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Short Communication

Introduction of NDM-1 and OXA-370 from Brazil into Chile in strains of *Klebsiella pneumoniae* isolated from a single patient

Sergio Carrasco-Anabalón[a,b], Carlos Orlando Conceição Neto[c], Ana Paula D'Alincourt Carvalho-Assef[c], Celia A. Lima[a,d], Marcela Cifuentes[e], Francisco Silva[e], Boris Barrera[e], Mariana Domínguez[a], Gerardo González-Rocha[a,f], Helia Bello-Toledo[a,*]

[a] *Laboratorio de Investigación en Agentes Antibacterianos, Universidad de Concepción, Departamento de Microbiología, Facultad de Ciencias Biológicas, Concepción, Chile*
[b] *Laboratorio Central, Hospital Regional Dr. Guillermo Grant Benavente, Concepción, Chile*
[c] *Laboratório de Pesquisa em Infecção Hospitalar, Instituto Oswaldo Cruz-FIOCRUZ, Rio de Janeiro, Brazil*
[d] *Departamento de Medicina Interna, Facultad de Medicina, Universidad de Concepción, Concepción, Chile*
[e] *Hospital Clínico Universidad de Chile, Santiago, Chile*
[f] *Nucleus Millennium on Interdisciplinary Approach to Antimicrobial Resistance, Microbe-R, Chile*

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ABSTRACT

Carbapenemase-producing Enterobacteriaceae have rapidly disseminated worldwide and can colonize patients in healthcare centers. As in Chile the first isolations of NDM-1 and OXA-370 carbapenemases were related with a patient arriving from Brazil, the genetic relatedness of *Klebsiella pneumoniae* strains producers of these enzymes and isolated in both countries was assessed. PFGE analyses revealed that the isolates were clonally related, illustrating how travel contributes to the spread of multidrug-resistant microorganisms. In addition, the occurrence of three different carbapenemases in three different *K. pneumoniae* strains isolated from a single patient is described.

According to the World Health Organization (WHO), carbapenemase-producing *Enterobacteriaceae* (CPE) represent a serious health problem worldwide due to being associated with high mortality rates, high hospital costs and, in recent years, to increasing dissemination.[1]

Travel, either by migration or tourism, from areas where CPE are endemic contribute to this phenomenon (Halaby et al., 2012; van der Bij and Pitout, 2012; Johnson and Woodford, 2013; Lee et al., 2016). Currently, in Latin America KPC-producing Enterobacteriaceae are endemic in countries like Colombia, Brazil and Argentina (Lee et al., 2016; Aires et al., 2017; Escandón-Vargas et al., 2017) and the prevalence of other carbapenemases, specifically, NDM-1 and OXA-48-*like* is increasing (Aires et al., 2017; Escandón-Vargas et al., 2017). In Chile, the first description of a KPC enzyme was in 2012 in a *K. pneumoniae* strain isolated from a patient coming from Italy (Cifuentes et al., 2012). Subsequently, in May 2014 two strains of carbapenemase-producing *K. pneumoniae* were isolated in a same hospital in Santiago de Chile: strain UC358, an OXA-370 producer, and strain UC361, a NDM-1 producer (Carrasco-Anabalón et al., 2018). Strain UC358 was isolated from a patient arriving from Brazil with prolonged hospitalizations in Rio de Janeiro, whereas strain UC361 was isolated from a patient with no history of travel abroad. Both patients shared the same room and the strains were detected in surveillance rectal swab cultures after the isolation of a *Serratia marcescens* strain carrying KPC-2, on April 2014, from the patient coming from Brazil few days after being hospitalized in Chile.

Considering that (a) NDM-1 and OXA-370 carbapenemases had not been previously found in Chile, (b) OXA-370-producing strain was detected in a patient coming from Brazil, (c) this variant of the OXA-48- group has been described only in Brazil, and (d) the similarity of ST and carbapenemase reported in *K. pneumoniae*

* Corresponding author at: Departamento de Microbiología, Facultad de Ciencias Biológicas, Universidad de Concepción, Barrio Universitario S/N, Concepción POB 160-C, Chile.
E-mail address: hbello@udec.cl (H. Bello-Toledo).
[1] http://www.who.int/medicines/publications/global-priority-list-antibiotic-resistant-bacteria/.

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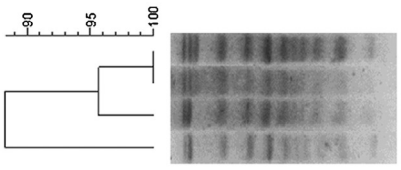
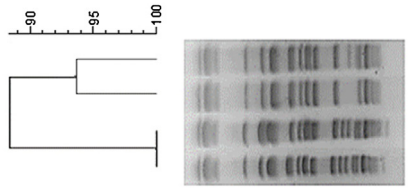


Strain	CBP	ST	Country/City	H	Date	Origin
CCBH14393	OXA-370	16	Brazil/Rio de Janeiro	H2	09 Oct 2013	Rectal swab
UC358	OXA-370	16	Chile/Santiago	H1	07 May 2014	Urine
CCBH14420	OXA-370	16	Brazil/Rio de Janeiro	H3	23 Oct 2013	Rectal swab
CCBH13791	OXA-370	16	Brazil/Rio de Janeiro	H3	20 Aug 2013	Rectal swab



Strain	CBP	ST	Country/City	H	Date	Origin
CCBH16046	NDM-1	1588	Brazil/Rio de Janeiro	H4	06 May 2014	Catheter tip
CCBH16328	NDM-1	1588	Brazil/Rio de Janeiro	H5	06 Mar 2014	Rectal swab
UC361	NDM-1	1588	Chile/Santiago	H1	07 May 2014	Rectal swab
CCBH16886	NDM-1	1588	Brazil/Rio de Janeiro	H5	30 Sept 2014	Rectal swab

Figure 1. Pulse-field gel electrophoresis dendrogram and epidemiological characteristics of NDM-1 and OXA-370 producing *Klebsiella pneumoniae* strains isolated in hospitals in Brazil and Chile. CBP: Carbapenemase, H: Hospital, ST: sequence-type (MLST).

isolates in both countries (Pereira et al., 2015; Aires et al., 2017; Carrasco-Anabalón et al., 2018), the aim of this study was to determine if any of the first strains producing NDM-1 and OXA-370 isolated in Chile correspond to imported cases.

Eight *K. pneumoniae* strains were included in the study, the two isolated in Chile plus six clinical strains from Rio de Janeiro, Brazil, producing the same carbapenemases and belonging to the same ST as the Chilean strains (three OXA-370 positive isolated in 2013 and three NDM-1 positive isolated in 2014). Furthermore, the strains carry similar determinants of antibiotic resistance such as bla_{CTX-M}, *qnrB, aac(6′)Ib-cr* (Pereira et al., 2015; Aires et al., 2017; Carrasco-Anabalón et al., 2018). The genetic relatedness between the strains producing the same type of carbapenemases was assessed by pulsed-field gel electrophoresis (PFGE) using *Xba*I endonuclease (Thermo Fisher Scientific Inc., Waltham, USA). Dendrogram were constructed with BioNumerics software version 6.6 (Maths, Kortrijk, Belgium), using the UPGMA algorithm and Dice coefficient and tolerance and optimization values of 1.5. Isolates with ≥85% similarity were considered as genetically related (Pereira et al., 2015; Aires et al., 2017; Carrasco-Anabalón et al., 2018).

The strains producing OXA-370 and NDM-1 belong to ST16 and ST1158, respectively and three pulsotypes with ≥88% genetic similarity were identified among the isolates producing OXA-370 and NDM-1 (Figure 1). The two Chilean strains were found to be clones with Brazilian strains, UC358 with CCBH14393 (OXA-370 producers) and UC361 with CCBH1688 (NDM-1-producers).

It seems that the patient with no history of travelling abroad was colonized by the NDM-1-producing *K. pneumoniae* strain, probably due to sharing the room with the patient coming from Brazil. This is supported by the isolation of a *K. pneumoniae* strain producing NDM-1 from a rectal swab culture from the patient from Brazil in days after. As such, it can be concluded that probably the patient travelled to Chile already colonized by three different strains, each one carrying a carbapenemase of high epidemiological relevance such as NDM-1, OXA-370 and KPC-2 (Lee et al., 2016).

According to these results and supported by the epidemiological background, the strains producing NDM-1 and OXA-370 isolated in Chile in 2014 correspond to cases imported from Brazil. It should be considered that in Chile in 2014, even though there were few CPE reports, there were no specific regulations on contact precautions or additional containment barriers regarding the management of patients arriving from abroad carrying multidrug resistant bacteria (Cifuentes et al., 2012, 2015). This finding, added to the imported case of KPC-2 in Chile in 2012 (Cifuentes et al., 2012), emphasizes the need for hospitals to reinforce infection control management practices. Some authors point out that it may be reasonable to rule out the colonization by CPE of any patient incoming from countries where these enzymes are endemic (van der Bij and Pitout 2012; Cifuentes et al., 2015; Lee et al., 2016).

These epidemiological results illustrate how travels facilitate the spread of multidrug resistant microorganisms.

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Conflict of interest statement

None.

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