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SPECIAL ARTICLE

Carbapenemases in *Acinetobacter baumannii*. Review of their dissemination in Latin America

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Abstract Carbapenem resistance in gram-negative bacteria by production of carbapenemases is one of the most challenging issues regarding healthcare worldwide. We review the epidemiology and prevalence of carbapenemases in carbapenem-resistant *Acinetobacter baumannii* isolates from Latin American countries. High resistance rates to antimicrobial agents, particularly to carbapenems, are observed in this region. OXA-23 is the most widely disseminated class D-carbapenemase; it is present in all the countries of the region and is frequently associated to endemic clones CC113/CC79, CC104/CC15, CC110/ST25 and CC109/CC1. The emergence of OXA-72 and NDM-1 represents a novel finding which is observed simultaneously and without clonal relatedness in different countries, some of which are distant from one another, whereas OXA-143 is only present in Brazil. Further collaborative intraregional studies would provide a better understanding of these issues in most of the countries and thus, policies to control the spread of these isolates could be implemented.

PALABRAS CLAVE
Acinetobacter baumannii;
América Latina;
Carbapenemasas;
Clase D carbapenemasas;
NDM-1

Carbapenemasas en *Acinetobacter baumannii*. Revisión de su diseminación en América Latina

Resumen En bacilos gram negativos, la resistencia a carbapenemes por producción de carbapenemasas es uno de los mayores problemas en la atención de la salud a nivel mundial. Reseñamos en este artículo la epidemiologia y la prevalencia de las carbapenemasas descritas en aislamientos de *Acinetobacter baumannii* recuperados en América Latina. En esta región se ha observado un alto porcentaje de resistencia a los antimicrobianos, particularmente a

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los carbapenemes. La carbapenemasa más frecuentemente descrita es OXA-23, que ha sido recuperada en todos los países de la región y fue asociada a los clones endémicos CC113/CC79, CC104/CC15, CC110/ST25 y CC109/CC1. La emergencia de OXA-72 y NDM-1 representa un nuevo hallazgo en varios países, algunos de los cuales se encuentran muy distantes entre sí. Por el momento, OXA-143 solo se recuperó de aislamientos obtenidos en Brasil. Serían necesarios estudios colaborativos dentro de la región para lograr una mejor comprensión de la resistencia a carbapenemes en *Acinetobacter baumannii*, a fin de poder instaurar medidas de control que eviten una mayor diseminación de esta bacteria.

Introduction

The genus *Acinetobacter*, as currently defined, comprises gram-negative, strictly aerobic, nonfermenting, nonfastidious, nonmotile, catalase-positive, oxidase-negative bacteria with a DNA G+C content of 39–47%[24].

Implementation of molecular techniques and mass spectrometry such as matrix-assisted laser desorption ionization-time and flight mass spectrometry (MALDI-TOF MS) in clinical microbiology laboratories has greatly improved the identification of *Acinetobacter* species. *Acinetobacter baumannii* is the most important in the clinical context. This is the genospecies which is most frequently associated with hospital outbreaks[24]. The ability to survive on inanimate surfaces and resistance to disinfectants or antimicrobials are crucial to this behavior[24].

Carbapenems are currently the antibiotics of choice against multidrug-resistant *Acinetobacter* infections. However, carbapenem-resistance (CR) is increasingly being reported, leaving few therapeutic options available[24,37,38].

The aim of this review is to analyze the prevalence and molecular epidemiology of carbapenem-resistant *A. baumannii* (CR-Ab) isolates in Latin American countries.

Literature associated with CR-Ab in Latin America (LA) was included. The articles in English and Spanish language were accessed through PubMed and Scientific Electronic Library Online (SciELO). Pan American Health Organization (PAHO) documents were also consulted[19–23]. It is important to mention that a heterogeneous distribution of molecular epidemiology studies performed in the region was noticed; although 60% of the countries in LA have presented data, more than 50% of these correspond to Brazil and Argentina.

Prevalence of carbapenem-resistant *A. baumannii*

Rates of carbapenem resistance in LA appear to be among the highest in the world. A wide range of resistance has been reported among the different countries (1–90%), the lowest values belong to Central America and the highest ones to some studies in Argentina and Brazil[12]. In addition, reports of the Latin American Antimicrobial Resistance Surveillance Network (ReLAVRA-PAHO) showed a progressive increase in the percentages of resistance reported during the period 2000–2013[19–23] (Table 1). Even though statistics do not show discrimination among genospecies, some studies conducted in the area evidence a participation of *A. baumannii* in nosocomial infections higher than 90%[27]. Therefore, it could be affirmed that resistance rates would not vary significantly if only *A. baumannii* isolates had been considered in the analysis[27].

Table 1 Evolution of carbapenem resistance in *Acinetobacter* spp. isolates recovered in several Latin American countries. Annual reports by ReLAVRA-PAHO

Percentage of carbapenem resistance in *Acinetobacter* spp. in the years studied					
Country	2000	2002	2005	2009	2013
Argentina	17	16	27	78	82
Bolivia				19	53
Brazil		14		56	33
Chile				30	
Colombia		32		60	56
Costa Rica		3			
Cuba					66
Ecuador	27	21	8	54	83
El Salvador		17	11	19	46
Guatemala	33	45	40	64	46
Honduras			27	23	28
México		4		59	
Nicaragua		6	6	15	79
Panamá			27	77	78
Paraguay	10		33	63	77
Perú					78
R. Dominicana			22	20	20
Uruguay				36	
Venezuela	20	31	46	33	73

Carbapenem resistance

Acquired carbapenem resistance in *Acinetobacter* spp. is often associated with acquired carbapenemase production. The most frequent ones are carbapenem-hydrolyzing class D

β-lactamases (CHDLs) and secondly, metalloenzymes (MBL) such as VIM, IMP and NDM[37,38].

OXA-type carbapenemases

Currently, there are six subclasses of CHDLs associated with *A. baumannii*: intrinsic chromosomal OXA-51-like enzymes and acquired OXA-23-like, OXA-24-like, OXA-58-like, OXA-143-like and OXA-235-like. CHDLs exhibit weak carbapenem hydrolysis; however, they can confer resistance mediated by the combination of natural low permeability and IS*Aba* elements located upstream of the gene. The $bla_{\text{OXA-51-like}}$ gene codes for the intrinsic carbapenemase found in *A. baumannii* although clinically significant resistance to carbapenems mediated by $bla_{\text{OXA-51-like}}$ has only been observed in isolates with the insertion sequence IS*Aba*1 located immediately upstream of the gene. However, plasmids harboring IS*Aba*1 – $bla_{\text{OXA-51-like}}$ have been detected in *A. baumannii*, *Acinetobacter nosocomialis* and *Acinetobacter pittii*, as well. This affects the accuracy of using $bla_{\text{OXA-51-like}}$ detection as a tool for differentiating *A. baumannii* from other *Acinetobacter* species.

The first reported OXA-type enzyme was a plasmid-encoded β-lactamase described in 1985 that was initially named ARI-1 and later OXA-23[24,37]. The $bla_{\text{OXA-23}}$ gene can be located either on the chromosome or on plasmids[37]. This carbapenemase was the first described in LA in addition to being the most frequently reported and geographically most disseminated in LA. Its presence has been reported in all the Latin American countries where molecular epidemiology studies have been published (Table 2 and Fig. 1).

The worldwide dissemination of $bla_{\text{OXA-23}}$ would be related to International clones I or II. In South America (SA) this carbapenemase has been commonly associated with CC113/CC79; however, it has also been detected in clones recovered in a lower proportion (CC104/CC15, CC110/ST25, CC109/CC1) and in many sporadic isolates[3,6,9,14–17,28–30,34,36]. Some OXA-23 allelic variants, such as OXA-239, have been described, which showed a major presence in studies conducted in the south of Mexico in the year 2014[1].

As it can be observed in Figure 1, OXA-23 predominates in all the countries of the region, it is the most frequently detected carbapenemase in the CR-Ab population, except for some studies carried out in the south of Mexico[1,4].

In the mid-1990s, $bla_{\text{OXA-58}}$ was reported in Argentina and Venezuela[2,32]. Ten years later, outbreaks by CR-Ab have shown the presence of OXA-58 as the main carbapenem-resistance mechanism in Bolivia and Chile[5,18]. Coincidentally to what has been detected in other regions in recent years, a total displacement of $bla_{\text{OXA-58}}$ by $bla_{\text{OXA-23}}$ was observed in LA. In Argentina, the presence of OXA-58 in the resistant population has gradually declined from 36% in 1995 to 0% in studies conducted after the year 2014[28]. It is also noteworthy to mention the low presence of this carbapenemase in Brazil, where the first isolate harboring OXA-58 was recovered in the year 2007, and so far, has only been detected sporadically[8,36]. In Brazil and Bolivia $bla_{\text{OXA-58}}$-producing isolates belonged to CC113/CC79, reaffirming its important presence in the CR-Ab population of LA, whereas in Argentina some strains were found to be associated to CC109/CC1[5,8,28].

The fact that both carbapenemases have been described in the same STs suggests that the prevalence of one enzyme over another does not only depend exclusively on the clone, but also on the ability to acquire resistance through horizontal gene transfer and the impact on the MIC value of the antimicrobial agents affected, among other factors[5,9,14,29,30,34,36].

Earlier, Opazo et al.[18] reported the presence of CR-Ab isolates belonging to the 24/40 group in LA, however, unfortunately, they were not sequenced. This carbapenemase, often plasmid-mediated, has been reported to cause hospital outbreaks in many Intensive Care Units (ICUs) worldwide[37]. In LA sporadic isolates were described in Brazil and Colombia in the middle of the last decade[3,31]. Since 2010 the first outbreaks have been detected in Guayaquil, Ecuador (2012) and in Brazil (2014). These isolates belonged to ST15 and CC113/CC79 in Ecuador and Brazil, respectively[17,36]. In Mexico, on the other hand, OXA-72 seems to be the most important contributor to carbapenem resistance in *A. baumannii* in several studies conducted in different cities in the north and center of the country[1,4].

Two new CHDL variants, OXA-143 and OXA-235, have been described in the last 10 years in LA; OXA-143, of plasmid encoding, possesses 40% similarity with OXA-40; there are two variants of this enzyme: OXA-231 and OXA-253[11]. As the $bla_{\text{OXA-143}}$ gene is undetectable using the current multiplex PCR assay available, Higgins et al. showed a modified multiplex PCR which can help to monitor the spread of this carbapenemase[20].

OXA-143 was detected for the first time in 2004 and to date, it has only been isolated in Brazil, its presence in the south of that country reaching about 70%. $bla_{\text{OXA-143}}$ like genes mainly belong to clonal complexes CC104/CC15, CC109/CC1 and CC113/CC79[3,7,10,16].

On the other hand, OXA-235 hydrolyzes penicillins and carbapenems but it does not show activity against extended-spectrum cephalosporins. Only one strain was isolated in Mexico in 2016[11].

Metallo-β-lactamase carbapenemases

Metallo-β-lactamases are divided into six families; of these, only IMP, VIM, SIM and NDM enzymes have been detected in *A. baumannii*[38]. We can differentiate 2 periods regarding the presence of MBLs in LA. The first period started in the mid-1990s, with the detection of IMP-1 in Brazil[35]. Even though more than 15 years have passed and that more allelic variants have been detected (IMP-10), these isolates have been restricted to a few hospitals located in e Sao Pablo State[6]. Apart from Brazil, sporadic isolates harboring bla_{IMP}, $bla_{\text{IM-1}}$ and $bla_{\text{VIM-4}}$ have been described in Mexico[1,4]. The second period started with the detection of the $bla_{\text{NDM-1}}$ gene almost simultaneously in Honduras (2012) and Brazil (2013) in *A. baumannii* isolates belonging to ST25[25,39]. Later in the following years, its presence was communicated in Argentina, Colombia, Nicaragua and Paraguay[21–23]. Moreover, this enzyme was also detected in other genospecies different from *A. baumannii* as well as in *Enterobacteriaceae*.

Table 2 Reports of epidemiological and microbiological features of carbapenemase-producing *A. baumannii* in Latin America

Country	Year	*n*	Type of surveillance	Carbapenemases	Epidemiological features	Reference
Argentina	1995	3	Local	OXA-58	Polyclonal	Afzal-Shah et al.[2]
Argentina	1995/2006	41	Regional	OXA-23 (63%), OXA-58 (36%)	Polyclonal	Merkier et al.[15]
Brazil	1993–2001	73	Local	IMP-1	Polyclonal	Togmin et al.[35]
Venezuela	1998–1999	2	Local	OXA-58	Monoclonal	Salazar de Vegas et al.[32]
Brazil	1997–1999	2	Regional	IMP-10	–	Cayô et al.[6]
Argentina	2006/2009	93	Regional	OXA-23 (90%), OXA-58 (10%)	CC113/CC79, CC103/CC15, CC110/ST25, CC109/CC1	Stietz et al.[34]
Argentina	2005/2012	129	Local	OXA-23 (90%), OXA-58 (10%)	Polyclonal	Rodríguez et al.[28]
Brazil	2004/2008	36	Regional	OXA-143 (52.5%), OXA-23, OXA-72, OXA-58	Polyclonal	Antonio et al.[3]
Brazil	2006/2007	96	Regional	OXA-23	bla_{OXA-66}, bla_{OXA-69}, bla_{OXA-95}, $bla_{OXA-132}$	Grosso et al.[9]
Brazil	2007/2008	60	Regional	OXA-23	CC109/CC1, CC110/CC110, CC113/CC79, CC104/CC15	Martins et al.[14]
Brazil	2007	1	Local	OXA-58	bla_{OXA-65}	de Souza Gusatti et al.[8]
Brazil	2008/2010	74	Regional	OXA-23 (72%), OXA-143 (25%)	CC104, CC109, CC113	Clímaco et al.[7]
Bolivia	2008/2009	15	Regional	OXA-58	bla_{OXA-65}	Bruno et al.[5]
Colombia	2004	30	Local	OXA-23	bla_{OXA-64}, bla_{OXA-69}, polyclonal	Saavedra et al.[30]
Colombia	2006	1	Local	OXA-72	clinical case	Saavedra et al.[31]
Mexico	2007	1	Local	OXA-253	IC-5, bla_{OXA-65}	Higgins et al.[11]
Argentina	2013/2014	33	Regional	OXA-23 (100%)	Polyclonal; ST79, ST1, ST25	Rodríguez et al.[29]
Brazil	2012	50		OXA-143 (86%), OXA-23 (20%), IMP-like (11%)	Polyclonal	Mostachio et al.[16]
Brazil	2013	1	Local	NDM-1	ST25	Pillonetto et al.[25]
Brazil	2014	142	National	OXA-23 (75%), OXA-72 (25%)	ST79, ST15, ST1	Vasconcelos et al.[36]
Chile	2010	2	Local	OXA-58 (100%)	Polyclonal	Opazo et al.[18]
Bolivia	2013	1	Local	OXA-23	ST25	Senati et al.[33]
Bolivia	2013/2014	20	Local	OXA-23 (100%)	Polyclonal, ST25	Rodríguez et al.[29]
Chile	2013/2014	20	Local	OXA-23 (100%)	ST15	Rodríguez et al.[29]
Ecuador	2012/2013	33	Regional	OXA-72 (88%), OXA-23 (12%)	Polyclonal; ST1, ST79	Rodríguez et al.[29]
Honduras	2012	1	Local	NDM-1	Clinical case	Waterman et al.[39]
Mexico	2007/2012	152	Regional	OXA-58 (28%), OXA-72 (25%)	ST762, ST763, ST229, ST369, ST777	Bocanegra-Ibarias et al.[4]
Mexico	2004/2011	303	Local	OXA-72 (50%), VIM-1 (1%)	Polyclonal	Alcantar-Curiel et al.[1]
Paraguay	2013/2014	10	Local	OXA-23 (100%)	Polyclonal, ST25, ST79	Rodríguez et al.[29]
Uruguay	2013/2014	10	Local	OXA-23 (100%)	ST25	Rodríguez et al.[29]

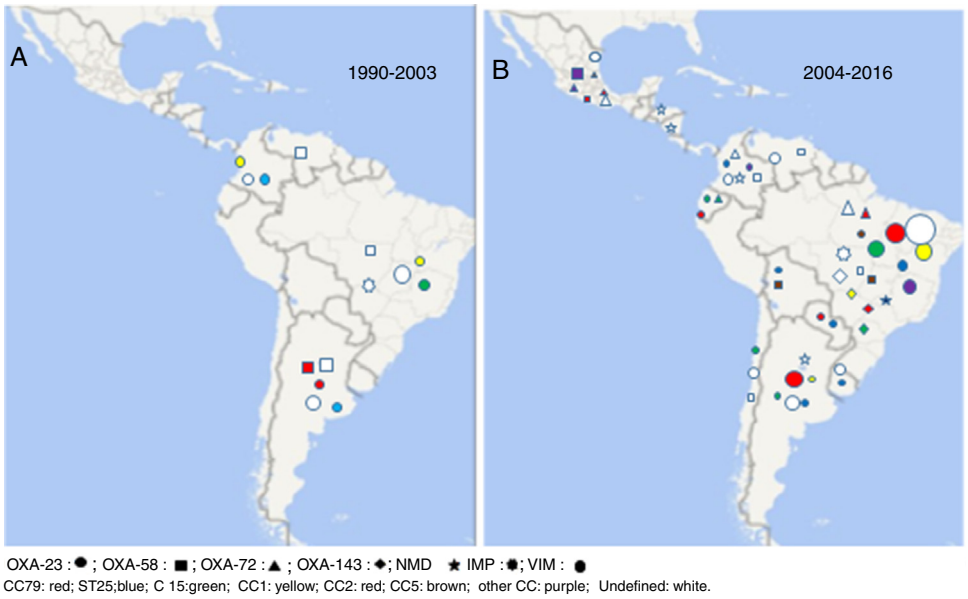

Figure 1 Comparative analysis of the carbapenemase distribution in *A. baumannii* isolates in Latin America (periods 1990–2003 and 2004–2016) and clonal relatedness.

Other carbapenemases

Carbapenemases different from CHDLs and MBLs are rare in *A. baumannii*[24]. However, it is noteworthy to mention the importance of the presence of KPC in *A. baumannii* isolates recovered in Puerto Rico[13-26]. The possibility of transmission of multidrug-resistant *A. baumannii* by tourism and/or human migration is a widely described phenomenon in *A. baumannii*. Therefore, the important interrelationship between the Caribbean country and SA would imply the need to implement measures to detect this enzyme in *A. baumannii*.

In the comparative analysis of the 2 symmetric periods shown in Figure 1, it can be observed that OXA-23 is the carbapenemase/oxacillinase mostly present in both periods (1990–2003 and 2006–2016), whereas OXA-58 was mainly detected in the first period and OXA-72; OXA-143 and NDM in the second one.

Clonal dissemination

Different tools have been proposed to investigate the epidemiology of *A. baumannii* outbreaks. Pulsed-field electrophoresis (PFGE) has been considered the gold-standard technique for fine-scale typing of *A. baumannii* isolates. The presence of multiple clones has been detected in most of the studies conducted in one hospital unit, which evidences endemic features in the CR-Ab population in LA. Conversely, the multilocus sequence typing technique (MLST) has a better ability to group isolates during large-sized epidemiological analyses. $bla_{\text{OXA-51-like}}$ sequence-based typing and 3-locus sequence typing represent economic and rapid methodologies which show a discriminatory power similar to MLST. Most recently, MALDI-TOF has shown to behave less effectively to perform *A. baumannii* clonal discrimination[24].

Despite the widely-accepted idea that a few genotypic groups are responsible for a large proportion of *A. baumannii* infections, particular characteristics of each region have been reported. Contrary to what was reported in Europe and other countries worldwide, in LA, the presence of the international clones II and III represented a minority in the year 2016[7,8,14,24,29,30,34,36].

Research performed in SA has shown a predominance of CC113/CC79. Stietz et al.[34] evidenced its presence in isolates recovered before the year 2000 in a retrospective study. Subsequent studies carried out mainly in Brazil, but also in Argentina and Colombia, confirmed the predominance of CC113/CC79 together with CC103/CC15 and CC109/CC1 in CR-Ab isolates[7,8,14,30,34,36]. In the year 2014 the first plurinational study performed in LA, which involved 9 hospitals belonging to 6 countries, evidenced that its predominance was also extended to countries such as Chile, Uruguay, Paraguay and Ecuador[29]. The spread of ST25 was also highlighted in the mentioned study in different LA countries, similarly to what was observed in other regions[12,29,30,34].

Summary

The main findings and recent changes in the molecular epidemiology of carbapenem-resistant *A. baumannii* clinical isolates in LA were revised in the present study. Among them, we have observed common features with other regions: (1) *A. baumanii* represents the predominant genospecies; (2) the main presence of *A. baumanii* in nosocomial infections and the progressive increase in carbapenem resistance rates; (3) the high prevalence of the $bla_{\text{OXA-23}}$ gene; (4) the emergence of OXA-72 and NDM-1, and other features such as the low predominance of international clones I, II and III. Therefore, we believe that being able to obtain our own results and figures will lead to the

elaboration of a regional casuistic report, which would guide the implementation of the adequate policies to prevent and/or control the spread of multidrug-resistant *A. baumannii* isolates.

Conflict of interest

The authors declare that they have no conflicts of interest.

References

1. Alcantar-Curiel MD, Garcia-Torres LF, Gonzalez-Chavez MI, Morfin-Otero R, Gayoso-Vazquez C, Jarillo-Quijada MD, Fernandez-Vazquez JL, Giono-Cerezo S, Rodriguez-Noriega E, Santos-Precieado JI. Molecular mechanisms associated with nosocomial carbapenem-resistant *Acinetobacter baumannii* in Mexico. Arch Med Res. 2014;45:553–60.
2. Afzal-Shah M, Villar HE, Livermore DM. Biochemical characteristics of a carbapenemase from an *Acinetobacter baumannii* isolate collected in Buenos Aires, Argentina. J Antimicrob Chemother. 1999;43:127–31.
3. Antonio CS, Neves PR, Medeiros M, Mamizuka EM, Elmor de Araújo MR, Lincopan N. High prevalence of carbapenem-resistant *Acinetobacter baumannii* carrying the $bla_{OXA-143}$ gene in Brazilian hospitals. Antimicrob Agents Chemother. 2011;55:1322–3.
4. Bocanegra-Ibarias P, Peña-Lopez C, Camacho-Ortiz A, Llaca-Diaz J, Silva-Sanchez J, Barrios H, Garza-Ramos U, Rodriguez-Flores AM, Garza-Gonzalez E. Genetic characterisation of drug resistance and clonal dynamics of *Acinetobacter baumannii* in a hospital setting in Mexico. Int J Antimicrob Agents. 2015;45:309–13.
5. Bruno LS, Gallego L, Amyes SGB. Multi-drug resistance profiles and the genetic features of *Acinetobacter baumannii* isolates from Bolivia. J Infect Dev Ctries. 2013;7:323–8.
6. Cayô R, Rodrigues-Costa F, Matos AP, Carvalhaes CG, Jové T, Gales AC. Identification of a new integron harboring *bla*(IMP-10) in carbapenem-resistant *Acinetobacter baumannii* clinical isolates. Antimicrob Agents Chemother. 2015;59:3687–9.
7. Clímaco EC, Oliveira ML, Pitondo-Silva A, Oliveira MG, Medeiros M, Lincopan N, da Costa Darini AL. Clonal complexes 104, 109 and 113 playing a major role in the dissemination of OXA-carbapenemase-producing *Acinetobacter baumannii* in Southeast Brazil. Infect Genet Evol. 2013;19:127–33.
8. de Souza Gusatti C, Martins Bertholdo L, Muner Otton L, Padilha Marchetti D, Alessandra Ferreira E, Corção G. First occurrence of bla_{OXA-58} in *Acinetobacter baumannii* isolated from a clinical sample in Southern Brazil. Braz J Microbiol. 2012;43:243–6.
9. Grosso F, Carvalho KR, Quinteira S, Ramos A, D'Alincourt Carvalho-Assef AP, Asensi MD, Peixe L. OXA-23-producing *Acinetobacter baumannii*: a new hotspot of diversity in Rio de Janeiro. J Antimicrob Chemother. 2011;66:62–5.
10. Higgins PG, Poirel L, Lehmann M, Nordman P, Seifert H. OXA-143 a novel carbapenem-hydrolyzing class D β-lactamase in *Acinetobacter baumannii*. Antimicrob Agents Chemother. 2009;53:5035–8.
11. Higgins PG, Perez-Llarena FJ, Zander E, Fernandez A, Bou G, Seifert H. OXA-235, a novel class D β-lactamase involved in resistance to carbapenems in *Acinetobacter baumannii*. Antimicrob Agents Chemother. 2013;57:2121–6.
12. Labarca JÁ, Salles MJ, Seas C, Guzman-Blanco M. Carbapenem resistance in *Pseudomonas aeruginosa* and *Acinetobacter baumannii* in the nosocomial setting in Latin America. Crit Rev Microbiol. 2016;42:276–92.
13. Martinez T, Martinez I, Vazquez GJ, Aquino EE, Robledo IE. Genetic environment of the KPC gene in *Acinetobacter baumannii* ST2 clone from Puerto Rico and genomics insights into drugs resistance. J Med Microbiol. 2016;65:92.
14. Martins AF, Kuchenbecker R, Sukiennik T, Boff R, Reiter KC, Lutz L, Machado AB, Barth AL. Carbapenem-resistant *Acinetobacter baumannii* producing the OXA-23 enzyme: dissemination in Southern Brazil. Infection. 2009;37:474–6.
15. Merkier AK, Catalano M, Ramirez MS, Quiroga C, Orman B, Ratier L, Famiglietti A, Vay C, Matino AD, Cetron D. Polyclonal spread of bla_{OXA-23} and bla_{oxa-58} in *Acinetobacter baumannii* isolates from Argentina. J Infect Dev Ctries. 2008;2:235–40.
16. Mostachio AK, Levin AS, Rizek FR, Zerbini J, Costa SF. High prevalence of OXA-143 and alteration of outer membrane proteins in carbapenem – resistant *Acinetobacter* spp. isolates in Brazil. Int J Antimicrob Agents. 2012;39:396–401.
17. Nuñez Quezada T, Rodríguez CH, Castro Cañarte G, Nastro M, Balderrama Yarhui N, Dabos L, Acosta Mosquera Y, Plaza Moreira N, Famiglietti A. Outbreak of bla_{OXA-72}-producing *Acinetobacter baumannii* in South America. J Chemother. 2016;13:1–4.
18. Opazo A, Dominguez M, Bello H, Amyes SGB, Gonzales GR. OXA-type carbapenemases in *Acinetobacter baummannii* in South America. J Infect Dev Ctries. 2012;6:311–6.
19. Organización, Panamericana de la Salud. Organización Mundial de la Salud. Informe Anual de la Red de Monitoreo/Vigilancia de la Resistencia a los Antibióticos, 2000 Asunción, Paraguay, 31/1 al 2/2; 2000.
20. Organización, Panamericana de la Salud. Organización Mundial de la Salud. Informe Anual de la Red de Monitoreo/Vigilancia de la Resistencia a los Antibióticos, 2002 Buenos Aires, Argentina, 10 al 13 de mayo; 2003.
21. Organización, Panamericana de la Salud. Organización Mundial de la Salud. Informe Anual de la Red de Monitoreo/Vigilancia de la Resistencia a los Antibióticos, 2005 Montevideo, Uruguay, 14 al 16 noviembre; 2006.
22. Organización, Panamericana de la Salud. Organización Mundial de la Salud. Informe Anual de la Red de Monitoreo/Vigilancia de la Resistencia a los Antibióticos, 2009 Lima, Perú, 3 y 4 de diciembre; 2009.
23. Organización, Panamericana de la Salud. Organización Mundial de la Salud. Informe anual de la red de monitoreo de la resistencia a los antimicrobianos y vigilancia de las infecciones asociadas a la atención de la salud. Rev Patol Trop. 2014;43:1–108.
24. Peleg AY, Seifert H, Paterson DL. *Acinetobacter baumannii*: emergence of a successful pathogen. Clin Microbiol Rev. 2008;21:538–82.
25. Pillonetto M, Arend L, Vespero EC, Pelisson M, Chagas TP, Carvalho-Assef AP, Asensi MD. First report of NDM-1-producing *Acinetobacter baumannii* sequence type 25 in Brazil. Antimicrob Agents Chemother. 2014;58:7592–4.
26. Robledo IE, Aquino EE, Sante MI, Santana JL, Otero DM, León CF, Vásquez GJ. Detection of KPC in *Acinetobacter* spp. in Puerto Rico. Antimicrob Agents Chemother. 2010;54:1354.
27. Rodríguez CH, Nastro M, Dabos L, Vay C, Famiglietti A. Frecuencia de aislamiento y resistencia a los antimicrobianos en *Acinetobacter* spp. en un Hospital Universitario de la Ciudad de Buenos Aires. Rev Argent Microbiol. 2014;46:320–4.
28. Rodríguez CH, Nastro M, Fiorilli G, Dabos L, Lopez Calvo J, Fariña ME, Vay C, Famiglietti A. Trends in the resistance profiles of *Acinetobacter baumannii* endemics clones in a university hospital of Argentina. J Chemother. 2014;30:25–7.
29. Rodríguez CH, Balderrama Yarhui N, Nastro M, Nuñez Quezada T, Castro Cañarte G, Magne Ventura R, Ugarte Cuba T, Valenzuela N, Roach F, Mota MI, Burger N, Velázquez Aguayo G, Ortellado-Canese J, Bruni G, Pandolfo C, Bastyas N, Famiglietti A. Molecular epidemiology of carbapenem-resistant *Acinetobacter baumannii* in South America. J Med Microbiol. 2016;65:1088–91.
30. Saavedra SY, Nuñez JC, Pulido IY, Gonzalez EB, Valenzuela EM, Reguero MT, Mantilla JR, Arango AI, Bravo P. Characterisation of

carbapenem-resistant *Acinetobacter calcoaceticus-baumannii* complex isolates in a third-level hospital in Bogotá Colombia. Int J Antimicrob Agents. 2008;31:389–91.
31. Saavedra SY, Cayõ R, Gales AC, Leal AL, Saavedra CH. Early dissemination of OXA-72-producing *Acinetobacter baumannii* strain in Colombia: a case report. Braz J Infect Dis. 2014;18:678–80.
32. Salazar De Vegas EZ, Nievesm B, Ruiz M, Ruíz J, Vila J, María A, Elsa V. Molecular epidemiology and characterization of resistance mechanisms to various antimicrobial agents in *Acinetobacter baumannii* isolated in Mérida Venezuela. Med Sci Monit. 2007;13:89–94.
33. Senati S, Vilagran AL, Bartoloini A, Rossolini GM, Pollecchi L. OXA-23 producing ST *Acinetobacter baumannii*: first report in Bolivia. J Glob Antimicrob Resist. 2016;4:70–1.
34. Stietz MS, Ramírez MS, Vilacoba E, Merkier AK, Limansky AS, Centrón D, Catalano M. *Acinetobacter baumannii* extensively drug resistant lineages in Buenos Aires hospitals differ from the international clones I-III. Infect Genet Evol. 2013;14:294–301.
35. Togmin M, Gales A, Penteado A, Silbert S, Sader H. Dissemination of IMP-1 metallo-beta-lactamase-producing *Acinetobacter* species in a Brazilian teaching hospital. Infect Control Hosp Epidemiol. 2006;27:742–7.
36. Vasconcelos AT, Barth AL, Zavascki AP, Gales AC, Levin AS, Lucarevschi BR, Cabral BG, Brasiliense DM, Rossi F, Furtado GH, Carneiro IC, da Silva JO, Ribeiro J, Lima KV, Correa L, Britto MH, Silva MT, da Conceição ML, Moreira M, Martino MD, de Freitas MR, Oliveira MS, Dalben MF, Guzman RD, Cayô R, Morais R, Santos SA, Martins WM. The changing epidemiology of *Acinetobacter* spp. producing OXA carbapenemases causing bloodstream infections in Brazil: a BrasNet report. Diagn Microbiol Infect Dis. 2015;83:382–5.
37. Walther-Rasmussen J, Hoiby N. OXA-type carbapenemases. J Antimicrob Chemother. 2006;57:373–83.
38. Walsh T, Toleman M, Poirel L, Nordmann P. Metallo-β-lactamases: the quiet before the storm? Clin Microbiol Rev. 2005;18:306–25.
39. Waterman PE, McGann P, Snersud E, Clifford RJ, Kwak YI, Muñoz-Urbizo IP, Tabora-Castellanos J, Milillo M, Preston L, Aviles R, Sutter DE, Lesho EP. Bacterial peritonitis due to *Acinetobacter baumannii* type ST25 with plasmid-borne New Delhi metallo-β-lactamase in Honduras. Antimicrob Agents Chemother. 2013;57:4584–6.