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Letter to the Editor

Emergence of *bla*$_{VIM-2}$, *bla*$_{NDM-1}$, *bla*$_{IMP-7}$ and *bla*$_{GES-1}$ in *bla*$_{KPC-2}$-harbouring *Pseudomonas aeruginosa* isolates in Brazil

Sir,

In 2018, during routine laboratory work at a public hospital in Recife, in the state of Pernambuco in northeast Brazil, when conducting phenotypic tests [1,2] we started to observe an increase in resistance to β-lactams. This included resistance to carbapenems in *Pseudomonas aeruginosa* coming from infection and colonisation samples, suspected of having other resistance mechanisms, in addition to which metallo-β-lactamases (MBLs) were being produced. Therefore, 14 of these *P. aeruginosa* isolates were investigated for the presence of the *bla*$_{KPC}$, *bla*$_{NDM}$, *bla*$_{VIM}$, *bla*$_{IMP}$, *bla*$_{SPM}$ and *bla*$_{GES}$ genes. Biochemical identification and antimicrobial susceptibility testing of the isolates was performed using a BD BACTEC™ 9120/Phoenix™ automated system and the results were interpreted according to Clinical and Laboratory Standards Institute (CLSI) breakpoints [1]. Antimicrobial resistance genes were investigated by PCR using primers and amplification conditions described previously [3]. The amplicons were purified using a Wizard® SV Gel and PCR Clean-Up System (Promega) and were sequenced using an Applied Biosystems 3500 Genetic Analyzer. Sequences were compared with those deposited in the GenBank database (http://www.ncbi.nlm.nih.gov/blast/) using BLAST (Basic Local Alignment Search Tool).

Enterobacterial repetitive intergenic consensus (ERIC)-PCR was used to determine the clonal relationship of the isolates using primers and amplification conditions according to Duan et al. [4]. *Pseudomonas aeruginosa* isolates showed a multidrug-resistant profile with resistance to β-lactams (carbapenems, monobactams and cephalosporins), aminoglycosides and quinolones (Table 1). PCR and sequencing analysis showed the presence of *bla*$_{VIM-2}$ ($n = 5$; 36%), *bla*$_{NDM-1}$ ($n = 4$; 29%), *bla*$_{KPC-2}$ ($n = 2$; 14%), *bla*$_{IMP-7}$ ($n = 1$; 7%) and *bla*$_{GES-1}$ ($n = 1$; 7%) genes. The *bla*$_{SPM}$ gene was not detected (Table 1).

To our knowledge, this is the first report of the *bla*$_{NDM-1}$ gene and of the *bla*$_{IMP-7}$ variant in *P. aeruginosa* isolates in Brazil. Detection of *bla*$_{NDM-1}$ in *P. aeruginosa* isolates indicates the emergence of *bla*$_{NDM-1}$ throughout the country. This gene has been widely reported in enterobacteria [3,5], but had not yet been described in non-fermenting bacilli, such as *P. aeruginosa*, in Brazil. During our research, it was with great concern that we detected an isolate harbouring *bla*$_{IMP-7}$, which shows the imminent risk of dissemination of this MBL in Brazil. Most IMP types have a defined global geographical distribution, but in *P. aeruginosa* the *bla*$_{IMP-7}$ variant is not limited to a specific geographical area and has been reported as being present in several countries but has not previously been reported in Brazil.

The *bla*$_{VIM-2}$ gene was also identified in this study. To our knowledge, this is the first description of this gene variant in

Table 1
Origin, sector, antimicrobial resistance genes (ARGs), ERIC-PCR profile and antimicrobial resistance profile of 14 *Pseudomonas aeruginosa* isolates from a public hospital in Recife-PE (Brazil).

Isolate ID	Origin	Sector	ARG(s)[a]	ERIC-PCR profile	MIC (mg/L) [susceptibility]										
					AMK	ATM	FEP	CAZ	CIP	GEN	IPM	LVX	MEM	TZP	CFO/TAZ
PS1-A	Tracheal aspirate	ICU	*bla*$_{VIM-2}$	1E	>32 [R]	8 [S]	>16 [R]	>16 [R]	>2 [R]	>8 [R]	>8 [R]	>4 [R]	>8 [R]	64/4 [I]	[S]
PS2-A	Catheter tip	ICU	*bla*$_{VIM-2}$	1E	>32 [R]	8 [S]	>16 [R]	>16 [R]	>2 [R]	>8 [R]	>8 [R]	>4 [R]	>8 [R]	64/4 [I]	[S]
PS4-A	Urine	ICU	*bla*$_{NDM-1}$, *bla*$_{VIM-2}$	2E	≤8 [S]	4 [S]	>16 [R]	>16 [R]	>2 [R]	>8 [R]	>8 [R]	>4 [R]	>8 [R]	≤4/4 [S]	[R]
PS5-A	Tracheal aspirate	CCU1	*bla*$_{NDM-1}$	3E	32 [I]	>16 [R]	8 [S]	>16 [R]	>2 [R]	8 [I]	4 [I]	>4 [R]	32 [R]	16/4 [S]	[S]
PS6-A	Tracheal aspirate	CCU1	*bla*$_{NDM-1}$, *bla*$_{IMP-7}$	4E	32 [I]	16 [I]	>16 [R]	>16 [R]	>2 [R]	>8 [R]	>8 [R]	4 [I]	>8 [R]	16/4 [S]	[R]
PS7-A	Tracheal aspirate	ICU	*bla*$_{VIM-2}$	1E	>32 [R]	8 [S]	>16 [R]	>16 [R]	>2 [R]	>8 [R]	>8 [R]	>4 [R]	>8 [R]	64/4 [I]	[R]
PS8-A	Tracheal aspirate	ICU	*bla*$_{NDM-1}$	5E	>32 [R]	>16 [R]	16 [I]	>16 [R]	>2 [R]	>8 [R]	>8 [R]	>4 [R]	>8 [R]	>64/4 [R]	[S]
PS9-A	Tracheal aspirate	ICU	–	6E	>32 [R]	>16 [R]	>16 [R]	>16 [R]	>2 [R]	>8 [R]	>8 [R]	>4 [R]	>8 [R]	>64/4 [R]	[S]
PS10-A	Catheter tip	ICU	–	6E	>32 [R]	>16 [R]	>16 [R]	>16 [R]	>2 [R]	>8 [R]	>8 [R]	>4 [R]	>8 [R]	>64/4 [R]	[S]
PS11-A	Rectal Swab	ICU	–	7E	≤8 [S]	16 [I]	≤1 [S]	2 [S]	≤0.5 [S]	≤2 [S]	2 [I]	≤1 [S]	8 [R]	≤4/4 [S]	[S]
PS12-A	Urine	ICU	*bla*$_{KPC-2}$	8E	>32 [R]	>16 [R]	>16 [R]	>16 [R]	>2 [R]	>8 [R]	>8 [R]	>4 [R]	>8 [R]	>64/4 [R]	[R]
PS13-A	Rectal Swab	CCU1	*bla*$_{KPC-2}$, *bla*$_{GES-1}$	9E	>32 [R]	>16 [R]	>16 [R]	>16[R]	>2 [R]	>8 [R]	>8 [R]	>4 [R]	>8 [R]	>64/4 [R]	[R]
PS14-A	Rectal Swab	CCU2	*bla*$_{VIM-2}$	1E	>32 [R]	>16 [R]	>16 [R]	>16 [R]	>2 [R]	>8 [R]	>8 [R]	>4 [R]	>8 [R]	>64/4 [R]	[R]
PS15-A	Tracheal aspirate	ICU	–	10E	≤8 [S]	>16 [R]	>16 [R]	>16 [R]	≤0.5 [S]	≤2 [S]	4 [I]	≤1 [S]	8 [R]	>64/4 [R]	[S]

ERIC-PCR, enterobacterial repetitive intergenic consensus PCR; MIC, minimum inhibitory concentration; AMK, amikacin; ATM, aztreonam; FEP, cefepime; CAZ, ceftazidime; CIP, ciprofloxacin; GEN, gentamicin; IPM, imipenem; LVX, levofloxacin; MEM, meropenem; TZP, piperacillin/tazobactam; CFO/TAZ, ceftolozane/tazobactam; ICU, intensive care unit; CCU, coronary care unit; R, resistant; I, intermediate; S, susceptible.

[a] Isolates were investigated for the presence of *bla*$_{KPC}$, *bla*$_{NDM}$, *bla*$_{GES}$, *bla*$_{VIM}$, *bla*$_{IMP}$ and *bla*$_{SPM}$ genes.

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P. aeruginosa in Northeast Brazil. We point out that there is a higher occurrence of bla_{VIM-2} compared with the other genes analysed in this study. Associations of bla_{VIM-2} and bla_{NDM-1} and of bla_{KPC-2} and bla_{GES-1} were also found. These associations have not been described previously in *P. aeruginosa* isolates in Brazil, thus demonstrating the potential of this micro-organism to accumulate resistance mechanisms.

Circulation of bla_{NDM-1}, bla_{IMP-7} and bla_{VIM-2} and the co-harbouring of bla_{KPC-2} with bla_{GES-1} and of bla_{VIM-2} with bla_{NDM-1} reveal a new epidemiological profile of resistance of *P. aeruginosa* in Brazil and show the decline in the occurrence of bla_{SPM} that was previously reported as endemic in Brazil. The emergence of a variety of new MBLs and associations of resistance genes circulating in Brazil promotes the survival and selection of clinically significant pathogenic strains. This emphasises the recombination and genetic variability of *P. aeruginosa*, which is visibly undergoing continuous evolution.

These data are alarming and may hamper treatment options and decrease patient survival, making *P. aeruginosa* a major concern for health systems. We alert that in view of this new epidemiological resistance profile, urgent measures are necessary to avoid the spread of these emerging resistance mechanisms.

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Competing interests

None declared.

Ethical approval

Not required.

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