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

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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 (HG) 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.
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 (\( n = 15 \)).
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 respiratory tract (73.3%, n = 112), followed by urinary (13.3%, n = 17) samples, with 3 PDR-PA infections from inpatients and 2 from outpatients.

### 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 = 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, cepafloxine (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
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 \textit{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 \textit{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 bacteremia; 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 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 vulgatus, E. coli, Entrococcus fcelis, 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, Stenotrophomonas 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.
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

| Antibiotics | 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 |
| MIC₅₀ | 32 | 48 | 24 | 64 | 32 | 256 | 32 | 1.5 |
| MIC₅₀ | 256 | 256 | 256 | 256 | 32 | 256 | 32 | 2 |

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, fluoroquinolone, levofloxacin, linezolid, meropenem, metronidazole, minocycline, moxifloxacin, nitrofurantoin, rifampcin, septrin, telcoplatin, tigecycline and vancomycin.

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.
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 Enterobacteraeceae 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 particular 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

### Table III

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

| Characteristics | Hospital | Total | p-value |
|-----------------|----------|-------|---------|
| **Disease severity** | | |
| Colonization | 92 (55.4) | 121 (59) | 0.184 |
| Sepsis | 36 (21.7) | 44 (21.5) | |
| Septic shock | 38 (22.9) | 40 (19.5) | |
| **Antibiotic treatment** | | |
| Amikacin | 12 (7.3) | 13 (6.3) | 0.32 |
| Meropenem | 53 (32.3) | 62 (30.2) | 0.3 |
| Piperacillin/tazobactam | 11 (6.7) | 12 (5.9) | 0.76 |
| Colistin | 47 (28.7) | 53 (25.9) | 0.4 |
| Ciprofloxacin | 6 (3.7) | 6 (2.9) | 0.69 |
| Gentamycin | 6 (3.7) | 6 (2.9) | 0.69 |
| Ceftime | 3 (1.8) | 4 (2) | 0.06 |
| Tobramycin | 0 | 0 | |
| **Number of antibiotic treatment(s)** | | |
| 0 | 92 (55.4) | 121 (59) | 0.55 |
| 1 | 20 (12.2) | 23 (11.2) | |
| 2 | 45 (27.4) | 51 (24.9) | |
| 3 | 6 (3.7) | 7 (3.4) | |
| 4 | 3 (1.8) | 3 (1.5) | |
| **Clinical outcome** | | |
| Not treated | 92 (55.4) | 121 (59) | 0.347 |
| Cured | 42 (25.3) | 54 (26.3) | |
| Relapsed | 5 (3) | 5 (2.4) | |
| Died | 27 (16.3) | 29 (14.1) | |
| 30-day mortality | 9 (5.4) | 10 (4.9) | |
| 30-90-day mortality | 14 (8.4) | 14 (6.8) | |
| >90-day mortality | 4 (2.4) | 5 (2.4) | |
| **Status** | | |
| Not admitted | 44 (26.5) | 51 (24.9) | 0.01 |
| Chronic care facility | 24 (14.5) | 35 (17.1) | |
| Home | 42 (25.3) | 50 (24.4) | |
| Overseas hospital | 11 (6.6) | 13 (6.3) | |
| Deceased | 27 (16.3) | 29 (14.1) | |
| Remain in hospital | 17 (10.2) | 26 (12.7) | |
| **Total** | 166 (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.
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 anti-pseudomonal 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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References

[1] Hidron AI, Edwards JR, Patel J, Horan TC, Sievert DM, Pollock DA, et al. NHSN annual update: antimicrobial-resistant pathogens associated with healthcare-associated infections: annual summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2006-2007. Infect Control Hosp Epidemiol 2008;29:996–1011.
[2] Tacconelli E, Cataldo MA, Dancer SJ, De Angelis G, Falcone M, Frank U, et al. ESCMID guidelines for the management of the infection control measures to reduce transmission of multidrug-resistant Gram-negative bacteria in hospitalized patients. Clin Microbiol Infect 2014;20(Suppl 1):1–55.
[3] McGowan Jr JE. Resistance in nonfermenting gram-negative bacteria: multidrug resistance to the maximum. Am J Infect Control 2006;34(5 Suppl 1):S29–37. discussion S64-73.
[4] Souli M, Galani I, Giarmarelli H. Emergence of extensively drug-resistant and pandrug-resistant Gram-negative bacilli in Europe. Euro Surveill 2008;13:19045.
[5] Gaynes R, Edwards JR. Overview of nosocomial infections caused by gram-negative bacilli. Clin Infect Dis 2005;41:848–54.
[6] European Centre for Disease Prevention and Control (ECDC). Antimicrobial resistance surveillance in Europe 2013 annual report of the European antimicrobial resistance surveillance network (EARS-Net). Stockholm: European Centre for Disease Prevention and Control; 2014.
[7] Williard C. The drug-resistant bacteria that pose the greatest health threats Nature, 543; 2017. p. 15.
[8] Chung DR, Song JH, Kim SH, Thamlikitkul V, Huang SG, Wang H, et al. High prevalence of multidrug-resistant nonfermenters in hospital-acquired pneumonia in Asia. Am J Respir Crit Care Med 2011;184:1409–17.
[9] Sievert DM, Ricks P, Edwards JR, Schneider A, Patel J, Srinivasan A, et al. Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009-2010. Infect Control Hosp Epidemiol 2013;34:1–14.
[10] Sader HS, Farrell DJ, Flamm RK, Jones RN. Antimicrobial susceptibility of Gram-negative organisms isolated from patients hospitalized in intensive care units in United States and European hospitals (2009-2011). Diagn Microbiol Infect Dis 2014;78:443–8.
[11] Zavascki AP, Carvalhaes CG, Picao RC, Gales AC. Multidrug-resistant \( Pseudomonas \) aeruginosa and \textit{Acinetobacter baumannii}: resistance mechanisms and implications for therapy. Expert Rev Anti Infect Ther 2010;8:71–93.
[12] Livermore DM. Multiple mechanisms of antimicrobial resistance in \textit{Pseudomonas aeruginosa}: our worst nightmare? Clin Infect Dis 2002;34:634–40.
[13] Mesaros N, Nordmann P, Plesiat P, Roussel-Delvallez M, Van Eldere J, Gicquazynski Y, et al. \textit{Pseudomonas aeruginosa}: resistance and therapeutic options at the turn of the new millennium. Clin Microbiol Infect 2007;13:560–78.
[14] Lister PD, Wolter DJ, Hanson ND. Antibacterial-resistant \textit{Pseudomonas aeruginosa}: clinical impact and complex regulation of chromosomally encoded resistance mechanisms. Clin Microbiol Rev 2009;22:582–610.
[15] Boucher HW, Talbot GH, Bradley JS, Edwards JE, Gilbert D, Rice LB, et al. Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. Clin Infect Dis 2009;48:1–12.
[16] European Centre for Disease Control & European Medicines Agency (ECDC/EMEA). The bacterial challenge: time to react. A call to narrow the gap between multidrug-resistant bacteria in the EU and the development of new antibacterial agents, Stockholm. 2009.
[17] Hamad Medical Corporation (HMC). Antibiogram, internal publication, Laboratory medicine and Pathology, Microbiology...
division, Hamad medical corporation Doha. Qatar: Hamad Medical Corporation; 2009. 2014.

[18] Clinical and Laboratory standards Institute (CLSI). Performance standards for antimicrobial susceptibility testing informational supplement. Wayne, PA: Clinical and Laboratory Standards Institute Twenty-Fifth; 2015. p. 100–5125.

[19] Sid Ahmed MA, Bansal D, Acharya A, Elmi AA, Hamid JM, Sid Ahmed AM, et al. Antimicrobial susceptibility and molecular epidemiology of extended-spectrum beta-lactamase-producing Enterobacteriaceae from intensive care units at Hamad Medical Corporation. Qatar Antimicrob Resist Infect Control 2016;5:4.

[20] O’Neill J. Tackling drug resistant infections globally: final report and recommendation. 2016.

[21] Gales AC, Jones RN, Turnidge J, Rennie R, Ramphal R. Characterization of Pseudomonas aeruginosa isolates: occurrence rates, antimicrobial susceptibility patterns, and molecular typing in the global SENTRY Antimicrobial Surveillance Program, 1997-1999. Clin Infect Dis 2001;32(Suppl 2):S146–55.

[22] Karlowsky JA, Jones ME, Thornsberry C, Evangelista AT, Yee YC, Sahm DF. Stable antimicrobial susceptibility rates for clinical isolates of Pseudomonas aeruginosa from the 2001-2003 tracking resistance in the United States today surveillance studies. Clin Infect Dis 2005;40(Suppl 2):S89–98.

[23] Babay HA. Antimicrobial resistance among clinical isolates of Pseudomonas aeruginosa from patients in a teaching hospital, Riyadh, Saudi Arabia, 2001-2005. Jpn J Infect Dis 2007;60:123–5.

[24] Ullah W, Qasim M, Rahman H, Bari F, Khan S, Rehman ZU, et al. Multidrug resistant Pseudomonas aeruginosa: Pathogen burden and associated antibiogram in a tertiary care hospital of Pakistan. Microb Pathog 2016;97:209–12.

[25] Micek ST, Wunderink RG, Kollef MH, Chen C, Rello J, Chastre J, et al. An international multicenter retrospective study of Pseudomonas aeruginosa nosocomial pneumonia: impact of multidrug resistance. Crit Care 2015;19:219.

[26] Defez C, Fabbro-Peray P, Bouziges N, Gouby A, Mahamat A, Daures JP, et al. Risk factors for multidrug-resistant Pseudomonas aeruginosa nosocomial infection. J Hosp Infect 2004;57:209–16.

[27] Alough VS, Navon-Venezia S, Seigman-Igra Y, Cabili S, Carmeli Y. Multidrug-resistant Pseudomonas aeruginosa: risk factors and clinical impact. Antimicrob Agents Chemother 2006;50:43–8.

[28] Hirsch EB, Tam VH. Impact of multidrug-resistant Pseudomonas aeruginosa infection on patient outcomes. Expert Rev Pharmaecon Outcomes Res 2010;10:441–51.

[29] Fishman N. Antimicrobial Stewardship Am J Med 2006;119(6 Suppl 1):S53–61. discussion S62-70.

[30] DeLisle S, Perl TM. Vancomycin-resistant enterococci: a road map on how to prevent the emergence and transmission of antimicrobial resistance. Chest 2003;123(5 Suppl):504s–18s.

[31] de Kraker MEA, Abbas M, Huttner B, Harbarth S. Good epidemiological practice: a narrative review of appropriate scientific methods to evaluate the impact of antimicrobial stewardship interventions. Clin Microbiol Infect 2017;23:819–25.