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Letter to the Editor

Detection of OXA-23, GES-11 and NDM-1 among carbapenem-resistant *Acinetobacter baumannii* in Dubai: A preliminary study



Sir,

Acinetobacter baumannii is a Gram-negative organism that has become a significant offender in health-care facilities, with the worldwide spread of carbapenem-resistant *Acinetobacter baumannii* (CRAB) significantly debilitating treatment options. Acquired carbapenemases of Ambler class D, or oxacillinases, namely OXA-23-like, OXA-24-like, OXA-58-like, OXA-143-like and OXA-235-like groups, have been largely described in CRAB. Non-OXA carbapenemases are also acquired by *A. baumannii*, including metallo- β -lactamases of Ambler class B, such as the NDM-group, as well as Ambler class A carbapenemases, KPC and GES [1]. Intrinsically, two β -lactam hydrolysing enzyme groups occur in CRAB, OXA-51 and *Acinetobacter*-derived cephalosporinases (ADCs). While these two intrinsic enzyme categories secure weak carbapenem hydrolysis, acquisition of insertion sequence (IS) elements such as *ISAbal* upstream of *bla*_{OXA-51} and *bla*_{ADC} may lead to enhanced expression, increasing resistance to cephalosporins, but only minimally to carbapenems. The existence of *ISAbal* upstream of acquired *bla*_{OXA-23} enhances expression, resulting in higher carbapenem hydrolysis [2].

In Dubai, a major attraction spot hosting over 150 nationalities, there are no published data defining current mechanisms of resistance in CRAB. We highlight here the molecular epidemiology and genetic relatedness of CRAB isolates recovered from Dubai hospitals between 1 June 2015 and 1 June 2016. CRAB isolates were delivered to Microbiology Research Laboratories of Zayed University, Dubai, for archiving and antibiotic susceptibility testing, then to Microbiology Laboratory of Saint-Joseph University, Beirut, for further phenotypic and genotypic analysis.

Antimicrobial susceptibility testing was performed for different antibiotic classes using a disk diffusion method, while for colistin and tigecycline, it was performed by broth microdilution according to CLSI 2017 criteria and FDA breakpoints for tigecycline.

All isolates were screened by PCR sequencing for carbapenemase genes of Ambler group A (*bla*_{KPC} and *bla*_{GES}), group B (*bla*_{IMP-1}, *bla*_{IMP-2}, *bla*_{NDM-1} and *bla*_{VIM-2}) and group D (*bla*_{OXA-23}, *bla*_{OXA-24}, *bla*_{OXA-58}), as described previously [3]. Isolates were screened for insertion sequence *ISAbal*. PCR mapping experiments using *ISAbal* forward and OXA-23 reverse primers was done on *bla*_{OXA-23}-positive isolates.

Also, *ISAbal* forward and *bla*_{OXA-51} or *bla*_{ADC} reverse primers were used for all isolates to locate *ISAbal* relative to *bla*_{OXA-51} or *bla*_{ADC}, respectively. Molecular typing was done by enterobacterial repetitive intergenic consensus PCR (ERIC-PCR).

A total of 341 *A. baumannii* was recovered by the participating hospitals during the study period, of which 167 (48.9%) were CRAB. Of these, a collection of 32 non-repetitive CRAB isolates were used for further analysis. Antibiotic susceptibility profiles and genotyping results are shown in Table 1. While resistance to β -lactams and other antibiotics was high, 16% of the isolates were colistin-resistant and none were tigecycline-resistant, suggesting possible utility of these two antibiotics for use in CRAB infections in Dubai. Ten isolates (31%) produced OXA-23, two (6%) produced GES-11 and one (3%) produced NDM-1. Seven isolates (22%) co-produced OXA-23 and GES-11, and one (3%) produced the three carbapenemases OXA-23, GES-11 and NDM-1; such a combination of three carbapenemases is scarcely reported in the literature. The major prevalence of OXA-23 in 56% of CRAB is similar to that in nearby countries [4]. GES-11 was observed in 31% of CRAB isolates, while 22% co-harboured OXA-23 and GES-11, as previously reported [5]. The detection of NDM-1, alone or in combination with both OXA-23 and GES-11, perhaps highlights the role of travel and cultural exchange in disseminating resistance determinants of CRAB.

The existence of intrinsic OXA-51 and ADCs was detected by mapping experiments, and may be an additional contributor to resistance. PCR mapping detected that sequences related to ADCs were close to *ISAbal* in 28 out of 31 (90.3%) isolates, while *bla*_{OXA-51} gene was close to *ISAbal* in 12 out of 32 (37.5%) isolates. Likewise, the sequence *ISAbal* was detectable in 83.3% of *bla*_{OXA-23} producers, potentially contributing to overexpressed carbapenem resistance. *ISAbal* plays the role of a promoter for *bla*_{OXA-23}, *bla*_{OXA-51} and *bla*_{ADC} contributing to increased expression of these genes and reduced susceptibility to β -lactams [6,7].

Fingerprinting by ERIC-PCR showed the existence of eight PCR types, each including from one to six isolates with heterogeneous genotypic profile, and from variable hospital sources. A correlation between resistance determinant and PCR type was not apparent, except for isolates representing PCR type 6, which originated from Dubai Hospital and was negative for the tested carbapenemases, probably revealing a hospital outbreak.

This study is the first report of CRAB isolates with OXA-23, GES-11 and NDM in Dubai and it highlights the role of *ISAbal* and horizontal spread of carbapenemase genes in CRAB. These preliminary data should support ongoing studies, increased surveillance and targeted measures towards CRAB in Dubai.

Table 1

Characteristics of 32 *Acinetobacter baumannii* isolates with antimicrobial susceptibility results, cumulative description of each of the three carbapenemases detected and PCR types.

| Carbapenemase | Percentage of isolates (n) | Antimicrobial susceptibility testing results | | | | | | | | | | | | | | PCR type |
|---|----------------------------|--|--------------|--------|--------------|--------|--------|--------------|-------------------|--------------------|--------|-------------|-------------------|--------------|-------------------|--------------|
| | | AMC | CTX | CPM | CAZ | IMI | MER | DOX | AKM | GMN | LEV | CIP | SXT | COL | TGC | |
| OXA-23 | 31 (10) | R (10) | R (10) | R (10) | R (10) | R (10) | R (10) | R (10) | R (3) I (5) | R (7) I (2) S (1) | R | R (10) | R (1) S (9) | S (10) | 1–5 | |
| GES-11 | 6 (2) | R (2) | R (2) | R (2) | R (2) | R (2) | R (2) | R (1) I (1) | R (2) | R (2) | R | R (1) I (1) | S (2) | S (2) | 1 and 2 | |
| NDM-1 | 3 (1) | R (1) | R (1) | R (1) | R (1) | R (1) | R (1) | R (1) | R (1) | R (1) | R | R (1) | S (1) | S (1) | 7 | |
| OXA-23+GES-11 | 22 (7) | R (7) | R (7) | R (7) | R (7) | R (7) | R (7) | R (7) | R (5) I (2) | R (7) | R | R (7) | R (3) S (4) | S (7) | 1, 3, 5, 7, and 8 | |
| OXA-23+GES-11+NDM-1 | 3 (1) | R (1) | I (1) | R (1) | R (1) | R (1) | R (1) | R (1) | R (1) | R (1) | R | R (1) | S (1) | S (1) | 1 | |
| No detection of tested carbapenemases | 34 (11) | R (11) | R (11) | R (11) | R (11) | R (11) | R (11) | R (10) S (1) | R (10) I (1) | R (9) I (2) | R | R (11) | R (8) I (2) S (1) | R (1) S (10) | 1, 2, 4–7 | |
| Cumulative carbapenemases detected in all isolates | | | | | | | | | | | | | | | | |
| OXA-23 | 56 (18) | R (18) | R (17) I (1) | R (18) | R (17) S (1) | R (18) | R (18) | R (18) | R (9) I (4) S (5) | R (15) I (2) S (1) | R (18) | R (18) | R (18) | R (4) S (14) | S (18) | All except 6 |
| GES-11 | 31 (10) | R (10) | R (9) I (1) | R (10) | R (9) S (1) | R (10) | R (10) | R (9) I (1) | R (8) I (2) | R (10) | R (10) | R (9) I (1) | R (3) S (7) | S (10) | 1–3, 5, 7 and 8 | |
| NDM-1 | 6 (2) | R (2) | R (1) I (1) | R (2) | R (1) S (1) | R (2) | R (2) | R (2) | R (2) | R (2) | R (2) | R (1) I (2) | S (2) | S (2) | 1 and 7 | |

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Competing interests

None declared.

Ethical approval

Ethical approval for the study was obtained from the Dubai Scientific Research Ethics Committee of Dubai Health Authority with the reference code DSREC-11.

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