# Determination of antibiotic resistance pattern and prevalence of OXA-type carbapenemases among *Acinetobacter baumannii* clinical isolates from inpatients in Isfahan, central Iran

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## SUMMARY

*Acinetobacter baumannii* is one of the most important bacterial species with the ability to produce OXA-type carbapenemases. We aimed to evaluate the prevalence of OXA-type carbapenemases among clinical isolates of *A. baumannii* in three major hospitals of Isfahan. In this cross-sectional descriptive study, 153 non-repeated strains of *A. baumannii* were isolated from various clinical samples of hospitalized patients in Al-Zahra, Imam Mousa Kazem, and Shariati hospitals from October 2015 to October 2016. Antimicrobial susceptibility testing for imipenem, meropenem, ertapenem, cefepime, ceftazidime, ceftriaxone, piperacillin-tazobactam, gentamicin, amikacin, ciprofloxacin, and tetracycline was performed using the disk diffusion method. In order to identify $bla_{OXA}$ genes, a multiplex polymerase chain reaction was used. The resistance rates in *A. baumannii* isolates to beta-lactam antibiotics including imipenem, ertapenem, meropenem, cefepime, ceftazidime, ceftriaxone, and piperacillin/tazobactam were 100%, 100%, 99.3%, 97.4%, 96.7%, 97.4%, and 98.6%, respectively. PCR assay showed the presence of $bla_{OXA}$ genes in all isolates. The $bla_{OXA-51}$ gene was recognized in all (100%) isolates, 90.8% and 62.1% of isolates possessed the $bla_{OXA-23}$ and $bla_{OXA-24}$ genes, respectively, while the $bla_{OXA-58}$ gene was not detected in any of the isolates. Also, 56.2% of isolates had both the $bla_{OXA-23}$ and $bla_{OXA-24}$ genes simultaneously. We found that the prevalence of OXA-type carbapenemases among carbapenem-resistant *A. baumannii* isolates is high in Isfahan, with OXA-23 being the major carbapenemase mechanism responsible for the resistance phenotype.

*Keywords*: *Acinetobacter baumannii*, carbapenemase, inpatients, OXA.

## INTRODUCTION

*Acinetobacter baumannii* (a well-known Gram-negative opportunistic nosocomial pathogen), is one of the most important bacteria with multi-drug resistance (MDR) phenotype. This organism is related with a variety of infections, such as septicemia, pneumonia, urinary tract infection, meningitis, wound infection etc [1, 2]. Carbapenems are one the members of the beta-lactam class of antibiotics that are used as a main choice for treatment of MDR *A. baumannii* infections, but recently the rise of carbapenem resistance strains have led to limited efficiency of these antibiotics [2]. Several mechanisms can be responsible of resistance of *A. baumannii* to carbapenems. One of the major mechanisms is the production of bacterial carbapenemases, which are enzymes that hydrolyze carbapenems. In *A. baumannii* three types of these enzymes have been reported belonging to class A, B and

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D of Ambler classification: class A including beta-lactamases inhibited by clavulanic acid such as KPC and GES; class B including metallo-beta-lactamases such as VIM, IMP, SIM, and NDM; and class D including oxacillinases [3, 4]. Six subclasses of oxacillinases (OXA-23, OXA-40, OXA-51, OXA-58, OXA-143, and OXA-235) have been known in *A. baumannii.* OXA-51 as an intrinsic subclass and five other subclasses are acquired [5]. Dissemination of OXA-type carbapenemase-producing *A. baumannii* strains have been reported from different geographical areas around the world [6-10]. In Iran, previous studies have described the presence of OXA-type carbapenemase-encoding genes among clinical isolates of *A. baumannii* from diverse areas; but no information is available from Isfahan, the most important central city of Iran [11-18]. So, the aim of this study was to evaluate the prevalence of OXA-type carbapenemases among clinical isolates of *A. baumannii* in three major hospitals of Isfahan.

## MATERIALS AND METHODS

*Bacterial isolates*

In this cross-sectional study, conducted from October 2015 to October 2016, one hundred fifty-three non-repeatedly *A. baumannii* strains were isolated from various clinical sources. All samples were collected from inpatients in three major hospitals (Al-Zahra, Imam Mousa Kazem, and Shariati) of Isfahan. The samples were cultured on standard laboratory media including blood agar and MacConkey agar (Merck, Germany) and incubated overnight at 37°C. The identification of *A. baumannii* strains were performed with Gram staining and routine biochemical tests such as oxidative or fermentative metabolism, catalase, oxidase, motility, production of acid from different sugars, urease, etc. [19]. The bacterial isolates were transferred in brain heart infusion broth medium containing 20% glycerol and stored at -20°C.

*Ethical considerations*

This study was evaluated and approved by the Ethics Committee of Isfahan University of Medical Sciences (No-395081).

*Antimicrobial susceptibility testing*

The antimicrobial susceptibility testing was performed based on Kirby-Bauer disk diffusion method using imipenem (10 µg), meropenem (10 µg), ertapenem (10 µg), cefepime (30 µg), ceftazidime (30 µg), ceftriaxone (30µg), piperacillin-tazobactam (100/10 µg), gentamicin (10 µg), amikacin (30 µg), ciprofloxacin (5 µg), and tetracycline (30 µg) disks (MAST, Merseyside, UK), and results were interpreted based on clinical and laboratory standards institute (CLSI) criteria. *Escherichia coli* ATCC 25922 was used as the control strain for antibiotic disks in susceptibility testing [20].

***Amplification of bla$_{OXA}$ genes***

Detection of bla$_{oxa}$ genes was performed with multiplex polymerase chain reaction (PCR) method. Primer sequences used for detection of blaOXA-51, blaOXA-23, blaOXA-24 and blaOXA-58 gene and their fragment size are presented in Table 1. The amplification was done with an initial denaturation step (5 min at 94ºC), followed by 30 cycles (1 min at 94ºC as denaturation, 1 min at 50ºC as annealing and 72ºC at 50 s as extension) and 10 min at 72ºC for the final extension [21]. Amplified fragments were separated by 2% agarose gel electrophoresis at 80V for 2h.

**Table 1** - List of primers used for amplification of *bla$_{OXA}$* gene.

| *Genes* | *Amplicon size (bp)* | *Sequences* | *Reference* |
|---|---|---|---|
| *bla$_{OXA-23}$* | 501 | 5´-GAT CGG ATT GGA GAA CCA GA-3´<br>5´-ATT TCT GAC CGC ATT TCC AT-3´ | 38 |
| *bla$_{OXA-24}$* | 246 | 5´-GGT TAG TTG GCC CCC TTA AA-3´<br>5´-AGT TGA GCG AAA AGG GGA TT-3´ | 38 |
| *bla$_{OXA-51}$* | 353 | 5´-CGG CCT TGTAA TGC TTT GAT-3´<br>5´-TGG ATT GCA CTT CAT CTT GG-3´ | 38 |
| *bla$_{OXA-58}$* | 599 | 5´-AAG TAT TGG GGC TTG TGC TG-3´<br>5´-CCC CTC TGC GCT CTA CAT AC-3´ | 38 |

## RESULTS

*Bacterial isolates*

In this study, 153 clinical isolates of *A. baumannii* were obtained from inpatient in three major hospitals of Isfahan: 126 (82.4%) isolates from Al-Zahra, 14 (9.1%) isolates from Imam Mousa Kazem, and 13 (8.5%) isolates from Shariati. Most isolates were related to the intensive care unit (64%), followed by the internal medicine (13.7%), surgical (12.5%), and emergency unit (9.8%), respectively. Bacterial strains were isolated from trachea (52.9%), wound (11.8%), cerebrospinal fluid (7.8%), sputum (7.2%), urine (5.9%), blood (4.6%), abscess (1.3%), catheter (1.3%), throat (1.3%), synovial fluid (1.3%), eye (1.3%), and other (3.3%) sources.

*Antimicrobial susceptibility testing*

The highest resistance rates in *A. baumannii* isolates were observed towards beta-lactam antibiotics including imipenem and ertapenem. Moreover, the highest susceptibility was demonstrated to amikacin. In Table 2 is reported the antibiotic resistance pattern of all *A. baumannii* isolates.

*Amplification of $bla_{OXA}$ genes*

PCR assay showed the presence of the $bla_{OXA}$ genes in all isolates. The $bla_{OXA-51}$ gene was recognized in all (100%) isolates. 90.8% and 62.1% of isolates possessed the $bla_{OXA-23}$ and $bla_{OXA-24}$ genes, respectively; but, the $bla_{OXA-58}$ gene was not detected in the studied isolates. Also, 86 (56.2%) of isolates had both the $bla_{OXA-23}$ and $bla_{OXA-24}$ genes, simultaneously. The highest frequency of the $bla_{OXA-23}$ and $bla_{OXA-24}$ genes was related to Al-Zahra hospital isolates with 93% and 63.4%, respectively. While, the lowest prevalence rate of $bla_{OXA-23}$ and $bla_{OXA-24}$ genes was observed among isolates of Imam Mousa Kazem and Shariati hospitals with 71.4% and 53.8%, respectively (Table 3). Figure 1 displays the electrophoretic pattern of the $bla_{OXA}$ genes.

## DISCUSSION

Nowadays, resistance to carbapenems in *A. baumannii* has become a global problem in the field of healthcare. High consumption of antibiotics

**Table 2** - Antimicrobial susceptibilities of the *Acinetobacter baumannii* isolates (n=153).

| *Antibiotic* | *Susceptible, No. (%)* | *Intermediate, No. (%)* | *Resistant, No. (%)* |
|---|---|---|---|
| Imipenem | 0 (0.0%) | 0 (0.0%) | 153 (100%) |
| Meropenem | 1 (0.07%) | 0 (0.0%) | 152 (99.3%) |
| Ertapenem | 0 (0.0%) | 0 (0.0%) | 153 (100%) |
| Cefepime | 1 (0.07%) | 3 (1.9%) | 149 (97.4%) |
| Ceftriaxone | 0 (0.0%) | 4 (2.6%) | 149 (97.4%) |
| Ceftazidime | 4 (2.6%) | 1 (0.07%) | 148 (96.7%) |
| Piperacillin/tazobactam | 1 (0.07%) | 1 (0.07%) | 151 (98.6%) |
| Tetracycline | 9 (5.9%) | 28 (18.3%) | 116 (75.8%) |
| Ciprofloxacin | 1 (0.07%) | 0 (0.0%) | 152 (99.3%) |
| Amikacin | 15 (9.8%) | 12 (7.8%) | 126 (82.4%) |
| Gentamycin | 7 (4.6%) | 2 (1.3%) | 144 (94.1%) |

**Table 3** - Amplification of $bla_{OXA}$ genes in *Acinetobacter baumannii* isolates.

| *Oxa type* | $bla_{OXA-51}$ | $bla_{OXA-23}$ | $bla_{OXA-24}$ | $bla_{OXA-58}$ | $bla_{OXA-23\&}$ $bla_{OXA-24}$ |
|---|---|---|---|---|---|
| Al-Zahra | 126 (100%) | 117(93%) | 80(63.4%) | 0(0.0%) | 72(57.1%) |
| Imam Mousa Kazem | 14 (100%) | 12(85.7%) | 8(57.1%) | 0(0.0%) | 7(50%) |
| Shariati | 13 (100%) | 10(77%) | 7(53.8%) | 0(0.0%) | 7(53.8%) |
| Total | 153(100%) | 139(90.8%) | 95(62.1%) | 0(0.0%) | 86(56.2%) |

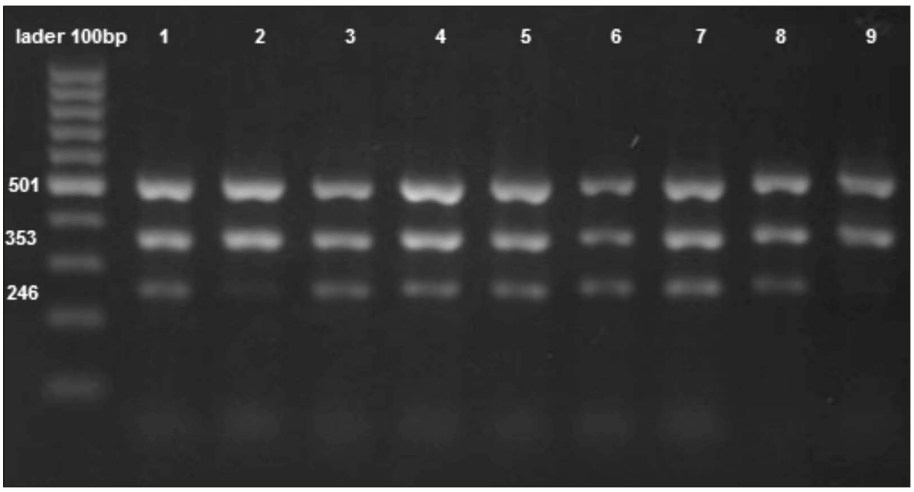


**Figure 1 -** PCR amplification of the *bla*OXA genes. Lane Ladder: 100 bp-3k b ladder, lane 1: positive control for *bla*OXA genes (*bla*OXA-51: 353bp, *bla*OXA-23: 501bp, and *bla*OXA-24: 246bp); lane 2: positive results for *bla*OXA-23 and *bla*OXA-51 genes; lane 3,4,5,6,7 and 8: positive results for *bla*-OXA-23, *bla*OXA-24, and *bla*OXA-51 genes; lane 9: positive results for *bla*-OXA-51 and *bla*OXA-23 genes.

particularly beta-lactams and long-term hospitalization may be two important causes of the isolation of carbapenem-resistant *A. baumannii* strains from inpatients. Infections caused by these strains are associated with high rates of mortality in hospitalized patients as well as the high cost of treatment [22, 23]. Therefore, awareness of the contribution of these strains in infectivity in hospitalized patients as well as continuous tracking of involved genes in each region can significantly contribute to the prevention and control of these infections.

In our study, the rate of resistance to imipenem was 100% that was higher than those reported from others Iranian cities by Shoja et al. (Ahvaz), Safari et al. (Hamadan), Akbari et al., Najar Peerayeh et al., Bahador et al., and Asadollahi et al. (Tehran) and Alaei et al. (Shiraz); but, it was similar to studies conducted by Zanganeh et al. and Salimizand et al. (Mashhad) [11, 13-15, 24-28].

In the present study, similar to other studies conducted in Iran, OXA-23 was the most prevalent acquired OXA-type carbapenemase among carbapenem-resistant isolates, followed by OXA-24 [18, 26, 29]. Nevertheless, OXA-58 was not detected in any of the isolates that in parallel with the results of above-mentioned studies.

At the regional level, in a study that was done by Zowawi and colleagues, OXA-23 was detected as a dominant type (91.5%) of carbapenemases in carbapenem-resistant *A. baumannii* isolates from hospitals of Saudi Arabia, United Arab Emirates, Oman, Qatar, Bahrain, and Kuwait, followed by OXA-24 (4.3%) [20]. Similary to our results, OXA-58 could not be identified by them in any of resistant isolates. Likewise, in the studies from other parts of the world have been reported that OXA-23 as a dominant type in carbapenem-resistant isolates has been associated with outbreaks [31-34].

Contrary to our findings, Kooti et al. and Sohrabi et al. have reported the low prevalence of OXA-58 among carbapenem-resistant isolates in their studies from (Shiraz) (0.5%), (Tehran) (3%), and (Tabriz) (3.2%) [17, 35]. However, two separate Turkish studies, have reported high prevalence of OXA-58 among carbapenem-resistant *A. baumannii* isolates [35, 36]. In addition, other studies from China, Brazil, France and Iran have reported the presence of $bla_{\text{OXA-58}}$ gene among resistant isolates [37-40]. These findings suggest that since the transfer of $bla_{\text{OXA-58}}$ gene is plasmid-mediated, the prevalence of OXA-58 among carbapenem-resistant *A. baumannii* isolates is geographically different.

To the best of our knowledge, this is the first documented report of prevalence of $bla_{\text{OXA}}$ genes among clinical isolates of *A. baumannii* from Isfahan. The results of this study demonstrated high prevalence of OXA-type carbapenemase among imipenem resistant *A. baumannii* in the different wards of hospitals, moreover, correct prescription of antibiotics and effective infection control polices for preventing extent of resistant strains is needed.

## CONCLUSIONS

In conclusion, we found that the prevalence of OXA-type carbapenemases among carbapenem-resistant *A. baumannii* isolates is high in Isfahan and OXA-23 is the major carbapenemase mechanism responsible for the resistance phenotype.

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**Conflict of interest**
None declared

## REFERENCES

[1] Neves F.C., Clemente W.T., Lincopan N., et al. Clinical and microbiological characteristics of OXA-23- and OXA-143-producing *Acinetobacter baumannii* in ICU patients at a teaching hospital., Brazil. *Braz. J. Infect. Dis.* 20, 556-563, 2016.
[2] Mathlouthi N., El Salabi A.A., Ben Jomaa-Jemili M., et al. Early detection of metallo-beta-lactamase NDM-1- and OXA-23 carbapenemase-producing *Acinetobacter baumannii* in Libyan hospitals. *Int. J. Antimicrob. Agents*. 48, 46-50, 2016.
[3] Zander E., Seifert H., Higgins P.G. Effects of saline, an ambient acidic environment, and sodium salicylate on OXA-Mediated carbapenem resistance in *Acinetobacter baumannii*. *Antimicrob. Agents Chemother*. 60, 3415-3418, 2016.
[4] Zenati K., Touati A., Bakour S., et al. Characterization of NDM-1- and OXA-23-producing *Acinetobacter baumannii* isolates from inanimate surfaces in a hospital environment in Algeria. *J. Hosp. Infect*. 92, 19-26, 2016.
[5] Higgins P.G., Perez-Llarena F.J., Zander E., et al. OXA-235, a novel class D beta-lactamase involved in resistance to carbapenems in *Acinetobacter baumannii*. *Antimicrob. Agents Chemother*. 57, 2121-2126, 2013.
[6] Sevillano E., Fernandez E., Bustamante Z., et al. Emergence and clonal dissemination of carbapenem-hydrolysing OXA-58-producing *Acinetobacter baumannii* isolates in Bolivia. *J. Med. Microbiol*. 61, 80-84, 2012.
[7] Kao C.Y., Udval U., Oyunchimeg R., et al. Dissemination of OXA-carbapenemase-producing *Acinetobacter baumannii* ST195 and ST642 in a Mongolian hospital. *Infect. Genet. Evo*l. 28, 313-316, 2014.
[8] de Sa Cavalcanti F.L., Almeida A.C., Vilela M.A., de Morais Junior M.A., de Morais M.M., Leal-Balbino T.C. Emergence of extensively drug-resistant OXA-72-producing *Acinetobacter baumannii* in Recife, Brazil: risk of clonal dissemination? *Diagn. Microbiol. Infect. Dis.* 77, 250-251, 2013.
[9] Strateva T., Markova B., Marteva-Proevska Y., et al. Widespread dissemination of multidrug-resistant *Acinetobacter baumannii* producing OXA-23 carbapenemase and ArmA 16S ribosomal RNA methylase in a Bulgarian university hospital. *Braz. J. Infect. Dis.* 16, 307-310, 2012.
[10] Rumbo C., Fernandez-Moreira E., Merino M., et al. Horizontal transfer of the OXA-24 carbapenemase gene via outer membrane vesicles: a new mechanism of dissemination of carbapenem resistance genes in *Acinetobacter baumannii*. *Antimicrob. Agents Chemother.* 55, 3084-3090, 2011.
[11] Shoja S., Moosavian M., Rostami S., Abbasi F., Tabatabaiefar M.A., Peymani A. Characterization of Oxacillinase and Metallo-beta-Lactamas genes and molecular typing of clinical isolates of *Acinetobacter baumannii* in Ahvaz, South-West of Iran. *Jundishapur J. Microbiol.* 9, e32388, 2016.
[12] Mohajeri P., Sharbati S., Farahani A., Rezaei Z. Evaluate the frequency distribution of nonadhesive virulence factors in carbapenemase-producing *Acinetobacter baumannii* isolated from clinical samples in Kermanshah. *J. Nat. Sci. Biol.Med*. 7, 58-61, 2016.
[13] Alaei N., Aziemzadeh M., Bahador A. Antimicrobial resistance profiles and genetic elements involved in carbapenem resistance in *Acinetobacter baumannii* isolates from a referral hospital in Southern Iran. *J. Glob. Antimicrob. Resist*. 5, 75-79, 2016.
[14] Zanganeh Z., Eftekhar F. Correlation of oxacillinase gene carriage with the genetic fingerprints of imipenem-resistant clinical isolates of *Acinetobacter baumannii*. *Jundishapur J. Microbiol*. 8, e26545, 2015.
[15] Salimizand H., Noori N., Meshkat Z., et al. Prevalence of *Acinetobacter baumannii* harboring ISAba1/bla OXA-23-like family in a burn center. *Burns* 41, 1100-1106, 2015.
[16] Mahdian S., Sadeghifard N., Pakzad I., et al. *Acinetobacter baumannii* clonal lineages I and II harboring different carbapenem-hydrolyzing-beta-lactamase genes are widespread among hospitalized burn patients in Tehran. *J. Infect. Public Health* 8, 533-542, 2015.
[17] Kooti S., Motamedifar M., Sarvari J. Antibiotic resistance profile and distribution of oxacillinase genes among clinical isolates of *Acinetobacter baumannii* in Shiraz teaching hospitals, 2012 - 2013. *Jundishapur J. Microbiol*. 8, e20215, 2015.
[18] Farsiani H., Mosavat A., Soleimanpour S., et al. Limited genetic diversity and extensive antimicrobial resistance in clinical isolates of *Acinetobacter baumannii* in north-east Iran. *J. Med. Microbiol*. 64, 767-773, 2015.

[19] Ionescu G., Constantiniu S. Biology of genus Acinetobacter. *Bacteriol. Virusol. Parazitol. Epidemiol.* 49,157-174, 2014.
[20] Jean B. Patel FRCI., Jeff Alder., et al. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Fourth Informational Supplement. Clinical and Laboratory Standards Institute. 34, 1-230, 2014.
[21] Woodford N., Ellington MJ., Coelho JM., et al. Multiplex PCR for genes encoding prevalent OXA carbapenemases in *Acinetobacter spp. Int. J. Antimicrob. Agents.* 27, 351-353, 2006.
[22] Al Atrouni A., Hamze M., Jisr T., et al. Wide spread of OXA-23-producing carbapenem-resistant *Acinetobacter baumannii* belonging to clonal complex II in different hospitals in Lebanon. *Int. J. Infect. Dis.* 52, 29-36, 2016.
[23] Pagano M., Rocha L., Sampaio J.L., et al. Emergence of OXA-72-producing *Acinetobacter baumannii* belonging to high-risk clones (CC15 and CC79) in different Brazilian states. *Infect. Control Hosp. Epidemiol*. 1-2, 2016.
[24] Safari M., Mozaffari Nejad A.S., Bahador A., et al. Prevalence of ESBL and MBL encoding genes in *Acinetobacter baumannii* strains isolated from patients of intensive care units (ICU). *Saudi J. Biol. Sci.* 22, 424-429, 2015.
[25] Akbari M., Niakan M., Taherikalani M., et al. Rapid identification of Iranian *Acinetobacter baumannii* strains by single PCR assay using BLA oxa-51 -like carbapenemase and evaluation of the antimicrobial resistance profiles of the isolates. *Acta Microbiol. Immunol. Hung.* 57, 87-94, 2010.
[26] Najar Peerayeh S., Karmostaji A. Molecular identification of resistance determinants, integrons and genetic relatedness of extensively drug resistant *Acinetobacter baumannii* isolated from hospitals in Tehran, Iran. *Jundishapur J. Microbiol.* 8, e27021, 2015.
[27] Bahador A., Raoofian R., Pourakbari B., et al. Genotypic and antimicrobial susceptibility of carbapenem-resistant *Acinetobacter baumannii:* analysis of IS Aba elements and Bla OXA-23-like genes including a new variant. *Front. Microbiol.* 6, 1249, 2015.
[28] Asadollahi P., Akbari M., Soroush S., et al. Antimicrobial resistance patterns and their encoding genes among *Acinetobacter baumannii* strains isolated from burned patients. *Burns* 38, 1198-1203, 2012.
[29] Bahador A., Raoo An R., Farshadzadeh Z., et al. The Prevalence of IS Aba 1 and IS Aba 4 in *Acinetobacter baumannii* species of different international clone lineages among patients with burning in Tehran, Iran. *Jundishapur J. Microbiol*. 8, e17167, 2015.
[30] Zowawi HM., Sartor A.L., Sidjabat H.E., et al. Molecular epidemiology of carbapenem-resistant *Acinetobacter baumannii* isolates in the Gulf Cooperation Council States: dominance of OXA-23-type producers. *J. Clin. Microbiol.* 53, 896-903, 2012.
[31] Peleg A.Y., Seifert H., Paterson DL. *Acinetobacter baumannii*: emergence of a successful pathogen. *Clin. Microbiol. Rev.* 21, 538-582, 2008.
[32] Merino M., Poza M., Roca I., et al. Nosocomial outbreak of a multiresistant *Acinetobacter baumannii* expressing OXA-23 carbapenemase in Spain. *Microb. Drug Resist.* 20, 259-263, 2014.
[33] Dettori M., Piana A., Deriu M.G., et al. Outbreak of multidrug-resistant *Acinetobacter baumannii* in an intensive care unit. *New Microbiol.* 37, 185-191, 2014.
[34] Perez F., Endimiani A., Ray AJ., et al. Carbapenem-resistant *Acinetobacter baumannii* and *Klebsiella pneumoniae* across a hospital system: impact of post-acute care facilities on dissemination. *J. Antimicrob. Chemother*. 65, 1807-1018, 2010.
[35] Metan G., Pala Ç., Kaynar L., Cevahir F., Alp E. A nightmare for haematology clinics:
extensively drug-resistant (XDR) *Acinetobacter baumannii. Infez. Med*. 22, 4, 277-282, 2014.
[36] Deveci O., Dal T., Tekin R., Bozkurt F., Tekin A., Dayan S. Carbapenem resistance in *Acinetobacter baumannii*: where is it heading? *Infez. Med*. 21, 3, 211-215, 2013.
[37] Fu Y., Jiang J., Zhou H., et al. Characterization of a novel plasmid type and various genetic contexts of bla OXA-58 in *Acinetobacter* spp. from multiple cities in China. *PLoS One*. 9, e84680, 2014.
[38] de Souza Gusatti C., Bertholdo L.M., Otton L.M., et al. First occurrence of bla OXA-58 in *Acinetobacter baumannii* isolated from a clinical sample in Southern Brazil. *Braz. J. Microbiol.* 43, 243-246, 2012.
[39] Barnaud G., Zihoune N., Ricard J.D., et al. Two sequential outbreaks caused by multidrug-resistant *Acinetobacter baumannii i*solates producing OXA-58 or OXA-72 oxacillinase in an intensive care unit in France. *J. Hosp. Infect*. 76, 358-360, 2010.
[40] Owlia P., Azimi L., Gholami A., Asghari B., Rastegar L.A. ESBL and MBL mediated resistance in *Acinetobacter baumannii*: a global threat to burnt patients. *Infez. Med.* 20, 3, 182-187, 2012.