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DETECTION OF THE OXA-58 CARBAPENEMASE IN CLINICAL ISOLATES OF *Acinetobacter baumannii* FROM COCHABAMBA, BOLIVIA

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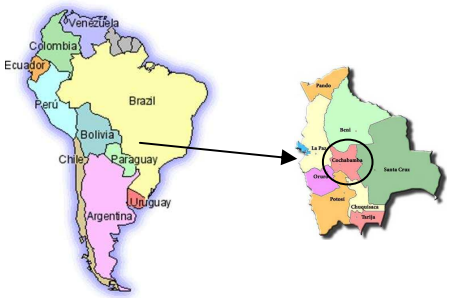
INTRODUCTION

Acinetobacter baumannii is a nosocomial pathogen responsible for severe infections such as pneumonia, septicaemia, urinary tract infections and wound infections. Carbapemens are considered as drugs of choice for treating these infections, but multidrug-resistant phenotypes are being reported worldwide. Mechanisms to develop carbapenem resistance include decreased permeability, efflux pump overexpression, and production of carbapenemases. Among these mechanisms, the acquisition of carbapenemases plays the major role in carbapenem resistance in most gram-negative bacilli, including *A. baumannii* clinical isolates. Enzymes with carbapenem-hydrolizing activity belongs to either class A, class B (metallo-β-lactamases), or class D (carbapenem-hydrolisisng oxacillinases) β-lactamases. Altough the highest level of carbapenem-hydrolising activity is provides by MBLs, the most common detected carbapenemases in *Acinetobacter baumannii* are carbapenem-hydrolyzing class D β-lactamases.

Although reports of these types of enzymes is high in Europe, Asia, and some countries of America, little is known about the situation in low income countries such as Bolivia.

In this study we analyse the antibiotic resistance in clinical isolates of *A. baumannii* obtained from several hospitals of Cochabamba (Bolivia); focusing specially on carbapenem resistance, and the presence of carbapenemases.



OBJECTIVES

The aim of this work was to analyse the antibiotic resistance in clinical isolates of *A. baumannii* obtained from several hospitals of Cochabamba (Bolivia), focusing specially on carbapenem resistance, presence of carbapenemases and their related genetic structures.

MATERIALS AND METHODS

The study included 12 *A. baumannii* isolates obtained in a hospital from Cochabamba, Bolivia (Hospital Gastroenterológico Boliviano-Japonés) during 2008.This hospital collects isolates from different hospitals of Cochabamba Department. Susceptibility to antimicrobial agents was done by determining the MIC following the CLSI recommendations. Antibiotics tested were amikacin, gentamicin, tobramicin, trimetroprim/sulfametoxazol, cefepime, ceftazidime, ceftriaxone, piperacilin/ tazobactam, criprofloxacin, imipenem and meropenem. Clonal relatedness was performed by PFGE, plasmids were determined by a commercial kit (Qiagen), and class 1 integrons and insertion sequences (ISAba 1, ISAba 2 and ISAba 3) by PCR experiments with the corresponding primers. OXA-type carbapenemases (-23, -40, -51 and –58) were detected by Multiplex PCR. Sequencing experiments were done with OXA-58 carbapenemase positive isolates.

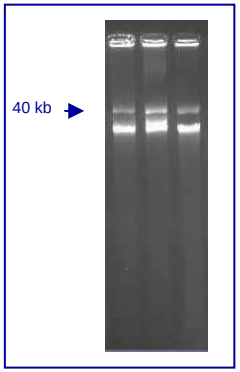
RESULTS

Genetic typing by PFGE clustered the isolates in 4 different clones. Clone A included 8 isolates, clone B: 2, and clones C and D: 1 one isolate each. Class 1 integrons were present in all strains. In most of the isolates (10) two simultaneous bands of 780 and 540 bp were present.

In our study, we found that among 12 strains studied, 8 were resistant to all antibiotics tested. These multirresistant isolates belonged to clones A and D, except for one isolate in clone A, susceptible to betalactams and quinolones. Clone B included isolates susceptible only to carbapenems, and clone C included the only isolate susceptible to all antibiotics tested.

All the isolates bored bla_{OXA-51} carbepenemase gene, and 7 of them, all belonging to clone A, also bored bla_{OXA-58} gene. Sequencing experiments of the coding region showed total homology with the sequence previously described and located the gene upstream of the IS*Aba*-3. Plasmid analysis and hybridization with an OXA-58 probe located the gene mainly in a 40 kb plasmid.

ISOLATE	PFGE	CMI (mg/L))		CARBAPENEMASES detected		Genetic location of bla_{OXA-58} gene
		IMI	MEM	OXA-51	OXA-58	
1	D	>8 R	>8 R	+	-	-
2	A	>8 R	>8 R	+	+	40 kb plasmid
3	A	>8 R	>8 R	+	+	40 kb plasmid
4	A	>8 R	>8 R	+	+	40 kb plasmid, chr*
5	A	>8 R	>8 R	+	+	40 kb plasmid, chr*
6	A	>8 R	>8 R	+	+	40 kb plasmid
8	B	2 S	>1 S	+	-	-
10	C	≤1 S	≤1 S	+	-	-
12	A	>8 R	>8 R	+	+	40 kb plasmid
13	A	>8 R	>8 R	+	+	40 kb plasmid
15	A	≤1 S	≤1 S	+	-	-
16	B	2 S	≤1 S	+	-	-



CONCLUSIONS

This is the first description of the OXA-58 carbapenemase in isolates of *A. baumannii* from Bolivia.

The detection of the enzyme in a multiresistant clone, named A, and its relationship with plasmids is of great concern as it means the possibility of spreading carbapenem resistance among the hospitals of the country.