Hindawi Publishing Corporation
BioMed Research International
Volume 2014, Article ID 305784, 11 pages
http://dx.doi.org/10.1155/2014/305784

Review Article

Epidemiology of Carbapenemase-Producing Enterobacteriaceae and *Acinetobacter baumannii* in Mediterranean Countries

Nassima Djahmi,[1,2] Catherine Dunyach-Remy,[1,3] Alix Pantel,[1,3] Mazouz Dekhil,[2] Albert Sotto,[1,4] and Jean-Philippe Lavigne[1,3]

[1] *National Institute of Health and Medical Research, U1047, Faculty of Medicine, Montpellier 1 University, 30908 Nîmes Cedex 02, France*
[2] *Department of Microbiology, University Hospital Ibn Rochd, 23000 Annaba, Algeria*
[3] *Department of Microbiology, University Hospital Caremeau, 30029 Nîmes Cedex 9, France*
[4] *Departement of Infectious Diseases, University Hospital Caremeau, 30029 Nîmes Cedex 9, France*

Correspondence should be addressed to Jean-Philippe Lavigne; jean.philippe.lavigne@chu-nimes.fr

Received 8 December 2013; Accepted 22 April 2014; Published 13 May 2014

Academic Editor: Selma Uzunović

The emergence and global spread of carbapenemase-producing Enterobacteriaceae and *Acinetobacter baumannii* are of great concern to health services worldwide. These β-lactamases hydrolyse almost all β-lactams, are plasmid-encoded, and are easily transferable among bacterial species. They are mostly of the KPC, VIM, IMP, NDM, and OXA-48 types. Their current extensive spread worldwide in Enterobacteriaceae is an important source of concern. Infections caused by these bacteria have limited treatment options and have been associated with high mortality rates. Carbapenemase producers are mainly identified among *Klebsiella pneumoniae*, *Escherichia coli*, and *A. baumannii* and still mostly in hospital settings and rarely in the community. The Mediterranean region is of interest due to a great diversity and population mixing. The prevalence of carbapenemases is particularly high, with this area constituting one of the most important reservoirs. The types of carbapenemase vary among countries, partially depending on the population exchange relationship between the regions and the possible reservoirs of each carbapenemase. This review described the epidemiology of carbapenemases produced by enterobacteria and *A. baumannii* in this part of the world highlighting the worrisome situation and the need to screen and detect these enzymes to prevent and control their dissemination.

1. Introduction

Carbapenems are β-lactam group of drugs that are often used as antibiotics of last resort for treating infection due to multidrug-resistant Gram-negative bacilli. They are also stable even in response to extended-spectrum (ESBL) and AmpC β-lactamases. However, this scenario has changed with the emergence in the last few years of carbapenem resistant bacteria both in nonfermenters (*Acinetobacter baumannii* and *Pseudomonas aeruginosa*) and in fermenters (Enterobacteriaceae) Gram-negative bacilli [1].

Resistance to carbapenems is mediated mostly by two main mechanisms: (i) production of a β-lactamase (derepressed cephalosporinase or ESBL) with nonsignificant carbapenemase activity combined with decreased permeability due to porin loss or alteration; (ii) production of a carbapenem-hydrolyzing β-lactamase [2].

Carbapenemases have now become a major concern worldwide [3, 4]. They are an increasing concern for global healthcare due to their association with resistance to β-lactam antibiotics and to other classes of antibiotics such as aminoglycosides, fluoroquinolones, and cotrimoxazole [5]. Thus they reduce the possibility of treating infections due to multidrug-resistant strains [6]. The first description of carbapenemase-producing enterobacteria (NmcA) was in 1993 [7]. Since then, large varieties of carbapenemases have been identified belonging to three molecular classes: the Ambler class A, B, and D β-lactamases [8]. They have

emerged and diffused in different parts of the world, including Mediterranean countries, in recent years [2–6, 9]. These enzymes are carried either on chromosome or acquired via plasmids [10].

The aim of this review is to describe the epidemiology of the main carbapenemases circulating in the Mediterranean countries, a region of the world with a great diversity and population mixing. This region includes 11 European countries (Albania, Bosnia, and Herzegovina, Croatia, Spain, France, Greece, Italia, Malta, Montenegro, Monaco and Slovenia), 5 Asian countries (Cyprus, Israel, Lebanon, Syria, Turkey) and 5 African countries (Algeria, Egypt, Libya, Morocco, Tunisia).

2. Class A Carbapenemases

2.1. Enterobacteriaceae. A variety of class A carbapenemases have been described: some are chromosome encoded (NmcA, Sme, IMI-1, SFC-1) and others are plasmid encoded (KPC, IMI-2, GES derivatives such as GES-1, GES-2, GES-4, and GES-5) but all effectively hydrolyze carbapenems and are partially inhibited by clavulanic acid [8].

KPCs (acronym for *K. pneumoniae* carbapenemase) are the most frequently encountered enzymes in this group [2]. Since the first report of this enzyme in 1996 isolated from a clinical *Klebsiella pneumonia* strain in North Carolina, USA [11], the KPC producers had spread around the world and are becoming a major clinical and public health concern [12].

Several KPC clones are disseminating harboring different multilocus sequence type, β-lactamase content, and plasmids. However the bla_{KPC} genes are flanked by the same transposon *Tn*4401 located on conjugative plasmids and are horizontally transferred [13]. This gives to this enzyme an extraordinary spreading capacity [14]. They have been detected more often in *Klebsiella* spp. [2] but have also been reported in other Enterobacteriaceae [15]. Thirteen variants of KPC are known so far; KPC-2 and KPC-3 are the most frequent worldwide variants [16]. The mortality rate due to infection with a KPC producer ranged from 25% to 69% [2, 17].

The first outbreak of KPC-producing *K. pneumoniae* outside the United States was described in Israel in 2006 [18]. This strain belonged to the pandemic clone ST258, suggesting an importation from the USA [19]. Moreover, a large range of enterobacteria producing these variants was described in Israel [20–26]. Since then, many studies have reported outbreaks of KPC producers in enterobacterial isolates in many Mediterranean countries (Figure 1), in which most cases have been reported so far in Greece, where the situation can be described as endemic [27, 28]. Moreover a recent study showed a wide dissemination of KPC-producing strains to many healthcare institutions in Italy [2, 29]. KPC producers became the most prevalent carbapenemase found in this country [30]. Spain and France have recently described a rapid increase of cases [31, 32]. Single or sporadic hospital outbreaks caused by KPCs isolated from various species were reported [32–34]. KPC-2 is clearly the most prevalent variant in Europe [12, 35]. In most of the cases reported from France, the patients had been transferred from a country where KPC enzymes are endemic (e.g., Israel, Greece, USA, or Italy) [34]. Croatia is another Mediterranean country affected [36].

To date, there is no description of class A carbapenemases from North African countries. However, KPC producers have already been isolated in an *E. coli* strain in Algeria (N. Djahmi et al., unpublished data).

2.2. Acinetobacter baumannii. Among the class A carbapenemases, KPCs and GES-type have been described in *A. baumannii* [37]. KPC-2, KPC-3, KPC-4, and KPC-10 variants were identified in 10 *A. baumannii* clinical isolates collected in 2009 from 17 hospitals in Puerto Rico [38].

In Mediterranean countries, only GES-type carbapenemase was reported. A GES-14-producing *A. baumannii* clinical strain was isolated in France. This strain was demonstrated to confer resistance to all β-lactams, including carbapenems [39]. Very recently, an emergence of GES-11 was reported from Turkey [40]. Some strains coexpressed both OXA-23 and GES-11. They belonged to ST2, being part of the worldwide distributed clone II group.

3. Class B Carbapenemases

3.1. Enterobacteriaceae. Class B metallo-β-lactamases (MBLs) are mostly of the Verona integron-encoded metallo-β-lactamase (VIM) and IMP types and, more recently, of the New Delhi metallo-β-lactamases-1 (NDM-1) type [8, 41]. MBLs can hydrolyze all β-lactams except monobactam (e.g., aztreonam) [41]. Their activity is inhibited by EDTA but not by clavulanic acid [41].

IMP-1 was the first MBL reported in *Serratia marcescens* from Japan in 1991 [42]. Since then, MBLs have been observed worldwide [8, 41]. The most commonly found class B carbapenemases are of the VIM type [43], which has been identified in all continents [44]. The death rates associated with MBL producers are high (18% to 67%) [2, 45].

Italy was the first Mediterranean country to report acquired metallo-β-lactamases, with sporadic isolates of VIM-4-producing *K. pneumoniae* and *Enterobacter cloacae* [8, 46]. Since then, single or sporadic hospital outbreaks caused by VIM-1 like enzymes were described from various regions in this country [47, 48]. However, such VIM-producing Enterobacteriaceae have not undergone wide dissemination, unlike that observed in Greece during the same period [49]. Endemicity of VIM- and IMP-producing *Klebsiella pneumoniae* strains has now been noted in Greece [8, 41]. Additionally, outbreaks and single reports of VIM- or IMP-type producers have been reported in several countries of Mediterranean area, such as France [50, 51], Spain [33], Morocco [52], Egypt [53, 54], Algeria [55], and Tunisia [56].

Most recently reported, NDM-1 enzyme is spreading rapidly worldwide [44] notably Central and South America that represented the last zone without description of this enzyme [57, 58]. NDM-1 was initially identified in *E. coli* and *K. pneumoniae* in a patient returning to Sweden from India in 2008 [59]. Most of the outbreaks indicated a link with the Indian subcontinent, in some cases with the Balkan countries [60], and the Middle East [61]. Five minor variants

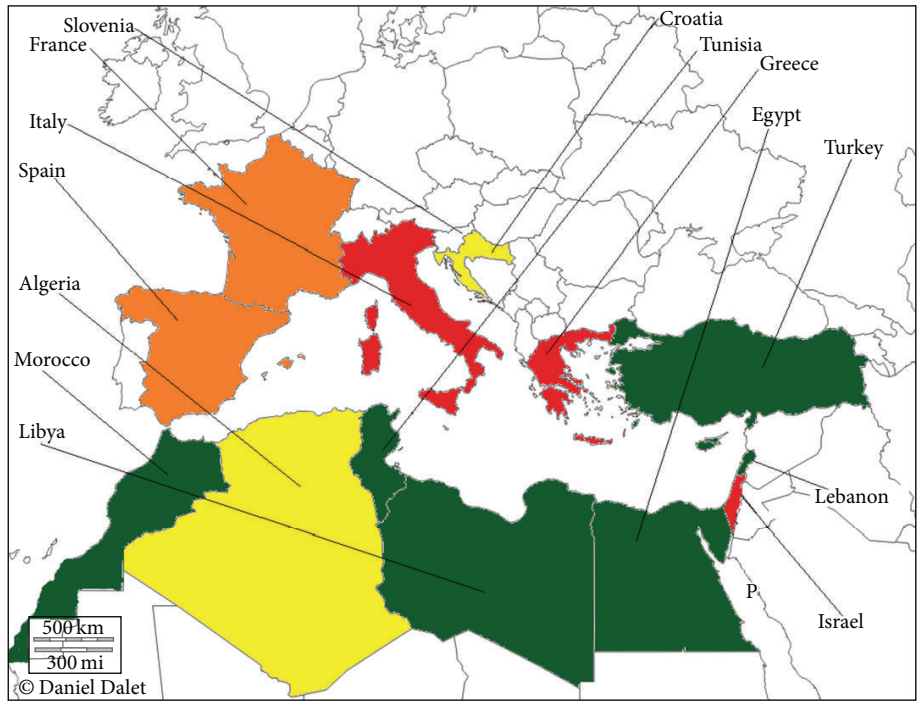

Figure 1: Geographic distribution of KPC enzymes in Mediterranean countries. White, no case reported; yellow, single KPC-producing isolates; green, some outbreaks of KPC-producing isolates; orange, several outbreaks of KPC-producing isolates; red, endemicity of KPC-producing isolates.

of NDM-1 (NDM-2 to NDM-6) have been now identified in enterobacteria and very recently, a novel variant NDM-7 was detected in *E. coli* in France [62]. Contrarily to other carbapenemase genes, $bla_{\text{NDM-1}}$ is not associated with a single clone. Thus NDM-1 has been identified mostly in nonclonally related *E. coli* and *K. pneumoniae* and to a lesser extent in other enterobacterial species [63]. These enzymes are encoded on highly transmissible plasmids that spread rapidly between bacteria, rather than relying on clonal proliferation. The strains harboring NDM are broadly resistant to many other drug classes in addition to β-lactams and carry a diversity of other resistance mechanisms, which leaves few treatment options (tigecycline or colistin) [63, 64]. NDM-1 producers have been reported in the environment and in the community [2, 63]. They have been identified in Enterobacteriaceae species around the world [59] highlighting the ability of this gene to disseminate in bacteria [65]. Moreover NDM-1 has been identified in *E. coli* ST131, a well-known source of community infections [66, 67].

Single or sporadic hospital outbreaks caused by NDM-1 producing enterobacterial strains were reported from many countries in Mediterranean area (Figure 2): France [68, 69], Italy [70], Lebanon [71], Morocco [52, 72], Spain [33, 73–75], Tunisia [76], and Turkey [77, 78]. Very recently, NDM-5 was identified in *E. coli* in Algeria (Sassi et al., unpublished data). There are no published data yet from Libya, but a very recent study has reported identification of NDM-1 in *K. pneumoniae* from patient transferred from Libya to Tunisia [76], indicating the emergence of this enzyme resistance in Mediterranean countries. Finally an emergence of NDM-producing *K. pneumoniae* was recently reported in Greece [79].

3.2. Acinetobacter baumannii. To date, four groups of MBLs have been identified in *A. baumannii*: IMP-like, VIM-like, SIM-like, and recently the NDMs [80].

The first MBL identified in *A. baumannii* strains was IPM-2 reported in 2000 from Italy [81]. Since then, IMP-like, VIM-like, and SIM-like have been sporadically reported in some parts of the world [82], including Mediterranean countries, especially in Greece and Italy [81–85]. Concerning NDM producers, *A. baumannii* bacteria harboring these enzymes were increasingly observed around the world [86] notably in Mediterranean countries. They were detected in North Africa: Algeria [87, 88] and Libya (isolated from a patient transferred from Libya to Denmark) [89]; in Europa: France [87, 90, 91] and Slovenia [86]; and in Turkey [92]. The isolation of an NDM-1-producing *A. baumannii* in a Czech patient repatriated in 2011 from Egypt was described [93]. In France, the emergence of imported cases of NDM-1-producing *A. baumannii* was linked with Algeria [87, 90]. The strains belonged to ST85, the main clone isolated in Mediterranean countries [90, 91]. Finally, another clone NDM variant, NDM-2, was found in *A. baumannii* isolates in Egypt [94] and Israel [95].

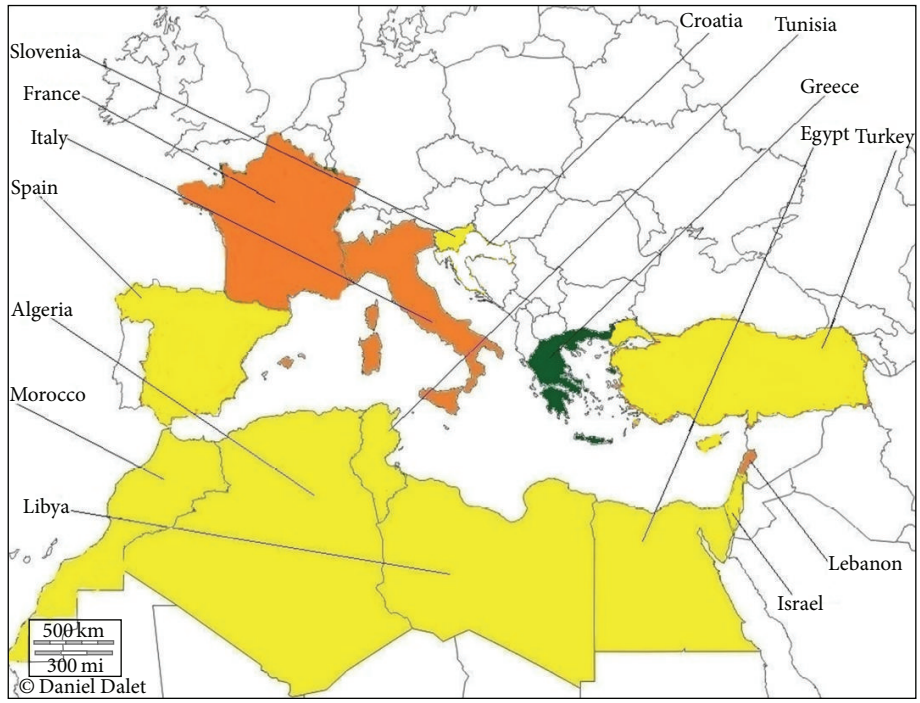

Figure 2: Geographic distribution of NDM type producers in Mediterranean countries. White, no case reported; yellow, sporadic NDM-producing isolates; green, emerging outbreak of NDM-producing isolates; orange, single hospital outbreaks of NDM-producing isolates.

4. Class D Carbapenemases

4.1. Enterobacteriaceae. Class D β-lactamases, also named OXAs for oxacillinases include 232 enzymes with few variants, possessing the same carbapenemase activity [96]. Initially OXA β-lactamases were reported from *P. aeruginosa* but until now, these carbapenemases have been detected in many other Gram-negative bacteria, including Enterobacteriaceae [16].

OXA-48 represents the main enzyme isolated around the world. This enzyme hydrolyses penicillins but has a weak activity against carbapenems or extended-spectrum cephalosporins (third generation cephalosporin, aztreonam) [2]. However, its frequent association with ESBL (notably CTX-M-15 enzyme) increases the level of resistance to carbapenem. Its activity is not inhibited by EDTA or clavulanic acid [2], tazobactam, and sulbactam, whereas its activity may be inhibited by NaCl *in vitro* [96, 97]. Its high level of resistance to temocillin is interesting to detect this enzyme [98, 99]. A point mutant analog of OXA-48, namely, OXA-181, with similar carbapenemase activity, has been identified in enterobacterial strains from India [100, 101] and from patients with a link to the Indian subcontinent [100, 102]. Further analysis of the OXA-48-producing isolates demonstrated that this enzyme was not exclusively linked with a single clone, and the $bla_{\text{OXA-48}}$ gene was associated with either transposon *Tn*1999 or transposon *Tn*1999.2 within transferable nontypable plasmids of 70 or 150 kb [103]. The death rates associated with OXA-producers are unknown.

OXA-48 was initially identified in *K. pneumoniae* isolate from Turkey in 2001 [104]. Since then, OXA-48 producing strains have been extensively reported as sources of nosocomial outbreaks in many parts of the world notably in Mediterranean countries [105–110] (Figure 3): Croatia [111], Egypt [54], France [109], Greece [112], Israel [113, 114], Italy [53], Lebanon [71, 115, 116], Libya [117], Slovenia [118], Spain [33, 119], Tunisia [120], and Turkey [106]. Moreover, this enzyme disseminated in various Enterobacteriaceae species [2, 96]. To date OXA-48 represents the most common carbapenemase type circulating in this part of the world notably in Spain [33] and France [109]. The Middle East and North Africa are considered as reservoirs of OXA-48 producers [121]. In the last few years, a nosocomial dissemination of OXA-48-producing Enterobacteriaceae has been reported in different hospitals in Morocco [122]. This problem was exacerbated by the occurrence of this enzyme in community [123] and in environment [124] suggesting that OXA-48 is endemic in this country [122]. More recently, the identification of the $bla_{\text{OXA-48}}$ gene in a *K. pneumoniae* isolate has been reported in Algeria (N. Djahmi, personal data).

4.2. Acinetobacter baumannii. The class D carbapenemases (oxacillinases) are by far the most prevalent carbapenemases in *A. baumannii* [125, 126]. They can be grouped into six subclasses: intrinsic chromosomal OXA-51-like, among which there are over 70 variants and the acquired OXA-23-like, OXA-24/40-like, OXA-58-like, OXA-143-like, and OXA-235-like β-lactamases [97, 127].

The first case of OXA-type enzyme was reported from a clinical *A. baumannii* isolate detected in Scotland in 1985. It was initially named ARI-1 (*Acinetobacter* resistant to imipenem) [128] and renamed OXA-23 after sequencing

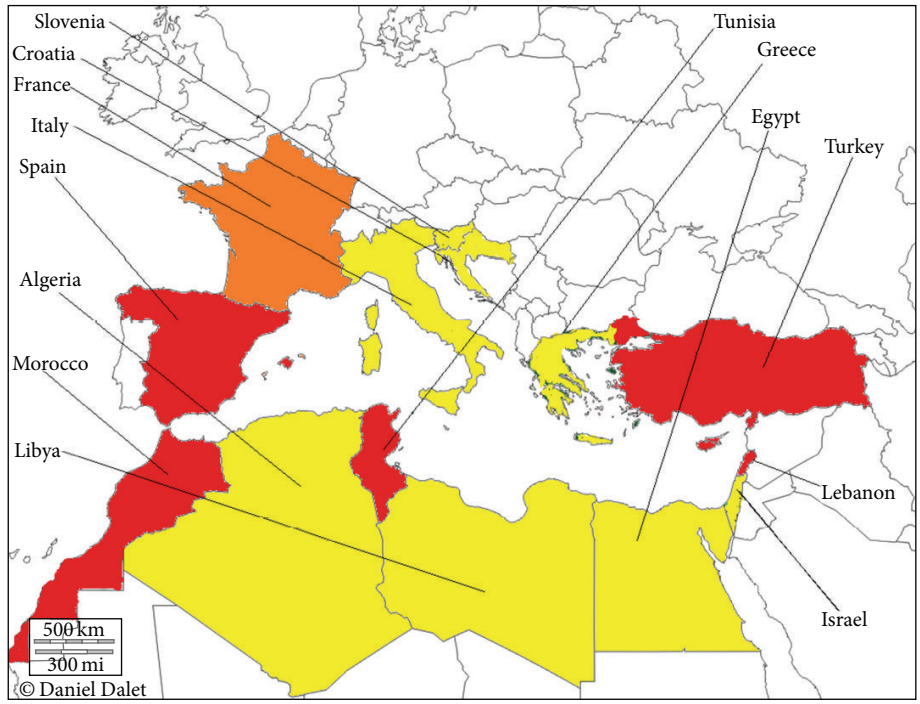

Figure 3: Geographic distribution of OXA-48 type producers in Mediterranean countries. White, no case reported; yellow, single OXA-48-producing isolates; orange, several outbreaks of OXA-48-producing isolates; red, nationwide distribution of OXA-48-producing isolates.

[129]. *A. radioresistens* was identified as the progenitor of the bla_{OXA23}-like gene [130].

Nosocomial outbreaks or sporadic cases caused by carbapenem-resistant *A. baumannii* producing these OXA-enzymes have been reported worldwide [80, 131–133]. *A. baumannii* epidemic strains were assigned to international clonal lineages I or II [134], with recent studies reporting the spread of genetically related epidemic clone of OXA-23-producing *A. baumannii* and belonging to IC-II within the Mediterranean region [135–137]. The $bla_{\text{OXA-23}}$ gene was either located on the chromosome or on plasmids and was associated with four different genetic structures, with the most frequent being transposons *Tn*2006 [134].

The emergence and spread of several outbreak or sporadic *A. baumannii* strains producing OXA-23-like enzymes have been reported around the world [134]. During a long period, the $bla_{\text{OXA-58}}$ carbapenemase gene has been predominated among carbapenem-resistant *A. baumannii* isolates in various Mediterranean countries [85]. Since 2009, a replacement of $bla_{\text{OXA-58}}$ gene with $bla_{\text{OXA-23}}$ gene has been reported and it became the most prevalent carbapenemase-encoding gene circulating in the Mediterranean region: Algeria [88, 136], Croatia [111], Egypt [138], France [139], Greece [140], Italy [135, 141], Israel [132], Spain [137, 142], Tunisia [143], and Turkey [83, 144]. The replacement of OXA-58 by OXA-23 might be explained by the selective advantage associated with the higher carbapenemase activity of OXA-23 [37, 142] and/or acquisition of carbapenem resistance through horizontal gene transfer [37].

Concerning other OXA-producers, outbreaks of OXA-72-producing *A. baumannii* were described in Croatia [145] and OXA-69 or OXA-97 in Tunisia [146, 147].

5. Conclusion

In recent years the emergence of carbapenem-resistant Gram-negative bacilli in Mediterranean region is an alarming problem. This part of the world is the cradle of western civilization representing nearly 475 million inhabitants (6.3% of world population). It is the location of a large population mixing explaining the importance of the dissemination of carbapenemase producers. This situation imposes a series of measures as soon as possible. These need the over-the-counter sale of indistinctly antibiotics, improving basic and extended knowledge on hygiene, the reinforcement of infection control measures, and the early and accurate detection, with restriction of the usage of carbapenems, to control the spread of these multidrug resistant organisms.

Conflict of Interests

The authors state that there is no conflict of interests.

References

[1] M. V. Jesudason, A. J. Kandathil, and V. Balaji, "Comparison of two methods to detect carbapenemase & metallo-β-lactamase production in clinical isolates," *Indian Journal of Medical Research*, vol. 121, no. 6, pp. 780–783, 2005.

[2] P. Nordmann, T. Naas, and L. Poirel, "Global spread of carbapenemase producing *Enterobacteriaceae*," *Emerging Infectious Diseases*, vol. 17, no. 10, pp. 1791–1798, 2011.

[3] Y. Carmeli, M. Akova, G. Cornaglia et al., "Controlling the spread of carbapenemase-producing Gram-negatives: therapeutic approach and infection control," *Clinical Microbiology and Infection*, vol. 16, no. 2, pp. 102–111, 2010.

[4] G. Cornaglia, H. Giamarellou, and G. M. Rossolini, "Metallo-β-lactamases: a last frontier for β-lactams?" *The Lancet Infectious Diseases*, vol. 11, no. 5, pp. 381–393, 2011.

[5] M. Souli, I. Galani, and H. Giamarellou, "Emergence of extensively drug-resistant and pandrug-resistant Gram-negative bacilli in Europe," *Euro Surveillance*, vol. 13, no. 47, 2008.

[6] H. Giamarellou and G. Poulakou, "Multidrug-resistant gram-negative infections: what are the treatment options?" *Drugs*, vol. 69, no. 14, pp. 1879–1901, 2009.

[7] T. Naas and P. Nordmann, "Analysis of a carbapenem-hydrolyzing class A β-lactamase from *Enterobacter cloacae* and of its LysR-type regulatory protein," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 91, no. 16, pp. 7693–7697, 1994.

[8] A. M. Queenan and K. Bush, "Carbapenemases: the versatile β-lactamases," *Clinical Microbiology Reviews*, vol. 20, no. 3, pp. 440–458, 2007.

[9] T. R. Walsh, "Emerging carbapenemases: a global perspective," *International Journal of Antimicrobial Agents*, vol. 36, no. 3, pp. S8–S14, 2010.

[10] F. Nahid, A. A. Khan, S. Rehman, and R. Zahra, "Prevalence of metallo-β-lactamase NDM-1-producing multi-drug resistant-bacteria at two Pakistani hospitals and implications for public health," *Journal of Infection and Public Health*, vol. 6, no. 6, pp. 487–493, 2013.

[11] H. Yigit, A. M. Queenan, G. J. Anderson et al., "Novel carbapenem-hydrolyzing β-lactamase, KPC-1, from a carbapenem-resistant strain of *Klebsiella pneumoniae*," *Antimicrobial Agents and Chemotherapy*, vol. 45, no. 4, pp. 1151–1161, 2001.

[12] P. Nordmann, G. Cuzon, and T. Naas, "The real threat of *Klebsiella pneumoniae* carbapenemase-producing bacteria," *The Lancet Infectious Diseases*, vol. 9, no. 4, pp. 228–236, 2009.

[13] G. Cuzon, T. Naas, H. Truong et al., "Worldwide diversity of *Klebsiella pneumoniae* that produces β-lactamase blaKPC-2 Gene," *Emerging Infectious Diseases*, vol. 16, no. 9, pp. 1349–1356, 2010.

[14] T. Naas, G. Cuzon, M.-V. Villegas, M.-F. Lartigue, J. P. Quinn, and P. Nordmann, "Genetic structures at the origin of acquisition of the β-lactamase *bla*KPC gene," *Antimicrobial Agents and Chemotherapy*, vol. 52, no. 4, pp. 1257–1263, 2008.

[15] L. M. Deshpande, P. R. Rhomberg, H. S. Sader, and R. N. Jones, "Emergence of serine carbapenemases (KPC and SME) among clinical strains of Enterobacteriaceae isolated in the United States Medical Centers: report from the MYSTIC Program (1999–2005)," *Diagnostic Microbiology and Infectious Disease*, vol. 56, no. 4, pp. 367–372, 2006.

[16] Y. Pfeifer, A. Cullik, and W. Witte, "Resistance to cephalosporins and carbapenems in Gram-negative bacterial pathogens," *International Journal of Medical Microbiology*, vol. 300, no. 6, pp. 371–379, 2010.

[17] A. Robustillo Rodela, C. Díaz-Agero Pérez, T. Sanchez Sagrado, P. Ruiz-Garbajosa, M. J. Pita López, and V. Monge, "Emergence and outbreak of carbapenemase-producing KPC-3 *Klebsiella pneumoniae* in Spain, September 2009 to February 2010: control measures," *Eurosurveillance*, vol. 17, no. 7, 2012.

[18] Z. Samra, O. Ofir, Y. Lishtzinsky, L. Madar-Shapiro, and J. Bishara, "Outbreak of carbapenem-resistant *Klebsiella pneumoniae* producing KPC-3 in a tertiary medical centre in Israel," *International Journal of Antimicrobial Agents*, vol. 30, no. 6, pp. 525–529, 2007.

[19] B. Kitchel, J. K. Rasheed, J. B. Patel et al., "Molecular epidemiology of KPC-producing *Klebsiella pneumoniae* isolates in the United States: clonal expansion of multilocus sequence type 258," *Antimicrobial Agents and Chemotherapy*, vol. 53, no. 8, pp. 3365–3370, 2009.

[20] C. Hidalgo-Grass, G. Warburg, V. Temper et al., "KPC-9, a novel carbapenemase from clinical specimens in Israel," *Antimicrob Agents Chemother*, vol. 56, pp. 6057–6059, 2012.

[21] Y. Geffen, A. Adler, S. Paikin et al., "Detection of the plasmid-mediated KPC-2 carbapenem-hydrolysing enzyme in three unusual species of the *Enterobacteriaceae* family in Israel," *Journal of Antimicrobial Chemotherapy*, vol. 68, pp. 719–720, 2013.

[22] A. Adler, S. Paikin, Y. Sterlin et al., "A swordless knight: epidemiology and molecular characteristics of the *bla*KPC-negative sequence type 258 *Klebsiella pneumoniae* clone," *Journal of Clinical Microbiology*, vol. 50, pp. 3180–3185, 2012.

[23] M. G. Goren, Y. Carmeli, M. J. Schwaber, I. Chmelnitsky, V. Schechner, and S. Navon-Venezia, "Transfer of Carbapenem-resistant plasmid from *Klebsiella pneumoniae* ST258 to *Escherichia coli* in patient," *Emerging Infectious Diseases*, vol. 16, no. 6, pp. 1014–1017, 2010.

[24] J. A. Lopez, A. Correa, S. Navon-Venezia et al., "Intercontinental spread from Israel to Colombia of a KPC- 3- producing *Klebsiella pneumoniae* strain," *Clinical Microbiology and Infection*, vol. 17, no. 1, pp. 52–56, 2011.

[25] I. Chmelnitsky, O. Hermesh, S. Navon-Venezia, J. Strahilevitz, and Y. Carmeli, "Detection of *aac*(6′)-Ib-cr in KPC-producing *Klebsiella pneumoniae* isolates from Tel Aviv, Israel," *Journal of Antimicrobial Chemotherapy*, vol. 64, no. 4, pp. 718–722, 2009.

[26] B. Kitchel, J. K. Rasheed, J. B. Patel et al., "Molecular epidemiology of KPC-producing *Klebsiella pneumoniae* isolates in the United States: clonal expansion of multilocus sequence type 258," *Antimicrobial Agents and Chemotherapy*, vol. 53, no. 8, pp. 3365–3370, 2009.

[27] P. Giakkoupi, C. C. Papagiannitsis, V. Miriagou et al., "An update of the evolving epidemic of *bla*KPC-2-carrying *Klebsiella pneumoniae* in Greece (2009-10)," *Journal of Antimicrobial Chemotherapy*, vol. 66, no. 7, pp. 1510–1513, 2011.

[28] M. Souli, I. Galani, A. Antoniadou et al., "An outbreak of infection due to β-lactamase *Klebsiella pneumoniae* carbapenemase 2-producing *K. pneumoniae* in a Greek university hospital: molecular characterization, epidemiology, and outcomes," *Clinical Infectious Diseases*, vol. 50, no. 3, pp. 364–373, 2010.

[29] H. Grundmann, D. M. Livermore, C. G. Giske et al., "Carbapenem-non-susceptible *Enterobacteriaceae* in Europe: conclusions from a meeting of national experts," *Eurosurveillance*, vol. 15, no. 46, 2010.

[30] P. Gaibani, S. Ambretti, A. Berlingeri et al., "Rapid increase of carbapenemase-producing *Klebsiella pneumoniae* strains in a large Italian hospital: surveillance period 1 March—30 September 2010," *Eurosurveillance*, vol. 16, no. 8, 2011.

[31] A. Carbonne, J. M. Thiolet, S. Fournier et al., "Control of a multihospital outbreak of KPC-producing *Klebsiella pneumoniae*

type 2 in France, September to October 2009," *Eurosurveillance*, vol. 15, no. 48, 2010.

[32] M. R. Gómez-Gil, J. R. Paño-Pardo, M. P. Romero-Gómez et al., "Detection of KPC-2-producing *Citrobacter freundii* isolates in Spain," *Journal of Antimicrobial Chemotherapy*, vol. 65, no. 12, pp. 2695–2697, 2010.

[33] J. Oteo, D. Saez, V. Bautista et al., "Spanish collaborating group for the antibiotic resistance surveillance program. Carbapenemase-producing enterobacteriaceae in Spain in 2012," *Antimicrob Agents Chemother*, vol. 57, pp. 6344–6347, 2013.

[34] G. Cuzon, T. Naas, M.-C. Demachy, and P. Nordmann, "Nosocomial outbreak of *Klebsiella pneumoniae* harbouring *bla*KPC-3 in France subsequent to a patient transfer from Italy," *International Journal of Antimicrobial Agents*, vol. 39, no. 5, pp. 448–449, 2012.

[35] V. Miriagou, G. Cornaglia, M. Edelstein et al., "Acquired carbapenemases in Gram-negative bacterial pathogens: detection and surveillance issues," *Clinical Microbiology and Infection*, vol. 16, no. 2, pp. 112–122, 2010.

[36] B. Bedenić, A. Mazzariol, V. Plečko et al., "First report of KPC-producing *Klebsiella pneumoniae* in Croatia," *Journal of Chemotherapy*, vol. 24, no. 4, pp. 237–239, 2012.

[37] R. Zarrilli, S. Pournaras, M. Giannoulia, and A. Tsakrisc, "Global evolution of multidrug-resistant *Acinetobacter baumannii* clonal lineages," *International Journal of Antimicrobial Agents*, vol. 41, no. 1, pp. 11–19, 2013.

[38] I. E. Robledo, E. E. Aquino, M. I. Santé et al., "Detection of KPC in *Acinetobacter* spp. in Puerto Rico," *Antimicrobial Agents and Chemotherapy*, vol. 54, no. 3, pp. 1354–1357, 2010.

[39] R. A. Bonnin, P. Nordmann, A. Potron, H. Lecuyer, J.-R. Zahar, and L. Poirel, "Carbapenem-hydrolyzing GES-type extended-spectrum β-lactamase in *Acinetobacter baumannii*," *Antimicrobial Agents and Chemotherapy*, vol. 55, no. 1, pp. 349–354, 2011.

[40] A. N. Zeka, L. Poirel, O. R. Sipahi et al., "GES-type and OXA-23 carbapenemase-producing *Acinetobacter baumannii* in Turkey," *Journal of Antimicrobial Chemotherapy*, vol. 69, no. 4, pp. 1145–1146, 2013.

[41] T. R. Walsh, M. A. Toleman, L. Poirel, and P. Nordmann, "Metallo-β-lactamases: the quiet before the storm?" *Clinical Microbiology Reviews*, vol. 18, no. 2, pp. 306–325, 2005.

[42] H. Ito, Y. Arakawa, S. Ohsuka, R. Wacharotayankun, N. Kato, and M. Ohta, "Plasmid-mediated dissemination of the metallo-β-lactamase gene *bla*(IMP) among clinically isolated strains of *Serratia marcescens*," *Antimicrobial Agents and Chemotherapy*, vol. 39, no. 4, pp. 824–829, 1995.

[43] A. Vatopoulos, "High rates of metallo-β-lactamase-producing *Klebsiella pneumoniae* in Greece—a review of the current evidence," *Euro Surveillance*, vol. 13, no. 4, 2008.

[44] P. Nordmann, L. Poirel, M. A. Toleman, and T. R. Walsh, "Does broad-spectrum β-lactam resistance due to NDM-1 herald the end of the antibiotic era for treatment of infections caused by Gram-negative bacteria?" *Journal of Antimicrobial Chemotherapy*, vol. 66, no. 4, pp. 689–692, 2011.

[45] G. L. Daikos, P. Petrikkos, M. Psichogiou et al., "Prospective observational study of the impact of VIM-1 metallo-β- lactamase on the outcome of patients with *Kebsiella pneumoniae* bloodstream infections," *Antimicrobial Agents and Chemotherapy*, vol. 53, no. 5, pp. 1868–1873, 2009.

[46] F. Luzzaro, J.-D. Docquier, C. Colinon et al., "Emergence in *Klebsiella pneumoniae* and *Enterobacter cloacae* clinical isolates of the VIM-4 metallo-β-lactamase encoded by a conjugative plasmid," *Antimicrobial Agents and Chemotherapy*, vol. 48, no. 2, pp. 648–650, 2004.

[47] R. Aschbacher, M. Doumith, D. M. Livermore, C. Larcher, and N. Woodford, "Linkage of acquired quinolone resistance (*qnrS1*) and metallo-β-lactamase (*bla*VIM-1) genes in multiple species of *Enterobacteriaceae* from Bolzano, Italy," *Journal of Antimicrobial Chemotherapy*, vol. 61, no. 3, pp. 515–523, 2008.

[48] R. Aschbacher, L. Pagani, M. Doumith et al., "Metallo-β-lactamases among *Enterobacteriaceae* from routine samples in an Italian tertiary-care hospital and long-term care facilities during 2008," *Clinical Microbiology and Infection*, vol. 17, no. 2, pp. 181–189, 2011.

[49] R. Cantón, M. Akóva, Y. Carmeli et al., "Rapid evolution and spread of carbapenemases among *Enterobacteriaceae* in Europe," *Clinical Microbiology and Infection*, vol. 18, no. 5, pp. 413–431, 2012.

[50] L. Poirel, A. Ros, A. Carricajo et al., "Extremely drug-resistant *Citrobacter freundii* isolate producing NDM-1 and other carbapenemases identified in a patient returning from India," *Antimicrobial Agents and Chemotherapy*, vol. 55, no. 1, pp. 447–448, 2011.

[51] M.-F. Lartigue, L. Poirel, and P. Nordmann, "First detection of a carbapenem-hydrolyzing metalloenzyme in an *Enterobacteriaceae* isolate in France," *Antimicrobial Agents and Chemotherapy*, vol. 48, no. 12, pp. 4929–4930, 2004.

[52] A. Barguigua, F. El Otmani, F. L. El Yaagoubi, M. Talmi, K. Zerouali, and M. Timinouni, "First report of a *Klebsiella pneumoniae* strain coproducing NDM-1, VIM-1 and OXA-48 carbapenemases isolated in Morocco," *APMIS*, vol. 121, pp. 675–677, 2013.

[53] T. Giani, A. Marchese, E. Coppo, V. Kroumova, and G. M. Rossolini, "VIM-1-producing *Pseudomonas mosselii* isolates in Italy, predating known VIM-producing index strains," *Antimicrobial Agents and Chemotherapy*, vol. 56, no. 4, pp. 2216–2217, 2012.

[54] L. Poirel, M. O. Abdelaziz, S. Bernabeu, and P. Nordmann, "Occurrence of OXA-48 and VIM-1 carbapenemase-producing *Enterobacteriaceae* in Egypt," *International Journal of Antimicrobial Agents*, vol. 41, pp. 90–91, 2013.

[55] F. Robin, N. Aggoune-Khinache, J. Delmas, M. Naim, and R. Bonnet, "Novel VIM metallo-β-lactamase variant from clinical isolates of *Enterobacteriaceae* from Algeria," *Antimicrobial Agents and Chemotherapy*, vol. 54, no. 1, pp. 466–470, 2010.

[56] S. Ktari, G. Arlet, B. Mnif et al., "Emergence of multidrug-resistant *Klebsiella pneumoniae* isolates producing VIM-4 metallo-β-lactamase, CTX-M-15 extended-spectrum β-lactamase, and CMY-4 AmpC β-lactamase in a Tunisian University Hospital," *Antimicrobial Agents and Chemotherapy*, vol. 50, no. 12, pp. 4198–4201, 2006.

[57] F. Pasteran, E. Albornoz, D. Faccone et al., "Emergence of NDM-1-producing *Klebsiella pneumoniae* in Guatemala," *Journal of Antimicrobial Chemotherapy*, vol. 67, no. 7, pp. 1795–1797, 2012.

[58] J. A. E. Pérez, N. M. O. Escobar, B. Castro-Cardozo et al., "Outbreak of NDM-1-producing *Klebsiella pneumonia* in a neonatal unit in Colombia," *Antimicrob Agents Chemother*, vol. 57, no. 4, pp. 1957–1960, 2013.

[59] D. Yong, M. A. Toleman, C. G. Giske et al., "Characterization of a new metallo-β-lactamase gene, *bla* NDM-1, and a novel

erythromycin esterase gene carried on a unique genetic structure in *Klebsiella pneumoniae* sequence type 14 from India," *Antimicrobial Agents and Chemotherapy*, vol. 53, no. 12, pp. 5046–5054, 2009.

[60] D. M. Livermore, T. R. Walsh, M. Toleman, and N. Woodford, "Balkan NDM-1: escape or transplant?" *The Lancet Infectious Diseases*, vol. 11, no. 3, p. 164, 2011.

[61] L. Poirel, N. Fortineau, and P. Nordmann, "International transfer of NDM-1-producing *Klebsiella pneumoniae* from Iraq to France," *Antimicrobial Agents and Chemotherapy*, vol. 55, no. 4, pp. 1821–1822, 2011.

[62] G. Cuzon, R. A. Bonnin, and P. Nordmann, "First Identification of Novel NDM Carbapenemase, NDM 7, in *Escherichia coli* in France," *PLoS ONE*, vol. 8, no. 4, 2010.

[63] K. K. Kumarasamy, M. A. Toleman, T. R. Walsh et al., "Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study," *The Lancet Infectious Diseases*, vol. 10, no. 9, pp. 597–602, 2010.

[64] A. Muir and M. J. Weinbren, "New Delhi metallo-β-lactamase: a cautionary tale," *Journal of Hospital Infection*, vol. 75, no. 3, pp. 239–240, 2010.

[65] P. Nordmann, L. Poirel, T. R. Walsh, and D. M. Livermore, "The emerging NDM carbapenemases," *Trends in Microbiology*, vol. 19, no. 12, pp. 588–595, 2011.

[66] M.-H. Nicolas-Chanoine, J. Blanco, V. Leflon-Guibout et al., "Intercontinental emergence of *Escherichia coli* clone O25:H4-ST131 producing CTX-M-15," *Journal of Antimicrobial Chemotherapy*, vol. 61, no. 2, pp. 273–281, 2008.

[67] G. Peirano, P. C. Schreckenberger, and J. D. D. Pitout, "Characteristics of NDM-1-producing *Escherichia coli* isolates that belong to the successful and virulent clone ST131," *Antimicrobial Agents and Chemotherapy*, vol. 55, no. 6, pp. 2986–2988, 2011.

[68] A. Birgy, C. Doit, P. Mariani-Kurkdjian et al., "Early detection of colonization by VIM-1-producing *Klebsiella pneumoniae* and NDM-1-producing *Escherichia coli* in two children returning to France," *Journal of Clinical Microbiology*, vol. 49, no. 8, pp. 3085–3087, 2011.

[69] C. Denis, L. Poirel, A. Carricajo et al., "Nosocomial transmission of NDM-1-producing *Escherichia coli* within a non-endemic area in France," *Clinical Microbiology and Infection*, vol. 18, no. 5, pp. E128–E130, 2012.

[70] T. Giani, B. Pini, F. Arena et al., "Epidemic diffusion of KPC carbapenemase-producing *Klebsiella pneumoniae* in Italy: results of the first countrywide survey," *Eurosurveillance*, vol. 18, no. 22, 2013.

[71] M. Baroud, I. Dandache, G. F. Araj et al., "Underlying mechanisms of carbapenem resistance in extended-spectrum β-lactamase-producing *Klebsiella pneumoniae* and *Escherichia coli* isolates at a tertiary care centre in Lebanon: role of OXA-48 and NDM-1 carbapenemases," *International Journal of Antimicrobial Agents*, vol. 41, no. 1, pp. 75–79, 2013.

[72] L. Poirel, A. Benouda, C. Hays, and P. Nordmann, "Emergence of NDM-1-producing *Klebsiella pneumoniae* in Morocco," *Journal of Antimicrobial Chemotherapy*, vol. 66, no. 12, pp. 2781–2783, 2011.

[73] M. Solé, C. Pitart, I. Roca et al., "First description of an *Escherichia coli* strain producing NDM-1 carbapenemase in Spain," *Antimicrobial Agents and Chemotherapy*, vol. 55, no. 9, pp. 4402–4404, 2011.

[74] Y. Gil-Romero, N. Sanz-Rodríguez, M. Almagro-Moltó, and J. L. Gómez-Garcés, "New description of a NDM-1 carbapenemase producing *Klebsiella pneumoniae* carrier in Spain," *Enfermedades Infecciosas y Microbiología Clínica*, vol. 31, no. 6, pp. 418–419, 2013.

[75] J. Oteo, D. Domingo-García, S. Fernández-Romero et al., "Abdominal abscess due to NDM-1-producing *Klebsiella pneumoniae* in Spain," *Journal of Medical Microbiology*, vol. 61, pp. 864–867, 2012.

[76] A. B. Nasr, D. Decré, F. Compain, N. Genel, F. Barguellil, and G. Arlet, "Emergence of NDM-1 in association with OXA-48 in *Klebsiella pneumoniae* from Tunisia," *Antimicrob Agents Chemother*, vol. 57, no. 8, pp. 4089–4090, 2013.

[77] L. Poirel, M. Özdamar, A. A. Ocampo-Sosa, S. Türkoglu, U. G. Ozer, and P. Nordmann, "NDM-1-producing *Klebsiella pneumoniae* now in Turkey," *Antimicrobial Agents and Chemotherapy*, vol. 56, no. 5, pp. 2784–2785, 2012.

[78] E. Alp, D. Perçin, S. Colakoğlu et al., "Molecular characterization of carbapenem-resistant *Klebsiella pneumoniae* in a tertiary university hospital in Turkey," *Journal of Hospital Infection*, vol. 84, pp. 178–180, 2013.

[79] P. Giakkoupi, K. Tryfinopoulou, F. Kontopidou et al., "Emergence of NDM-producing *Klebsiella pneumonia* in Greece," *Diagnostic Microbiology and Infectious Disease*, vol. 77, pp. 382–384, 2013.

[80] M. Kempf and J.-M. Rolain, "Emergence of resistance to carbapenems in *Acinetobacter baumannii* in Europe: clinical impact and therapeutic options," *International Journal of Antimicrobial Agents*, vol. 39, no. 2, pp. 105–114, 2012.

[81] M. L. Riccio, N. Franceschini, L. Boschi et al., "Characterization of the metallo-β-lactamase determinant of *Acinetobacter baumannii* AC-54/97 reveals the existence of *bla*(IMP) allelic variants carried by gene cassettes of different phylogeny," *Antimicrobial Agents and Chemotherapy*, vol. 44, no. 5, pp. 1229–1235, 2000.

[82] S. Figueiredo, L. Poirel, A. Papa, V. Koulourida, and P. Nordmann, "First identification of VIM-4 metallo-β-lactamase in *Acinetobacter* spp.," *Clinical Microbiology and Infection*, vol. 14, no. 3, pp. 289–290, 2008.

[83] A. Di Popolo, M. Giannouli, M. Triassi, S. Brisse, and R. Zarrilli, "Molecular epidemiological investigation of multidrug-resistant *Acinetobacter baumannii* strains in four Mediterranean countries with a multilocus sequence typing scheme," *Clinical Microbiology and Infection*, vol. 17, no. 2, pp. 197–201, 2011.

[84] A. Ikonomidis, E. Ntokou, A. N. Maniatis, A. Tsakris, and S. Pournaras, "Hidden VIM-1 metallo-β-lactamase phenotypes among *Acinetobacter baumannii* clinical isolates," *Journal of Clinical Microbiology*, vol. 46, no. 1, pp. 346–349, 2008.

[85] A. Tsakris, A. Ikonomidis, S. Pournaras et al., "VIM-1 metallo-β-lactamase in *Acinetobacter baumannii*," *Emerging Infectious Diseases*, vol. 12, no. 6, pp. 981–983, 2006.

[86] R. A. Bonnin, L. Poirel, T. Naas et al., "Dissemination of New Delhi metallo-β-lactamase-1-producing *Acinetobacter baumannii* in Europe," *Clinical Microbiology and Infection*, vol. 18, no. 9, pp. E362–E365, 2012.

[87] A. Boulanger, T. Naas, N. Fortineau, S. Figueiredo, and P. Nordmann, "NDM-1-producing *Acinetobacter baumannii* from Algeria," *Antimicrobial Agents and Chemotherapy*, vol. 56, no. 4, pp. 2214–2215, 2012.

[88] E. Mesli, M. Berrazeg, M. Drissi, S. N. Bekkhoucha, and J. M. Rolain, "Prevalence of carbapenemase-encoding genes including New Delhi metallo-β-lactamase in *Acinetobacter* species,

Algeria," *International Journal of Infectious Diseases*, vol. 17, no. 9, pp. 739–743, 2013.

[89] A. M. Hammerum, A. R. Larsen, F. Hansen et al., "Patients transferred from Libya to Denmark carried OXA-48-producing *Klebsiella pneumoniae*, NDM-1-producing *Acinetobacter baumannii* and meticillin-resistant *Staphylococcus aureus*," *International Journal of Antimicrobial Agents*, vol. 40, no. 2, pp. 191–192, 2012.

[90] J. W. Decousser, C. Jansen, P. Nordmann et al., "Outbreak of NDM-1-producing *Acinetobacter baumannii* in France," *Eurosurveillance*, vol. 18, no. 31, 2013.

[91] R. A. Bonnin, G. Cuzon, L. Poirel, and P. Nordmann, "Multidrug-resistant *Acinetobacter baumannii* clone, France," *Emerging Infectious Diseases Journal*, vol. 19, no. 5, pp. 822–823, 2013.

[92] A. C. Cicek, A. Saral, M. Iraz et al., "OXA- and GES-type β-lactamases predominate in extensively drug-resistant *Acinetobacter baumannii* isolates from a Turkish University Hospital," *Clinical Microbiology and Infection*, 2013.

[93] J. Hrabák, M. Stolbová, V. Studentová, M. Fridrichová, E. Chudáčková, and H. Zemlickova, "NDM-1 producing *Acinetobacter baumannii* isolated from a patient repatriated to the Czech Republic from Egypt," *Eurosurveillance*, vol. 17, no. 7, 2012.

[94] M. Kaase, P. Nordmann, T. A. Wichelhaus, S. G. Gatermann, R. A. Bonnin, and L. Poirel, "NDM-2 carbapenemase in *Acinetobacter baumannii* from Egypt," *Journal of Antimicrobial Chemotherapy*, vol. 66, no. 6, pp. 1260–1262, 2011.

[95] P. Espinal, G. Fugazza, Y. López et al., "Dissemination of an NDM-2-producing *Acinetobacter baumannii* clone in an Israeli Rehabilitation Center," *Antimicrobial Agents and Chemotherapy*, vol. 55, no. 11, pp. 5396–5398, 2011.

[96] P. Nordmann, L. Dortet, and L. Poirel, "Carbapenem resistance in *Enterobacteriaceae*: here is the storm!," *Trends in Molecular Medicine*, vol. 18, no. 5, pp. 263–272, 2012.

[97] L. Poirel, T. Naas, and P. Nordmann, "Diversity, epidemiology, and genetics of class D β-lactamases," *Antimicrobial Agents and Chemotherapy*, vol. 54, no. 1, pp. 24–38, 2010.

[98] N. Woodford, R. Pike, D. Meunier, R. Loy, R. Hill, and K. L. Hopkins, "*In vitro* activity of temocillin against multidrug-resistant clinical isolates of *Escherichia coli*, *Klebsiella* spp. and *Enterobacter* spp., and evaluation of high-level temocillin resistance as a diagnostic marker for OXA-48 carbapenemase," *Journal of Antimicrobial Chemotherapy*, 2013.

[99] R. Hartl, S. Widhalm, H. Kerschner, and P. Apfalter, "Temocillin and meropenem to discriminate resistance mechanisms leading to decreased carbapenem susceptibility with focus on OXA-48 in *Enterobacteriaceae*," *Clinical Microbiology and Infection*, vol. 19, no. 5, pp. 230–232, 2013.

[100] M. Castanheira, L. M. Deshpande, D. Mathai, J. M. Bell, R. N. Jones, and R. E. Mendes, "Early dissemination of NDM-1- and OXA-181-producing *Enterobacteriaceae* in Indian hospitals: report from the SENTRY Antimicrobial Surveillance Program, 2006–2007," *Antimicrobial Agents and Chemotherapy*, vol. 55, no. 3, pp. 1274–1278, 2011.

[101] J. S. Kalpoe, N. Al Naiemi, L. Poirel, and P. Nordmann, "Detection of an ambler class D Oxa-48-type β-lactamase in a *Klebsiella pneumoniae* strain in the netherlands," *Journal of Medical Microbiology*, vol. 60, no. 5, pp. 677–678, 2011.

[102] A. Potron, P. Nordmann, E. Lafeuille, Z. Al Maskari, F. Al Rashdi, and L. Poirel, "Characterization of OXA-181, a carbapenem-hydrolyzing class D β-lactamase from *Klebsiella pneumoniae*," *Antimicrobial Agents and Chemotherapy*, vol. 55, no. 10, pp. 4896–4899, 2011.

[103] A. Potron, J. Kalpoe, L. Poirel, and P. Nordmann, "European dissemination of a single OXA-48-producing *Klebsiella pneumoniae* clone," *Clinical Microbiology and Infection*, vol. 17, no. 12, pp. E24–E26, 2011.

[104] L. Poirel, C. Héritier, V. Tolün, and P. Nordmann, "Emergence of oxacillinase-mediated resistance to imipenem in *Klebsiella pneumoniae*," *Antimicrobial Agents and Chemotherapy*, vol. 48, no. 1, pp. 15–22, 2004.

[105] A. Carrër, L. Poirel, H. Eraksoy, A. A. Cagatay, S. Badur, and P. Nordmann, "Spread of OXA-48-positive carbapenem-resistant *Klebsiella pneumoniae* isolates in Istanbul, Turkey," *Antimicrobial Agents and Chemotherapy*, vol. 52, no. 8, pp. 2950–2954, 2008.

[106] A. Carrër, L. Poirel, M. Yilmaz et al., "Spread of OXA-48-encoding plasmid in Turkey and beyond," *Antimicrobial Agents and Chemotherapy*, vol. 54, no. 3, pp. 1369–1373, 2010.

[107] L. Poirel, A. Ros, A. Carrër et al., "Cross-border transmission of OXA-48-producing *Enterobacter cloacae* from Morocco to France," *Journal of Antimicrobial Chemotherapy*, vol. 66, no. 5, pp. 1181–1182, 2011.

[108] G. Cuzon, J. Ouanich, R. Gondret, T. Naas, and P. Nordmann, "Outbreak of OXA-48-positive carbapenem-resistant *Klebsiella pneumoniae* isolates in France," *Antimicrobial Agents and Chemotherapy*, vol. 55, no. 5, pp. 2420–2423, 2011.

[109] A. Potron, L. Poirel, E. Rondinaud, and P. Nordmann, "Intercontinental spread of OXA-48 beta-lactamase-producing *Enterobacteriaceae* over a 11-year period, 2001 to 2011," *Eurosurveillance*, vol. 18, no. 31, 2013.

[110] A. Benouda, O. Touzani, M.-T. Khairallah, G. F. Araj, and G. M. Matar, "First detection of oxacillinase-mediated resistance to carbapenems in *Klebsiella pneumoniae* from Morocco," *Annals of Tropical Medicine and Parasitology*, vol. 104, no. 4, pp. 327–330, 2010.

[111] M. Vranić-Ladavac, B. Bedenić, F. Minandri et al., "Carbapenem resistance and acquired class D β-lactamases in *Acinetobacter baumannii* from Croatia 2009–2010," *European Journal of Clinical Microbiology & Infectious Diseases*, vol. 33, no. 3, pp. 471–478, 2014.

[112] E. Voulgari, O. Zarkotou, K. Ranellou et al., "Outbreak of OXA-48 carbapenemase-producing *Klebsiella pneumoniae* in Greece involving an ST11 clone," *Journal of Antimicrobial Chemotherapy*, vol. 68, no. 1, pp. 84–88, 2013.

[113] A. Adler, M. Shklyar, M. J. Schwaber et al., "Introduction of OXA-48-producing enterobacteriaceae to israeli hospitals by medical tourism," *Journal of Antimicrobial Chemotherapy*, vol. 66, no. 12, pp. 2763–2766, 2011.

[114] M. G. Goren, I. Chmelnitsky, Y. Carmeli, and S. Navon-Venezia, "Plasmid-encoded OXA-48 carbapenemase in *Escherichia coli* from Israel," *Journal of Antimicrobial Chemotherapy*, vol. 66, no. 3, pp. 672–673, 2011.

[115] G. M. Matar, I. Dandache, A. Carrër et al., "Spread of OXA-48-mediated resistance to carbapenems in Lebanese *Klebsiella pneumoniae* and *Escherichia coli* that produce extended spectrum β-lactamase," *Annals of Tropical Medicine and Parasitology*, vol. 104, no. 3, pp. 271–274, 2010.

[116] G. M. Matar, G. Cuzon, G. F. Araj et al., "Oxacillinase-mediated resistance to carbapenems in *Klebsiella pneumoniae*

from Lebanon," *Clinical Microbiology and Infection*, vol. 14, no. 9, pp. 887–888, 2008.

[117] M. Kaase, N. Pfennigwerth, F. Szabados, and S. Gatermann, "OXA-48, OXA-23 and NDM-1 carbapenemases in Gram-negative bacteria from patients from Libya," in *Abstracts of the Twenty-Second European Congress of Clinical Microbiology and Infectious Diseases*, London, UK, 2012.

[118] M. Pirš, A. Andlovic, T. Cerar et al., "A case of OXA-48 carbapenemase-producing *Klebsiella pneumoniae* in a patient transferred to Slovenia from Libya, November 2011," *Euro Surveillance*, vol. 16, no. 50, 2011.

[119] J. Oteo, J. M. Hernández, M. Espasa et al., "Emergence of OXA-48-producing *Klebsiella pneumoniae* and the novel carbapenemases OXA-244 and OXA-245 in Spain," *Journal of Antimicrobial Chemotherapy*, vol. 68, no. 2, pp. 317–321, 2013.

[120] S. Ktari, B. Mnif, F. Louati et al., "Spread of *Klebsiella pneumoniae* isolates producing OXA-48 β-lactamase in a Tunisian university hospital," *Journal of Antimicrobial Chemotherapy*, vol. 66, no. 7, pp. 1644–1646, 2011.

[121] L. Poirel, A. Potron, and P. Nordmann, "OXA-48-like carbapenemase: the phantom menace," *Journal of Antimicrobial Chemotherapy*, vol. 67, no. 7, pp. 1597–1606, 2012.

[122] C. Hays, A. Benouda, L. Poirel, M. Elouennass, and P. Nordmann, "Nosocomial occurrence of OXA-48-producing enterobacterial isolates in a Moroccan hospital," *International Journal of Antimicrobial Agents*, vol. 39, no. 6, pp. 545–547, 2012.

[123] A. Barguigua, F. El Otmani, M. Talmi, K. Zerouali, and M. Timinouni, "Emergence of carbapenem-resistant *Enterobacteriaceae* isolates in the Moroccan community," *Diagnostic Microbiology & Infectious Disease*, vol. 73, no. 3, pp. 290–291, 2012.

[124] A. Potron, L. Poirel, F. Bussy, and P. Nordmann, "Occurrence of the carbapenem-hydrolyzing β-lactamase gene *bla*OXA-48 in the environment in Morocco," *Antimicrobial Agents and Chemotherapy*, vol. 55, no. 11, pp. 5413–5414, 2011.

[125] L. S. Munoz-Price and R. A. Weinstein, "Acinetobacter infection," *The New England Journal of Medicine*, vol. 358, no. 12, pp. 1214–1281, 2008.

[126] J. Walther-Rasmussen and N. Høiby, "OXA-type carbapenemases," *Journal of Antimicrobial Chemotherapy*, vol. 57, no. 3, pp. 373–383, 2006.

[127] P. G. Higgins, F. J. Perez-Llarena, E. Zander, A. Fernández, G. Bou, and H. Seifert, "OXA-235, a novel class D beta-lactamase involved in resistance to carbapenems in *Acinetobacter baumannii*," *Antimicrobial Agents and Chemotherapy*, vol. 57, pp. 2121–2126, 2013.

[128] R. Paton, R. S. Miles, J. Hood, and S. G. B. Amyes, "ARI 1: β-lactamase-mediated imipenem resistance in *Acinetobacter baumannii*," *International Journal of Antimicrobial Agents*, vol. 2, no. 2, pp. 81–88, 1993.

[129] H. M. Donald, W. Scaife, S. G. B. Amyes, and H.-K. Young, "Sequence analysis of ARI-1, a novel OXA β-lactamase, responsible for imipenem resistance in *Acinetobacter baumannii* 6B92," *Antimicrobial Agents and Chemotherapy*, vol. 44, no. 1, pp. 196–199, 2000.

[130] L. Poirel, S. Figueiredo, V. Cattoir, A. Carattoli, and P. Nordmann, "*Acinetobacter radioresistens* as a silent source of carbapenem resistance for *Acinetobacter* spp," *Antimicrobial Agents and Chemotherapy*, vol. 52, no. 4, pp. 1252–1256, 2008.

[131] J. K. Valenzuela, L. Thomas, S. R. Partridge, T. Van Der Reijden, L. Dijkshoorn, and J. Iredell, "Horizontal gene transfer in a polyclonal outbreak of carbapenem-resistant *Acinetobacter baumannii*," *Journal of Clinical Microbiology*, vol. 45, no. 2, pp. 453–460, 2007.

[132] P. G. Higgins, C. Dammhayn, M. Hackel, and H. Seifert, "Global spread of carbapenem-resistant *Acinetobacter baumannii*," *The Journal of Antimicrobial Chemotherapy*, vol. 65, no. 2, pp. 233–238, 2010.

[133] T. R. Walsh, "Emerging carbapenemases: a global perspective," *International Journal of Antimicrobial Agents*, vol. 36, no. 3, pp. S8–S14, 2010.

[134] P. D. Mugnier, L. Poirel, T. Naas, and P. Nordmann, "Worldwide dissemination of the *bla*OXA-23 Carbapenemase gene of *Acinetobacter baumannii*," *Emerging Infectious Diseases*, vol. 16, no. 1, pp. 35–40, 2010.

[135] S. D'Arezzo, L. Principe, A. Capone, N. Petrosillo, A. Petrucca, and P. Visca, "Changing carbapenemase gene pattern in an epidemic multidrug-resistant *Acinetobacter baumannii* lineage causing multiple outbreaks in central Italy," *Journal of Antimicrobial Chemotherapy*, vol. 66, no. 1, pp. 54–61, 2011.

[136] M. Touati, S. M. Diene, A. Racherache, M. Dekhil, A. Djahoudi, and J. M. Rolain, "Emergence of bla_{OXA-23} and bla_{OXA-58} carbapenemase-encoding genes in multidrug-resistant *Acinetobacter baumannii* isolates from University Hospital of Annaba, Algeria," *International Journal of Antimicrobial Agents*, vol. 40, no. 1, pp. 89–91, 2012.

[137] N. Mosqueda, P. Espinal, C. Cosgaya et al., "Globally expanding carbapenemase finally appears in Spain: nosocomial outbreak of *Acinetobacter baumannii* producing plasmid-encoded OXA-23 in Barcelona, Spain," *Antimicrobial Agents and Chemotherapy*, vol. 57, no. 10, pp. 5155–5157, 2013.

[138] M. Vranic-Ladavac, B. Bedenic, F. Minandri et al., "Carbapenem resistance and acquired class D β-lactamases in *Acinetobacter baumannii* from Croatia 2009–2010," *European Journal of Clinical Microbiology & Infectious Diseases*, vol. 33, no. 3, pp. 471–478, 2014.

[139] M. Fouad, A. S. Attia, W. M. Tawakkol, and A. M. Hashem, "Emergence of carbapenem-resistant *Acinetobacter baumannii* harboring the OXA-23 carbapenemase in intensive care units of Egyptian hospitals," *International Journal of Infectious Diseases*, vol. 17, pp. 1252–1254, 2013.

[140] C. Bourigault, S. Corvec, C. Bretonnière et al., "Investigation and management of multidrug-resistant *Acinetobacter baumannii* spread in a French medical intensive care unit: one outbreak may hide another," *American Journal of Infection Control*, vol. 41, pp. 652–653, 2013.

[141] A. Liakopoulos, V. Miriagou, E. A. Katsifas et al., "Identification of OXA-23-producing *Acinetobacter baumannii* in Greece, 2010 to 2011," *Eurosurveillance*, vol. 17, no. 11, 2012.

[142] C. Mammina, D. M. Palma, C. Bonura et al., "Epidemiology and clonality of carbapenem-resistant *Acinetobacter baumannii* from an intensive care unit in Palermo, Italy," *BMC Research Notes*, vol. 5, p. 365, 2012.

[143] P. Espinal, M. D. Macià, I. Roca et al., "First report of an OXA-23 carbapenemase-producing *Acinetobacter baumannii* clinical isolate related to *Tn*2006 in Spain," *Antimicrobial Agents and Chemotherapy*, vol. 57, no. 1, pp. 589–591, 2013.

[144] W. Mansour, L. Poirel, D. Bettaieb, O. Bouallegue, N. Boujaafar, and P. Nordmann, "Dissemination of OXA-23-producing and carbapenem-resistant *Acinetobacter baumannii* in a university hospital in Tunisia," *Microbial Drug Resistance*, vol. 14, no. 4, pp. 289–292, 2008.

[145] I. H. . Ciftci, G. Aşık, E. Karakeçe et al., "Distribution of *bla*OXA genes in *Acinetobacter baumannii* strains: a multicenter study," *Mikrobiyoloji Bülteni*, vol. 47, pp. 592–602, 2013.

[146] I. Goic-Barisic, K. J. Towner, A. Kovacic et al., "Outbreak in Croatia caused by a new carbapenem-resistant clone of *Acinetobacter baumannii* producing OXA-72 carbapenemase," *Journal of Hospital Infection*, vol. 77, no. 4, pp. 368–369, 2011.

[147] W. Mansour, O. Bouallegue, S. Dahmen, and N. Boujaafar, "Characterization of the resistance mechanism to β-lactams in *Acinetobacter baumannii* strains isolated in the university hospital Sahloul in Tunisia (2005)," *Pathologie Biologie*, vol. 56, no. 3, pp. 116–120, 2008.