Journal of Medical Microbiology and Infectious Diseases

JoMMID
ISSN: 2345-5349
eISSN: 2345-5330

The *adeH* and *adeS* Efflux Pump Genes in Imipenem and Colistin-Resistant *Acinetobacter baumannii* Clinical Isolates

Azam Aghili Amjad[1], Mohammad Niakan[1*], Fatemeh Sameni[1], Shahriar Bakhti[1], Mansoor Khaledi[2] Hamed Afkhami[1], Reza Mirnejad[2]

[1]Department of Microbiology, Faculty of Medicine, Shahed University, Tehran, Iran; [2]Biology Research Center, System Biology and Poisoning Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran.

ARTICLE INFO

Original Article

Keywords: *Acinetobacter baumannii*, Efflux pump, *adeS* gene, *adeH* gene

Received: 21 Sep. 2021
Received in revised form: 26 Oct. 2022
Accepted: 08 Nov. 2022
DOI: 10.52547/JoMMID.10.4.186

***Correspondence**
Email: niakan@shahed.ac.ir
Tel: +982188964792
Fax: +982151215285

ABSTRACT

Introduction: *Acinetobacter baumannii* is one of the most important causes of nosocomial infections. In this bacteria, several mechanisms contribute to resistance against antimicrobial agents. The present study investigated the prevalence of *adeS* and *adeH* genes and the role of efflux pumps in imipenem and colistin-resistant *A. baumannii* clinical isolates. **Methods:** This study included 60 *A. baumannii* isolates collected from medical centers affiliated with the Shahid Beheshti University of Medical Science, Tehran, Iran. The antibiotic susceptibility pattern was examined using the broth microdilution MIC method according to Clinical and Laboratory Standards Institute (CLSI) guidelines. Also, the *adeS* and *adeH* genes were amplified by PCR. **Results:** The isolates were 100% imipenem-resistant and 86.7% colistin-resistant. All isolates were positive for the *51-blaOXA* gene. The *adeH* and *adeS* genes were detected in 95% and 80% of the isolates. **Conclusion:** The high frequency of *adeS* and *adeH* efflux pump genes and the high drug resistance in *A. baumannii* clinical isolates indicated that *adeS* and *adeH* efflux pump genes contribute to antibiotic resistance in this species. Therefore, our results provide essential information about high drug resistance in *A. baumannii* clinical isolates that can help limit the horizontal and vertical transmission of efflux pump genes in antibiotic-resistant *A. baumannii* isolates that causes nosocomial infections in susceptible strains.

INTRODUCTION

A. baumannii is a nonfermenting Gram-negative bacillus and poses a severe threat, particularly in intensive care units (ICUs) [1-3]. This species can cause blood, respiratory tract, urinary tract (UTI), and ventilator-associated infections, which are severe medical challenges [4, 5]. Bacterial antibiotic resistance is of great concern for public health authorities, particularly for bacteria causing nosocomial infections[6]. High multidrug-resistant (MDR) *A. baumannii* infections in Iran are challenging health problems [7, 8]. The bacterium is typically multidrug-resistant and shows resistance to aminoglycosides, fluoroquinolones, and third-generation cephalosporins [9, 10].

In MDR *A. baumannii* strains, the enzymes such as beta-lactamases and efflux pump genes are involved in resistance to various antibiotics [11-13]. Efflux pumps may lead to inherent bacterial resistance by expelling a wide range of toxic substrates such as antibiotics, biocides, and chemicals from bacteria [14]. Overexpression of efflux pumps in *A. baumannii* is a common MDR mechanism. Efflux pumps increase the minimum inhibitory concentration (MIC), resulting from the intracellular reduction of the antibiotic [15].

A. baumannii encodes *AdeA*, *AdeB*, and *AdeC* genes through the adeABC operon, which are involved in the resistance-nodulation-division (RND) efflux systems [16, 17]. The RND efflux systems are found only in Gram-negative bacteria and are effective in antibiotic resistance against fluoroquinolones and other antibiotic groups, such as those affecting the bacterial cell walls [18].

Knowledge of RND efflux systems and their relationship to antibiotic resistance in *A. baumannii* can be helpful from different perspectives, e,g., reducing antibiotic resistance in *A. baumannii*-resistant isolates.

The current study investigated the relationship between the RND efflux pump system and the imipenem and colistin resistance to provide essential information about high drug resistance in *A. baumannii* clinical isolates that

[DOI: 10.52547/JoMMID.10.4.186]

can help limit the horizontal and vertical transmission of efflux pump genes in antibiotic-resistant *A. baumannii* isolates that causes nosocomial infections in susceptible strains.

Material and Methods

Bacterial Isolation and Identification. In this cross-sectional descriptive study, from October 2018 to April 2019, among 200 clinical samples collected from the medical centers of Shahid Beheshti University of Tehran, Iran, 60 isolates from blood and wound specimens were identified as *A. baumannii*. Samples were cultured on general and specific culture media such as MacConkey Agar (Merck Company, Germany) and incubated for 24 hours at 37 ºC. The isolates were examined by Gram staining and biochemical tests such as motility, fermentation, catalase, oxidase, hemolysis, citrate, Methyl Red, and Vogues-Proskauer (MR and VP). Then, the housekeeping 16S rRNA gene was amplified to confirm the identity of *A. baumannii* isolates [19]. The amplification program included an initial cycle at 95 ºC for 5 min, followed by 30 cycles of 95 ºC for 45 s, 85 ºC for 55 s, 72 ºC for 60 s, and a final cycle at 72 ºC for 5 min.

Amplification of *bla*OXA- 51-like. A PCR assay was used to amplify *bla*OXA-51-like gene to confirm *A. baumannii* diagnosis. Bacterial DNA was first extracted using a DNA extraction kit (DENAzist Bacterial DNA isolation kit), followed by amplification using specific primers [20]. The amplification program included a cycle at 95 ºC for 5 min, followed by 30 cycles at 95 ºC for 45 s, 85ºC for 55 s, 72 ºC for 60 s, and a final cycle at 72 ºC for 5 min. The standard *A. baumannii* strain, ATCC®19606TM, was used as a positive control. PCR products were then electrophoresed in 2% agarose gel containing SYBR-safe dye and visualized under a gel documentation device.

Amplification of *adeS* and *adeH* genes. The standard *A. baumannii* strain, ATCC®19606TM containing *adeS* and *adeH* genes, was used as a control. The PCR uses proprietary primers (Table 1), and the amplification program included an initial denaturation at 94 º C for 5 min, followed by 30 cycles of denaturation at 94 ºC for 1 min, annealing at 55.5 ºC for the *adeH* gene and 54.5 º C for *adeS* gene C for 1 min, extension at 72 º C for 1 min, and a final extension at 72 º C for 7 min.

Table 1. Primers used to amplify genes encoding antibiotic resistance in *A. baumannii* isolates.

Genes	Primers	Sequence (5' to 3')	Size (bp)	References
adeS	adeS-F	GGTCGTTTACAAGGCATCATC	130	This study
	adeS-R	CAATATACAGGAGTGGAAGTTAGG		
adeH	adeH-F	GTTACACCGCATCTCGTTCC	120	This study
	adeH-R	CGCCGTTGATTGACTCTTCG		

Antimicrobial susceptibility testing. The efflux pump is involved in resistance to various antibiotics in *A. baumannii*. However, due to high resistance to imipenem and colistin in Iran. The minimum inhibitory concentration (MIC) for these two antibiotics (Sigma Aldrich Co. USA) was tested according to Clinical and Laboratory Standards Institute (CLSI 2020) guidelines [21]. The MIC value was determined in microplate wells containing the newly prepared Mueller Hinton broth culture medium (Merck, Co., Germany) using serial dilution, as previously described [22]. The final bacterial concentration was 5×10^5 CFU/mL in the 100 µl final volume. The microplates were placed at 37 ºC and examined for bacteria growth through turbidity after 24 h. *Escherichia coli* ATCC®25922TM and *Pseudomonas aeruginosa* ATCC®27853TM were used as positive controls [23].

Statistical method. Data analysis was performed using SPSS statics 23.0. Classified variables were compared using the chi-square or Fisher's exact test. The *P*-value <0.05 was considered statistically significant.

This study followed the Declaration of Helsinki. Informed written consent was obtained from all the participants, and the Ethics Committee of Shahed University of Medical Sciences approved this study (Code No.: IR.SHAHED.REC.1397.058).

RESULTS

Identification of 16S rRNA and *bla*OXA- 51-like genes. Sixty *A. baumannii* isolates were identified via microscopic observation of Gram-negative coccobacilli followed by biochemical tests, including motility, non-fermentation, positive catalase, negative oxidase, non-hemolysis, positive citrate, negative MR, and positive VP). Amplifying a 342-bp sequence of the 16S rRNA gene confirmed the identity of all isolates. The *blaOXA-51-like* gene was present in all samples.

Amplification of *adeS* and *adeH* genes. Of the 60 *A. baumannii* isolates, 57 (95%) had the *adeH* gene, and 48 (80%) had the *adeS* gene (Figs 1 and 2). Also, *AdeH* and *adeS* genes were observed in 59 (98.3%) imipenem-resistant *A. baumannii* isolates and 51 (85%) colistin-resistant isolates.

[DOI: 10.52547/JoMMID.10.4.186]

Fig. 1. Gel electrophoresis of PCR-amplified *adeH* gene (120 bp). Of the 60 *A. baumannii* isolates, 57 (95%) had the *adeH* gene. From left to right: 50 bp DNA ladder, positive control (C+), negative control (C-), 1-10 …

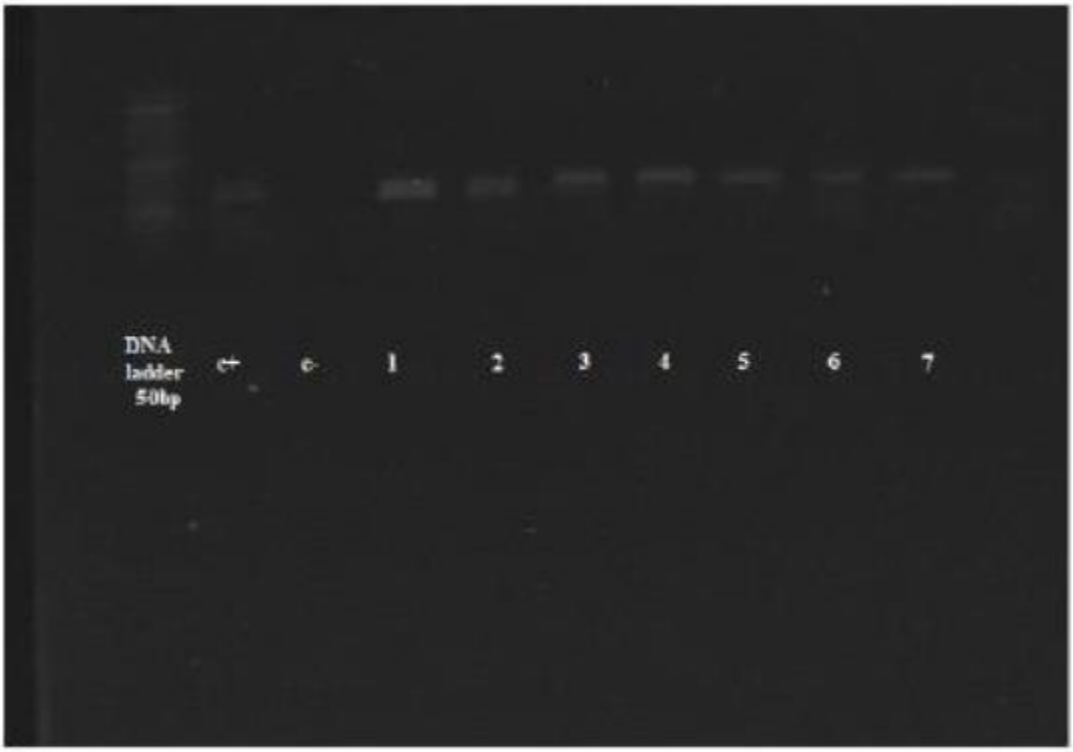

Fig. 2. Gel electrophoresis of PCR-amplified *ade S* gene (130 bp). Of the 60 *A. baumannii* isolates, 48 (80%) had the *adeS* gene. From left to right: 50 bp DNA ladder, positive control (C+), negative control (C-), 1-7 …

[DOI: 10.52547/JoMMID.10.4.186]

Microdilution Susceptibility testing method. All 60 isolates (100%) were imipenem-resistant, and 52 (86.7%) were colistin-resistant.

The MIC value for imipenem in 60 *A. baumannii* samples was 16 µg/ml, much higher than the 2 µg/ml for the *A. baumannii* ATCC®19606TM, the sensitive control strain. So all (100%) *A. baumannii* samples were imipenem-resistant. The MIC value for colistin in 52 samples was 6 µg/ml, which was also higher than the control strain (MIC= 0.5 µg/ml). Thus, 86.7% of samples were colistin-resistant, and 13.3% were not.

DISCUSSION

A. baumannii infections are among the most severe types of nosocomial infections. Evidence suggests that the overexpression of efflux pumps is a resistance mechanism in some bacteria, including *A. baumannii* [24]. The emergence of antibiotic-resistant *A. baumannii* is a global concern. In the present study, the results of the antibiotic resistance test showed 100% and 86.7% resistance to imipenem and colistin, respectively.

According to our results and similar studies in Iran, there seems to be a significant relationship between colistin and imipenem resistance of *A. baumannii* strains and efflux pump genes, *adeS* and *adeH*. Yousefian *et al*. (2014) showed that out of 96 clinical samples, 51 (30%) were resistant to colistin, and the MIC value of resistant strains was more than 128 µg/ml [25]. However, our study showed that the colistin resistance was 86.7%, and the MIC for resistant strains was higher than 8 µg/ml. Previous studies on the drug resistance pattern of *A. baumannii* isolates in Iran showed that 100% of strains were susceptible to colistin [26, 27], which is inconsistent with the present study. In Slovenia, 45.1% of isolates were resistant to colistin [28]. Consequently, we observed a significant increase in antibiotic resistance in the present study. Our results and similar studies in other countries indicated increased resistance in this bacteria due to antibiotic overuse.

In Iran, *A. baumannii* resistance rate to imipenem has increased from 26.6% (25) to 88.7% [29] from 2012 to 2015 and 100% in the present study. Another similar study in 2019 [26] showed an increase in imipenem resistance, which is entirely consistent with the present study, indicating that carbapenems are unsuitable for treating *A. baumannii* infections. Imipenem resistance rates of 98% and 99.4% by Angoti *et al.* (2016) in Iran and Boral *et al.* (2019) in Turkey [30, 31] disapproved of this antibiotic for *A. baumannii* infections.

In China, an evaluation of the relationship between *adeDE*, *adeM*, and *adeABC*efflux pumps among A. *baumannii* strains showed that 80% of the imipenem-resistant strains carried the *adeB, adeR, adeS, and adeJ* genes, indicating that efflux pumps were associated with antibiotic resistance, consistent with the results of the present study [32].

In a study by Asadolah-Malayeri *et al*., the imipenem and colistin resistance was 97% and 0%, respectively, and 98.3% of the isolates had *adeS* gene. Moreover, the *OXA-23* gene was prevalent in 95% of the isolates [29]. According to Noori *et al*. [33], colistin was the most effective antibiotic against *A. baumannii*, with a sensitivity value of 97%, which differs significantly from the present study. Moreover, the prevalence of the *adeS* gene was 91%, which is probability consistent with the present study. The *OXA-23* and *adeH* genes were observed in all 10 (100%) MDR *A. baumannii* isolates, and the *OXA-23* gene was associated with carbapenem resistance [34].

Feizabadi *et al*. (2019) reported that the MIC value forimipenem [35]was higher than the value reported by Taheri Kalani (2008) [36], and the present study exhibited increased imipenem resistance over the years.

The most recent study identified 60 clinical isolates of *A. baumannii* and later confirmed by detecting *blaOXA-51*-like and *16S rRNA* genes. This study showed that 98.37% of *A. baumannii* isolates were 100% resistant against piperacillin, meropenem, cefotaxime, ceftriaxone, ceftazidime, ceftazidime, and ciprofloxacin. Most *A. baumannii* isolates had antibiotic efflux pumps, and more than 73% of *A. baumannii* isolates were resistant to the target antibiotics, indicating the significant role of efflux pumps in developing resistance against these antibiotics. In addition, 95% of all *A. baumannii* isolates possessed *adeH* and 80% *adeS* efflux pumps [37].

The present study revealed increasing colistin and imipenem-resistant *A. baumannii* rates in Iran, similar to previous studies. This trend is a warning sign for health systems. According to the present and other studies, efflux pumps play a significant role in resistance to different antibiotics. Thus, it is necessary to use new treatment regimens and be more alert in the timely diagnosis and control of nosocomial infections.

ACKNOWLEDGMENT

This manuscript is part of the MSc thesis of Azam Aghili Amjad. This study was financially supported by Shahed University of Medical Sciences in 2018. The authors would like to express their sincere thanks to all laboratory staff of Shahed University of Medical Sciences. Funding was used to purchase equipment and tools.

CONFLICT OF INTEREST

The authors declare thare are no conflicts of interest associated with this manuscript.

REFERENCES

1. Ravi NS, Anandan S, Vijayakumar S, Gopi R, Lopes BS, Veeraraghavan B. The potential of different molecular biology

[DOI: 10.52547/JoMMID.10.4.186]

methods in tracking clones of *Acinetobacter baumannii* in an ICU setting. J Med Microbiol . 2018; 67 (9): 1340-7.

2. Basatian-Tashkan B, Niakan M, Khaledi M, Afkhami H, Sameni F, Bakhti S, et al. Antibiotic resistance assessment of *Acinetobacter baumannii* isolates from Tehran hospitals due to the presence of efflux pumps encoding genes (*adeA* and *adeS* genes) by molecular method. BMC Res Notes. 2020; 13 (1): 543.

3. Nazari M, Youzbashi Z, Khaledi M, Fathi J, Afkhami H. Detection of carbapenem resistance and virulence genes among *Acinetobacter baumannii* isolated from hospital environments in center of Iran. J Curr Biomed Rep. 2021; 2 (1): 14.

4. Khaledi M, Abadi MSS, Validi M, Zamanzad B, Vafapour R, Gholipour A. Phenotypic and genotypic detection of metallo-β-lactamases in *A. baumanii* isolates obtained from clinical samples in Shahrekord, southwest Iran. BMC Res Notes. 2019; 12 (1): 1-6.

5. Harding CM, Hennon SW, Feldman MF. Uncovering the mechanisms of *Acinetobacter baumannii* virulence. Nat Rev Microbiol. 2018; 16 (2): 91-102.

6. Sameni F, Esmaeili A, Dabiri H, Azargun R, Goudarzi H, Mohammadzadeh A. Distribution of Integron Class I in Drug Resistant *Pseudomonas aeruginosa* Isolated from Clinical Samples. Res Med. 2020; 44 (1): 301-7.

7. Potron A, Poirel L, Nordmann P. Emerging broad-spectrum resistance in *Pseudomonas aeruginosa* and *Acinetobacter baumannii*: mechanisms and epidemiology. Int J Antimicrob Agents. 2015; 45 (6): 568-85.

8. Hashemi B, Afkhami H, Khaledi M, Kiani M, Bialvaei AZ, Fathi J, et al. Frequency of Metalo beta Lactamase genes, *bla IMP1*, *INT 1* in *Acinetobacter baumanii* isolated from burn patients North of Iran. Gene Rep. 2020; 21: 100800.

9. Hawkey J, Ascher DB, Judd LM, Wick RR, Kostoulias X, Cleland H, et al. Evolution of carbapenem resistance in *Acinetobacter baumannii* during a prolonged infection. Microbial genomics. 2018; 4 (3): e000165.

10. Zhanel GG, Golden AR, Zelenitsky S, Wiebe K, Lawrence CK, Adam HJ, et al. Cefiderocol: a siderophore cephalosporin with activity against carbapenem-resistant and multidrug-resistant Gram-negative bacilli. Drugs. 2019; 79 (3): 271-89.

11. Elbrolosy AM, Labeeb AZ, Hassan DM. New Delhi metallo-β-lactamase-producing Acinetobacter isolates among late-onset VaP patients: Multidrug-resistant pathogen and poor outcome. Infect Drug Resist. 2019; 12: 373-84.

12. Jiang L, Yu Y, Zeng W, Guo J, Lv F, Wang X, et al. Whole-genome analysis of New Delhi metallo-beta-lactamase-1-producing *Acinetobacter haemolyticus* from China. J Glob Antimicrob Resist. 2020; 20: 204-8.

13. Patil HV, Mohite ST, Patil VC. Metallo-beta-lactamase-producing multidrug-pesistant acinetobacter isolates in patients with ventilator-associated pneumonia. J Nat Sci Biol. 2021; 12 (1): 64.

14. Rumbo C, Gato E, López M, de Alegría CR, Fernández-Cuenca F, Martínez-Martínez L, et al. Contribution of efflux pumps, porins, and β-lactamases to multidrug resistance in clinical isolates of *Acinetobacter baumannii*. Antimicrob Agents Chemother. 2013; 57 (11): 5247-57.

15. Pagdepanichkit S, Tribuddharat C, Chuanchuen R. Distribution and expression of the Ade multidrug efflux systems in *Acinetobacter baumannii* clinical isolates. Can J Microbiol. 2016; 62 (9): 794-801.

16. Kaviani R, Pouladi I, Niakan M, Mirnejad R. Molecular Detection of *Adefg* Efflux Pump Genes and their Contribution to Antibiotic Resistance in *Acinetobacter baumannii* Clinical Isolates. Rep Biochem Mol Biol. 2020; 8 (4): 413-8.

17. Yoon E-J, Courvalin P, Grillot-Courvalin C. RND-type efflux pumps in multidrug-resistant clinical isolates of *Acinetobacter baumannii*: major role for *AdeABC* overexpression and *AdeRS* mutations. Antimicrob Agents Chemother. 2013; 57 (7): 2989-95.

18. Webber M, Piddock L. The importance of efflux pumps in bacterial antibiotic resistance. J Antimicrob Chemother. 2003; 51 (1): 9-11.

19. Sepahvand S, Davarpanah MA, Roudgari A, Bahador A, Karbasizade V, Jahromi ZK. Molecular evaluation of colistin-resistant gene expression changes in *Acinetobacter baumannii* with real-time polymerase chain reaction. Infect Drug Resist. 2017; 10: 455-62.

20. Hou C, Yang F. Drug-resistant gene of *blaOXA-23*, *blaOXA-24*, *blaOXA-51* and *blaOXA-58* in *Acinetobacter baumannii*. Int J Clin Exp Med. 2015; 8 (8): 13859-63.

21. Lob S, Hackel M, Badal R, Young K, Motyl M, Sahm D, editors. Global Prevalence of colistin and carbapenem-resistant Gram-negative organisms: SMART 2015–2016. Open Forum Infect Dis; 2017.

22. Wiegand I, Hilpert K, Hancock RE. Agar and broth dilution methods to determine the minimal inhibitory concentration (MIC) of antimicrobial substances. Nat Protoc. 2008; 3 (2): 163-75.

23. Leu H-S, Ye J-J, Lee M-H, Su L-H, Huang P-Y, Wu T-L, et al. Synergy of imipenem/colistin methanesulfonate combinations against imipenem-nonsusceptible multidrug-resistant *Acinetobacter baumannii*. J Microbiol Immunol Infect. 2014; 47 (5): 406-11.

24. Coyne S, Courvalin P, Périchon B. Efflux-mediated antibiotic resistance in Acinetobacter spp. Antimicrob Agents Chemother. 2011; 55 (3): 947-53.

25. Yousefian R. Identification and frequency of colistin-resistant *acintobacter baumanii* in clinical isolates using polymerase chain reaction. J Isfahan Med Sch. 2014; 301: 1466-74.

26. Malekzadegan Y, Abdi A, Heidari H, Moradi M, Rastegar E, Ebrahim-Saraie HS. *In vitro* activities of colistin, imipenem and ceftazidime against drug-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii* isolates in the south of Iran. BMC Res Notes. 2019;12 (1): 301.

27. Gholami M, Hashemi A, Hakemi-Vala M, Goudarzi H, Hallajzadeh M. Efflux pump inhibitor phenylalanine-arginine B-naphthylamide effect on the minimum inhibitory concentration of imipenem in *Acinetobacter baumannii* strains isolated from hospitalized patients in Shahid Motahari burn hospital, Tehran, Iran. Jundishapur J Microbiol. 2015; 8 (10); e19048.

28. Germ J, Poirel L, Kisek TC, Spik VC, Seme K, Premru MM, et al. Evaluation of resazurin-based rapid test to detect colistin resistance in *Acinetobacter baumannii* isolates. Eur J Clin Microbiol Infect Dis. 2019; 38 (11): 2159-62.

[DOI: 10.52547/JoMMID.10.4.186]

29. Asadolah-Malayeri HO, Hakemi-Vala M, Davari K. Role of *Aders* and *OXA23* genes among imipenem resistant *Acinetobacter baumannii* isolates from two hospitals of Tehran, Iran. Iran J Pathol. 2016; 11 (4): 345-53.

30. Angoti G, Bandehpour M, Goudarzi H, Hajizadeh M, Zarringhalam Moghaddam M, Kouchaki A. Detection of Efflux Pump Genes (*adeA*, *adeB*, *adeC* and *abeM*) in *Acinetobacter baumannii* Isolated from Hospitalize Patients, North-west of Iran. Infect epidemiol microbiol. 2016; 2 (4): 8-11.

31. Boral B, Unaldi Ö, Ergin A, Durmaz R, Eser ÖK. A prospective multicenter study on the evaluation of antimicrobial resistance and molecular epidemiology of multidrug-resistant *Acinetobacter baumannii* infections in intensive care units with clinical and environmental features. Ann Clin Microbiol Antimicrob. 2019; 18 (1): 19.

32. Pu L, Jian Z, Pan F, Geng Y, He M, Liao P. Comparative genomic analysis and multi-drug resistance differences of *Acinetobacter baumannii* in Chongqing, China. Infect Drug Resist. 2019; 12: 2827-38.

33. Noori M, Mohsenzadeh B, Bahramian A, Shahi F, Mirzaei H, Khoshnood S. Characterization and frequency of antibiotic resistance related to membrane porin and efflux pump genes among *Acinetobacter baumannii* strains obtained from burn patients in Tehran, Iran. J Acute Dis. 2019; 8 (2): 63-6.

34. Nigro SJ, Hall RM. Antibiotic resistance islands in A320 (RUH134), the reference strain for *Acinetobacter baumannii* global clone 2. J Antimicrob Chemother. 2012; 67 (2): 335-8.

35. Feizabadi M, Fathollahzadeh B, Taherikalani M, Rasoolinejad M, Sadeghifard N, Aligholi M, et al. Antimicrobial susceptibility patterns and distribution of *blaOXA* genes among Acinetobacter spp. Isolated from patients at Tehran hospitals. Jpn J Infect Dis. 2008; 61 (4): 274-8.

36. Taherikalani M, Maleki A, Sadeghifard N, Mohammadzadeh D, Soroush S, Asadollahi P, et al. Dissemination of class 1, 2 and 3 integrons among different multidrug resistant isolates of *Acinetobacter baumannii* in Tehran hospitals, Iran. Iran Pol J Microbiol. 2011; 60 (2): 169-74.

37. Beikmohammadi H, Viesy S, Kaviani R, Pouladi I. Detection of efflux pump genes conferring multidrug resistance in clinical isolates of *Acinetobacter Baumannii* in Tehran province. Rev Med Microbiol. 2022; 33 (1): 31-6.

Cite this article:
Aghili Amjad A, Niakan M, Sameni F, Bakhti Sh, Khaledi M, Afkhami H, Mirnezad R. The adeH and adeS Efflux Pump Genes in Imipenem and Colistin-Resistant *Acinetobacter baumannii* Clinical Isolates. J Med Microbiol Infect Dis, 2022; 10 (4): 186-191. DOI: 10.52547/JoMMID.10.4.186

[DOI: 10.52547/JoMMID.10.4.186]