First Report of New Delhi Metallo-β-Lactamase Carbapenemase–Producing *Acinetobacter baumannii* in Peru

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Abstract. Here we report the first incidence of New Delhi metallo-β-lactamase (NDM-1)–producing *Acinetobacter baumannii* in Peru, identified via a strain-based nosocomial surveillance project carried out in Lima and Iquitos. The *bla*<sub>NDM-1</sub> gene was detected by multiplex polymerase chain reaction (PCR) and confirmed by loci sequencing. *Acinetobacter baumannii* is a nearly ubiquitous and promiscuous nosocomial pathogen, and the acquisition of *bla*<sub>NDM-1</sub> by *A. baumannii* may facilitate an increase in the prevalence of this important resistance marker in other nosocomial pathogens.

INTRODUCTION

Health-care–associated infections (HAI) and antimicrobial resistance are of great public health concern worldwide.¹ Bacterial pathogens causing HAI have become increasingly more resistant over the past 10–15 years as a result of various mechanisms, including gene-mediated enzymes such as class A, B, and D β-lactamases.² Numerous factors, from the horizontal transfer of gene-encoded enzymes to global travel, have allowed resistance and resistant organisms to rapidly spread with great clinical and epidemiological impact.²,³,⁴ The recently described carbapenemase, New Delhi metallo-β-lactamase (NDM-1) class B, is of particular epidemiological and clinical concern. Since its discovery in 2008, NDM-1 has rapidly spread worldwide and confers resistance to almost all lactams, with the exception of aztreonam, leaving limited therapeutic options against pathogens harboring resistance to almost all lactams, with the exception of aztreonam, leaving limited therapeutic options against pathogens harboring NDM-1, typically colistin, tigecycline, and fosfomycin.²,⁵,⁶ In Latin America, the *bla*<sub>NDM-1</sub> gene was first reported in 2011 from Guatemala and Colombia, and later from Mexico in 2012, Brazil in 2013, and Uruguay in 2013, with all instances from Enterobacteriaceae.⁵ The *bla*<sub>NDM-1</sub> gene in non-fermentative pathogens was first reported in Latin America from Honduras (*Acinetobacter baumannii*) and Paraguay (*Acinetobacter pittii*) in 2012, and later from Brazil (*A. baumannii*) in 2014, Cuba (*Acinetobacter soli*) in 2015, Argentina (*Acinetobacter junii*) in 2016, and Colombia (*A. baumannii*) in 2017.⁵,⁶,⁹ In Peru, the first report of *bla*<sub>NDM-1</sub> was in May 2017 in a set of nine *Klebsiella pneumoniae* infecting or colonizing critically ill neurological patients from one hospital in Lima.⁵ Here, we describe the identification of the first three strains of *A. baumannii* harboring *bla*<sub>NDM-1</sub> in Peru as part of a strain-based surveillance project carried out by the Naval Medical Research Unit No Six (NAMRU-6) in Lima, Peru.

MATERIALS AND METHODS

In June 2016, NAMRU-6 began ongoing strain collection from Lima (three hospitals) and Iquitos (two hospitals), Peru. Strain collection for this effort focuses on, but is not limited to,
RESULTS

From June 2016 to November 2017, 875 ESKAPE and 213 Escherichia coli isolates were collected from Lima and Iquitos hospitals (Table 1). The most frequent pathogen collected from Lima was P. aeruginosa (36%), whereas that of Iquitos was E. coli (46%). Enterobacteriaceae (K. pneumoniae, Enterobacter spp., and E. coli) represented 45% of all pathogens collected, whereas A. baumannii represented 11%. From the total 1,088 strains collected, 978 were Gram-negative pathogens and AST was performed on 974. Of the 974 isolates, 472 (48%) were non-susceptible (resistant or intermediate phenotype) to carbapenem. PCR was performed on 764 (78%) of the 974 strains with AST results, and 155 (20%) of those were for at least one of the four carbapenemase-encoding genes tested. Interestingly, 8 (5%) strains harboring PCR-detectable carbapenemase-encoding genes were susceptible to carbapenems, indicating not only a general agreement between PCR and AST but also that there are pseudogenes for carbapenem resistance present in the susceptible clinical isolates here. Such sequences likely have an interesting role in the dynamics of resistance within bacterial populations, and further analysis of such sequences in populations of clinical isolates in Peru is needed. From these 155 strains, an additional eight non-susceptible strains harboring blaNDM-1 were detected: five Enterobacteriaceae (one E. coli and four K. pneumoniae, all from Lima) and three A. baumannii (one from Lima and two from Iquitos).

The only A. baumannii harboring blaNDM-1 from Lima was isolated in January 2017 from a hemoculture taken in a tertiary care oncology hospital and was classified as XDR. This strain was resistant to all β-lactams with the exception of aztreonam, to which it showed intermediate resistance, and colistin and fosfomycin. In addition, this strain also showed intermediate resistance to ciprofloxacin but was sensitive to tetracycline, trimethoprim–sulfamethoxazole, levofoxacin, aminoglycosides, and colistin. The second A. baumannii from Iquitos was isolated in February 2017 from a postoperative wound and was classified as MDR. This strain was resistant to all antibiotics tested except ampicillin–sulbactam, to which it showed intermediate resistance, and colistin and tetracycline, to which it was sensitive (Table 2). Amplicon sequencing of all three A. baumannii strains returned a 99% match to blaNDM-1.

DISCUSSION

Carbapenem-resistant A. baumannii is a serious public health concern worldwide.2,6,15,16 Acinetobacter baumannii has spread throughout the world acquiring antibiotic resistance, first to the most common antibiotics (β-lactams, sulfonamides, and aminoglycosides) and later to carbapenems.15,17,18 The clinical

| Code | NSC2058 | NSI1409 | NSI1428 |
|------|---------|---------|---------|
| Study site | Lima | Iquitos | Iquitos |
| Sample type | Hemoculture | CVC tip | Wound |
| Sample date | January 27, 2017 | January 18, 2017 | January 17, 2017 |
| AMK | S | S | R |
| GEN | S | S | R |
| AMP | R | R | R |
| SAM | R | R | I |
| TIC | R | R | R |
| TIM | R | R | R |
| TAZ | R | I | R |
| ATM | R | I | R |
| CAZ | R | R | R |
| CFZ | R | R | R |
| CRO | R | R | R |
| FOX | R | R | R |
| FEP | R | R | R |
| LVX | S | S | R |
| CIP | S | I | R |
| IPM | R | R | R |
| MEM | R | R | R |
| FOF | R | R | R |
| SXT | S | S | S |
| TET | I | S | S |
| CST | S | S | S |
| Definition for acquired resistance | MDR | MDR | XDR |

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| CRO | R | R | R |
| FOX | R | R | R |
| FEP | R | R | R |
| LVX | S | S | R |
| CIP | S | I | R |
| IPM | R | R | R |
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| FOF | R | R | R |
| SXT | S | S | S |
| TET | I | S | S |
| CST | S | S | S |
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AMK = amikacin; AMP = ampicillin; ATM = amoxicillin; CAZ = cefazolin; CFZ = cefazolin; CIP = ciprofloxacin; CRO = ceftriaxone; GST = colistin; CVG = central venous catheter; FEP = cefepime; FOX = fosfomycin; FOX = cefoxitin; GEN = gentamicin; I = intermediate; IPM = imipenem; LVX = levofoxacin; MDR = multidrug resistant; MEM = meropenem; NDM-1 = New Delhi metallo-β-lactamase; R = resistant; S = sensitive; SAM = ampicillin–sulbactam; SXT = trimethoprim–sulfamethoxazole; TET = tetracycline; TIC = ticarcillin; TIM = ticarcillin–clavulanic acid; T2P = piperacillin–tazobactam; XDR = extremely drug resistant.
impact of this pathogen stems from its ability to upregulate or readily acquire resistance determinants and survive for prolonged periods in nosocomial environments, thus enhancing its rapid dissemination.\textsuperscript{5,16,17} Carbenapenem-resistant \textit{A. baumannii} is mainly thought to produce OXA-\(\beta\)-lactamas (oxacillin-hydrolysing) and is less frequently an NDM-1 producer.\textsuperscript{15–17} Conversely, some studies have found truncated forms of the \textit{bla}\textsubscript{NDM-1}–harboring composite transposons Tn125 in Enterobacteriaceae species, whereas the complete sequence can be found in \textit{A. baumannii}. Taken together, this suggests that \textit{A. baumannii} may serve as a reservoir of \textit{bla}\textsubscript{NDM-1} that can be transferred to other pathogens.\textsuperscript{2,6,19,20} Furthermore, the spread of \textit{A. baumannii} harboring \textit{bla}\textsubscript{NDM-1} is likely not a matter of a single lineage but may involve different contemporary clones.

NSC2058 and NSI1409 were found in Lima and Iquitos, respectively; yet they have similar patterns of resistance for strains.\textsuperscript{1,2,6} A.\textit{baumannii} resistance pattern, suggesting this may be a different clone.

We report here the first instances of \textit{bla}\textsubscript{NDM-1} in \textit{A. baumannii} in Peru, isolated from two different and geographically distinct regions at essentially the same time. This finding highlights the urgent need to implement surveillance and infection control measures for carbapenem-resistant pathogens, not only to mitigate the spread of resistant strains but also to limit or prevent the transfer of these resistance markers between pathogens in Peru and globally.\textsuperscript{1}

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