin.

Table III
Clinical diagnosis and outcome of patients with MDR-PA infection.

Characteristics[c]	Hospital[a,b]				Total (%)	p-value
	HGH	RH	NCCCR	HH		
	Frequency (%)					
Disease severity						
Colonization	92 (55.4)	22 (78.6)	3 (50)	4 (80)	121 (59)	0.184
Sepsis	36 (21.7)	5 (17.9)	2 (33.3)	1 (20)	44 (21.5)	
Septic shock	38 (22.9)	1 (3.6)	1 (16.7)	0	40 (19.5)	
Antibiotic treatment						
Amikacin	12 (7.3)	0	1 (16.7)	0	13 (6.3)	0.32
Meropenem	53 (32.3)	5 (17.9)	3 (50)	1 (20)	62 (30.2)	0.3
Piperacillin/tazobactam	11 (6.7)	1 (3.6)	0	0	12 (5.9)	0.76
Colistin	47 (28.7)	4 (14.3)	1 (16.7)	1 (20)	53 (25.9)	0.4
Ciprofloxacin	6 (3.7)	0	0	0	6 (2.9)	0.69
Gentamycin	6 (3.7)	0	0	0	6 (2.9)	0.69
Cefepime	3 (1.8)	0	1 (16.7)	0	4 (2)	0.06
Tobramycin	0	0	0	0	0	NA
Number of antibiotic treatment(s)						
0	92 (55.4)	22 (78.6)	3 (50)	4 (80)	121 (59)	0.55
1	20 (12.2)	2 (7.1)	1 (16.7)	0	23 (11.2)	
2	45 (27.4)	4 (14.3)	1 (16.7)	1 (20)	51 (24.9)	
3	6 (3.7)	0	1 (16.7)	0	7 (3.4)	
4	3 (1.8)	0	0	0	3 (1.5)	
Clinical outcome						
Not treated	92 (55.4)	22 (78.6)	3 (50)	4 (80)	121 (59)	0.347
Cured	42 (25.3)	5 (17.9)	2 (33.3)	5 (100)	54 (26.3)	
Relapsed	5 (3)	0	0	0	5 (2.4)	
Died	27 (16.3)	1 (3.6)	1 (16.7)	0	29 (14.1)	
30-day mortality	9 (5.4)	0	1 (16.7)	0	10 (4.9)	
30-90-day mortality	14 (8.4)	0	0	0	14 (6.8)	
>90-day mortality	4 (2.4)	1 (3.6)	0	0	5 (2.4)	
Status						
Not admitted	44 (26.5)	5 (17.9)	1 (16.7)	1 (20)	51 (24.9)	0.01
Chronic care facility	24 (14.5)	10 (35.7)	1 (16.7)	0	35 (17.1)	
Home	42 (25.3)	3 (10.7)	3 (50)	2 (40)	50 (24.4)	
Overseas hospital	11 (6.6)	1 (3.6)	0	1 (20)	13 (6.3)	
Deceased	27 (16.3)	1 (3.6)	1 (16.7)	0	29 (14.1)	
Remain in hospital	17 (10.2)	8	0	1 (20)	26 (12.7)	
Total	166 (100)	28 (100)	6 (100)	5 (100)	205 (100)	

[a] HGH, Hamad General Hospital; RH, Rumailah Hospital; NCCCR, National Center for Cancer Care and Research; HH, Heart Hospital.
[b] WH, No MDR-PA isolates were recovered from the Women's hospital.
[c] Colonization - patients with MDR-PA isolates if there were no clinical signs and symptoms of ongoing infection, and no antibiotics were required for treatment. Infection - patients considered having an infection when they received antibiotics based on the primary team's decision. Cured - the resolution of symptoms after antibiotic treatment and no further treatment of the same MDR-PA was required for 30 days. Relapsed - the clinical sign of infection secondary to MDR-PA isolates within 30 days of previously treated MDR-PA infection.

not require antibiotic treatment but rather strict infection control measures. From the phenotypic analyses, carbapenems and colistin remained the most effective drugs in to combat MDR-PA. These findings are reassuring given that the combination of colistin and meropenem is the recommended routine presumptive management recommended by the institution antimicrobial guidelines as first line regimen for suspected MDR–PA infections. It was noted that more isolates were resistant to meropenem than amikacin and gentamicin, and this was possibly due to higher consumption of carbapenems compared to aminoglycosides, as observed during monitoring of the hospital antimicrobial stewardship program (ASP). The main use of carbapenem in HMC institutions is likely related to

its broader indications, in particular the coverage of ESBL-producing Enterobacteriaceae which have become a significant problem during recent years [17].

Although HMC has had an antimicrobial prescribing policy since 2006 that is regularly updated based on local antibiogram, there was a significant increase in antimicrobial consumption with a peak in 2014 and is coupled to increase prevalence of AMR. This led to the introduction of an ASP in 2015, restricting most broad-spectrum antibiotics, in particularly parenterally administered ones. Despite this policy, majority of MDR-PA cases received antibiotic treatment within the preceding 90 days before acquiring the infection, while the extremely resistant PDR-PA cases received multiple antibiotic

regimens, which affirms the importance of an effectual ASP as advocated by many similar healthcare institutions [29,30]. Addressing the rising challenges of AMR, most modern healthcare facilities adopted an effective ASP as a rapid intervention to curb and control overuse and misuse of antibiotics, with some success in controlling AMR, as well as improving the cost effectiveness of antibiotics treatment. These findings, together with similar reports, enhanced the need to introduce ASP in 2015 to all hospitals in Qatar [31]. The study also highlights the importance of a clear interface between infection control and prevention and the spread of AMR, since majority of MDR-PA were shown to be healthcare acquired.

AMR is a global issue requiring an international alliance. The WHO has joined forces to produce various initiatives by raising antibiotic awareness and encourage best practices among the public, physicians, health workers and policy makers, to avoid further emergence and spread of antibiotic resistance. Crucial to this process is the provision of available regional data to set benchmarks to establish regional epidemiological surveillance. The paucity of data reporting MDR infections in the Middle East and Northern Africa needs to be rectified, to achieve a more accurate global perspective. Thus, an important strength of the present study lies in the use of a MDR-PA registry, a nationally comprehensive database program that tracks every clinical isolate of MDR-PA. The registry was established on September 2014, prior to starting data collection. It promises to be a good and reliable indicator of the regional AMR levels.

Conclusions

The present epidemiological study of the demographic characteristics *P. aeruginosa* in Qatar highlighted significant prevalence of MDR-PA with substantial AMR to most antipseudomonal drugs, including the isolation of pandrug resistant isolates. The study aims to be part of a national surveillance program to curtail the growing problem of antibiotic resistance.

Conflict of interest

All authors declare no conflict of interest.

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Ethics approval

This study was approved by the Research Ethics Committee (Protocol number IRGC-01-51-033) at Hamad Medical Corporation (HMC), Doha, Qatar.

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