Prevalence of Imipenem-Resistant *Acinetobacter baumannii* isolates in Iran: A Meta-Analysis

**ABSTRACT**

**Background:** *Acinetobacter baumannii* is a gram-negative pathogen that is highly resistant to antibiotics. This bacterium can cause severe systemic infections, especially in hospitalized patients. Recently, antimicrobial-resistant *Acinetobacter baumannii* has become a life-threatening pathogen in Iran and around the world.

**Materials & Methods:** In this study, several Iranian and English databases were systematically searched to find all original and review articles investigating the prevalence of imipenem resistance in their sample size, while mentioning the source of clinical isolates, as well as the prevalence of antimicrobial resistance genes.

**Findings:** Among genes, *bla* carbAp2 with a prevalence of 31% to 100% was responsible for global outbreaks of imipenem-resistant *Acinetobacter baumannii* and was presented in most of the hospital isolates. Our meta-analysis also revealed that 74.2% of *Acinetobacter baumannii* were resistant to imipenem in 122 clinical studies.

**Conclusion:** Our study highlighted a rapid increase in the rate of imipenem resistance in clinical isolates of *Acinetobacter baumannii* in Iran. The need for periodic antibiotic care system programs to monitor the administration and use of antibiotics is strongly recommended.

**Keywords:** Imipenem, Resistance, *Acinetobacter baumannii*, Iran.

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Introduction

Acinetobacter baumannii is an opportunistic, nosocomial Gram-negative pathogen that causes severe infections especially in intensive care units (ICUs) [1]. Recently, prevalence of multidrug-resistant (MDR) or extensively-drug resistant (XDR) A. baumannii becomes a life-threatening problem [2]. Since 1985 the broad-spectrum β-lactam antibiotics e.g. carbapenems such as imipenem, meropenem, ertapenem, and doripenem have been the effective agent against multidrug-resistant A. baumannii infections [2, 3]. According to worldwide reports on the prevalence of carbapenem-resistant A. baumannii, it can have a negative impact on the treatment of patients [4]. Producing different β-lactamases that harbor insertion sequences (ISs) encoded through mobile elements on integrons, transposons or plasmids genes plays a critical role in carbapenem-resistant A. baumannii. Moreover, A. baumannii uses different mechanism such as modified penicillin-binding proteins (PBPs) and efflux pumps which decreased cell membranes permeability as well as biofilm formation or mutation in some drug targets to resist and survive in harsh environments (Figure 1) [5]. So, the rapid prevalence of A. baumannii strains producing carbapenemases, cephalosporinases (AmpCs), extended-spectrum β-Lactamases (ESBLs), and metallo-β-lactamases (MBLs) is becoming a global concern [6]. During recent years different studies published on the carbapenem-resistant A. baumannii in Iran. However, more studies on the mechanism of resistance and prevalence of the resistance bacteria should be done to reach the best treatment strategies for controlling outbreaks of carbapenem-resistant A. baumannii [7]. Detection of carbapenem resistance needs phenotypic methods such as disc diffusion and different inhibition tests recommended by CLSI as well as genotypic methods such as PCR to identify carbapenem resistance genes in clinical isolates [8].

This study described the frequency of imipenem-resistant A. baumannii in different cities of Iran. So, our aim was to evaluate the distribution and prevalence of resistance genes during the last two decades in Iran.

Materials and Methods

Search Strategies: Our research was performed on several related keywords such as “A. baumannii”, “carbapenemase”, “carbapenem-resistant A. baumannii”, “prevalence of carbapenem-resistant A. baumannii strains in Iran”, imipenem”, “imipenem resistance”, “imipenem resistance in Iran”, “multidrug resistance A. baumannii in Iran”, which were as inclusion criteria. Keywords were monitored both original and review articles in Persian and English in all research centers e.g. PubMed, MEDLINE, Google Scholar, Iranian data base, Web of sciences, and Scopus during 2006-2020. Out of 483 articles obtained, 143 articles were finally reviewed. For all studies, published date, sample size, and genes related to imipenem were also considered (Table 1).

![Fig. 1] The most prevalent mechanism of carbapenem resistance in A. baumannii [9]
Table 1) Studies included on resistance of *A. baumannii* to imipenem in Iran.

| Author               | Year | City      | Sample size | No. of Imipenem resistant isolates | %     | Isolated from                                                                 | Ref  |
|----------------------|------|-----------|-------------|-----------------------------------|-------|-------------------------------------------------------------------------------|------|
| Sadeghifard et al.,  | 2006 | Tehran    | 66          | 66                                | 100   | NR                                                                           | [10] |
| Ardebili et al.,     | 2012 |           | 65          | 60                                | 92.38 | Burned or hospitalized patients in ICU                                       | [11] |
| Davoodi et al.,      | 2015 |           | 104         | 70                                | 67.30 | Clinical isolates                                                            | [12] |
| Dehghani et al.,     | 2012 |           | 50          | 39                                | 78    | Blood, respiratory secretions, urine, skin ulcer, and oral mucosa            | [13] |
| Erfani et al.,       | 2017 |           | 107         | NR*                               | NR    | Clinical isolates                                                            | [14] |
| Dehbalaei et al.,    | 2017 |           | 48          | 37                                | 77.08 | Wound, trachea, urine, catheter, sputum, and burn                           | [15] |
| Mirnejad et al.,     | 2012 |           | 50          | 39                                | 78    | Blood, tracheal, wound swab samples, urine and five samples with unknown origin | [16] |
| Karmostaji et al.,   | 2013 |           | 123         | 103                               | 83.74 | Aspirated sputum, trachea, burn, wound and urinary tract infections         | [17] |
| Pajand et al.,       | 2013 |           | 75          | 64                                | 85.33 | Aspirates, urine, wound, blood and sputum, burn wound                       | [18] |
| Azimi et al.,        | 2015 |           | 65          | 65                                | 100   | Burn wound                                                                   | [19] |
| Alavi-Moghadam et al.| 2014 |           | 61          | 61                                | 100   | Ventilator associated pneumonia, Sputum, wounds, urine, central venous line, blood | [20] |
| Saderi et al.,       | 2015 |           | 106         | 102                               | 96.22 | Clinical isolates                                                            | [21] |
| Sharif et al.,       | 2014 |           | 200         | 171                               | 85.5  | Endotracheal biopsy, sputum, blood, catheter, urine, wound                    | [22] |
| Fallah et al.,       | 2014 |           | 108         | 99                                | 91.66 | Urinary specimens                                                            | [23] |
| Bahador et al.,      | 2015 |           | 62          | 38                                | 61.29 | ICU patients                                                                  | [24] |
| Haeili et al.,       | 2013 |           | 136         | 102                               | 75    | Broncho alveolar lavage (BAL), mini BAL, tracheal aspirates, and sputum       | [25] |
| Goudarzi et al.,     | 2013 |           | 221         | 214                               | 96.83 | Specimens, environmental isolates which were obtained from patients' surroundings, medical equipment and hands of staff | [26] |
Continue Table 1) Studies included on resistance of *A. baumannii* to imipenem in Iran.

| Author                     | Year | City    | Sample size | No. of Imipenem resistant isolates | %    | Isolated from                                                                 | Ref |
|----------------------------|------|---------|-------------|----------------------------------|------|-------------------------------------------------------------------------------|-----|
| Goudarzi et al.            | 2016 | NR      | 108         | NR                               | NR   | Blood, wound, urine, sputum and respiratory tract                              | [27]|
| Maspi et al.               | 2016 | 78      | 86          | 90.69                            | NR   |                                                                                  | [28]|
| Malayeri et al.            | 2016 | 51      | 60          | 85                               | Clinical samples                      | [29]|
| Khaledi et al.             | 2016 | NR      | 100         | NR                               | ICU patients                          | [30]|
| Zanganeh et al.            | 2015 | 58      | 58          | 100                              | Burn and non-burn isolates of hospitalize patients | [31]|
| Azimi et al.               | 2013 | 80      | 93          | 86.02                            | Burn wounds                          | [32]|
| Khalilzadegan et al.       | 2016 | 131     | 131         | 100                              | ICU patients                          | [33]|
| Azimi et al.               | 2012 | 6       | 7           | 85.72                            | Burn wounds, environmental isolates which were obtained from patients' surroundings, medical equipment | [34]|
| Azimi et al.               | 2016 | NR      | 50          | NR                               | Burn patients                         | [35]|
| Owlia et al.               | 2012 | 107     | 126         | 84.92                            | Burn wounds                          | [36]|
| Asadollahi et al.          | 2012 | 11      | 23          | 47.82                            | Burn wounds                          | [37]|
| Aminzadeh et al.           | 2012 | 16      | 39          | 41.02                            | CSF                                  | [38]|
| Vafaei et al.              | 2013 | 76      | 100         | 76                               | Burn wounds                          | [39]|
| Talebi-Taher et al.        | 2012 | 34      | 34          | 100                              | Endobronchial aspirates               | [40]|
| Mirnejad et al.            | 2013 | 39      | 50          | 78                               | Sputum, trachea, wounds, urine, blood | [41]|
| Asadollahi et al.          | 2011 | 49      | 100         | 49                               | Clinical isolates                    | [42]|
| Shahcheraghii et al.       | 2011 | 100     | 203         | 43.47                            | Blood, wound, urine, sputum, and respiratory tract | [43]|
| Mohammadi et al.           | 2017 | 96      | 103         | 93.20                            | Ventilated patients                  | [44]|
| Mohammadi et al.           | 2016 | 98      | 100         | 98                               | Burn wounds                          | [45]|
| Babapour et al.            | 2017 | 142     | 156         | 91.02                            | Blood, burn wound, urine, sputum, and respiratory tract, CSF | [46]|
### Table 1
Studies included on resistance of *A. baumannii* to imipenem in Iran.

| Author                   | Year  | City                      | Sample size | No. of Imipenem resistant isolates | %     | Isolated from                        | Ref   |
|--------------------------|-------|---------------------------|-------------|------------------------------------|-------|--------------------------------------|-------|
| Tarashi et al.,          | 2016  | 189                       | 187         | 98.94                              | Burn wounds | [47]                                 |
| Jazani et al.,           | 2011  | 48                        | 7           | 14.58                              | Burn wounds | [48]                                 |
| Asadollahi et al.,       | 2011  | 100                       | 39          | 39                                 | Clinical isolates | [49]                             |
| Vahdani et al.,          | 2011  | 101                       | 19          | 18.81                              | Respiratory tube, urine, wound, and blood | [50]                        |
| Mohammad taheri et al.,  | 2010  | 136                       | 126         | 92.64                              | Respiratory tube, urine, blood, wound | [51]                        |
| Akbari et al.,           | 2010  | 100                       | 53          | 53                                 | Wound, trachea, pleural fluid, blood, sputum, urine, catheter, CSF | [52]                        |
| Moradi–Tabriz et al.,    | 2010  | 166                       | 45          | 27.10                              | Blood      | [53]                                 |
| Rahbar et al.,           | 2010  | 88                        | 1           | 1.13                               | Respiratory tube, urine, blood, wound | [54]                        |
| Rahbar et al.,           | 2011  | 88                        | 4           | 4.54                               | Respiratory tract, urine, blood, wound and other clinical specimens | [55]                        |
| Goudarzit et al.,        | 2015  | 128                       | 127         | 99.21                              | ICU patients | [56]                                 |
| Soroush et al.,          | 2009  | 145                       | 73          | 50.34                              | NR         | [57]                                 |
| Aliamezani et al.,       | 2016  | 8                         | 5           | 62.50                              | Environmental surfaces and equipment | [58]                        |
| Taherikalani et al.,     | 2009  | 80                        | 42          | 52.50                              | Clinical isolates | [59]                                 |
| Owrang et al.,           | 2017  | 105                       | 103         | 98.09                              | Clinical isolates | [60]                                 |
| Peerayeh et al.,         | 2015  | 123                       | 123         | 100                                | Sputum, urine, CSF and pleural effusion | [61]                      |
| Noori et al.,            | 2014  | 84                        | 67          | 79.76                              | NR         | [62]                                 |
| Zafari et al.,           | 2017  | 536                       | 429         | 80.03                              | Hospitalized patients | [63]                       |
| Navidinia et al.,        | 2017  | 37                        | 32          | 86.48                              | Trachea, urine, wound, discharges, ascites fluid, pleural fluid, blood, synovial fluid, and catheter | [64]                       |
| Shahcheraghi et al.,     | 2009  | 95                        | 65          | 68.42                              | ICU patients | [65]                                 |
| Mirshekar et al.,        | 2017  | 72                        | 61          | 84.72                              | NR         | [66]                                 |
Studies included on resistance of *A. baumannii* to imipenem in Iran.

| Author                  | Year | City            | Sample size | No. of Imipenem resistant isolates | %     | Isolated from                               | Ref  |
|-------------------------|------|-----------------|-------------|-----------------------------------|-------|---------------------------------------------|------|
| Tavakol et al.,         | 2014 | NR              | 121         | NR                                | NR    | Clinical isolates                           | [67] |
| Momtaz et al.,          | 2017 | NR              | 121         | NR                                | NR    | Blood, phlegms, urine, CSF, pus             | [68] |
| Boroumand et al.        | 2009 | 191             | 47          | 24.60                             |       | Clinical isolates                           | [69] |
| Aghamiri et al.,        | 2015 | 176             | 169         | 96.02                             |       | Hospitalized patients                       | [70] |
| Beigverdi et al.,       | 2019 | 6281            | 4899        | 77.99                             | NR    | Burn ward                                   | [71] |
| Hosseini-Jazani et al., | 2009 | 48              | 7           | 14.58                             |       | Burn ward                                   | [72] |
| Pournajafi et al.       | 2019 | 73              | 22          |                                   |       | Burn wounds                                 | [73] |
| Feizabadi et al.,       | 2008 | 108             | 55          | 50.92                             |       | Wounds, trachea, blood, CSF, urine, other tissues | [74] |
| Farshadzadeh et al.,    | 2015 | 92              | NR          |                                   |       | Burn wounds                                 | [75] |
| Gholami et al.,         | 2020 | 60              | 60          | 100                               |       | Burn wounds                                 | [76] |
| Rahbaar et al.,         | 2007 | 65              | 18          | 27.69                             |       | Hospitalized patients                       | [77] |
| Mahdian et al.,         | 2015 | 37              | NR          | NR                                |       | Burn wounds                                 | [78] |
| Tafreshi et al.,        | 2019 | 84              | 31          | 36.90                             |       | Wound infections                            | [79] |
| Savari et al.,          | 2017 | 120             | NR          | NR                                |       | Tracheal aspiration, blood, CSF, burn wound, urine infections | [80] |
| Nasrolahei et al.,      | 2014 | Tehran/ Sari    | 100         | 67                                | 67    | ICU patients                                | [81] |
| Hojabri et al.,         | 2014 | Tehran/ Tabriz  | 71          | 60                                | 84.50 | Clinical isolates                           | [82] |
| Rahmani et al.,         | 2015 | Tehran/ Shiraz  | 140         | 129                               | 92.14 | Hospitalized patients                       | [83] |
| Peymani et al.,         | 2012 | Tabriz          | 134         | 74                                | 55.22 | Hospitalized patients                       | [84] |
### Continue Table 1) Studies included on resistance of A. baumannii to imipenem in Iran.

| Author               | Year | City                  | Sample size | No. of Imipenem resistant isolates | %    | Isolated from                                                                 | Ref |
|----------------------|------|-----------------------|-------------|-----------------------------------|------|-------------------------------------------------------------------------------|-----|
| Peymani et al.,      | 2011 | 100                   | 54          | 54                                |      | Tracheal aspirate, urine, blood, bronchial washing, wound, sputum, abscess drainage, CSF, catheter, pleural effusion, and ascites | [85]|
| Sohrabi et al.,      | 2012 | 100                   | 62          | 62                                |      | Blood, tracheal aspirates, wound, sputum, abscess drainage, wound, bronchial washing, urine | [86]|
| Ranjbar et al.,      | 2019 | Markazi, Khozestan, Kermanshah | 163         | 154                               | 94.47| Wound infections                                                                | [87]|
| Ezadia et al.,       | 2019 | Gorgan                | 71          | 44                                | 61.97| Urine, respiratory tract secretions, blood, and wound swab                     | [88]|
| Shirmohammadlou et al, | 2018 | Zanjan                | 100         | 100                               | 100  | Blood, sputum, wound swabs, chest tube secretions and urine                    | [89]|
| Khosroshahi et al.,  | 2020 | Qazvin                | 15          | 4                                 | 26.66| ICU patients                                                                   | [90]|
| Farsianii et al.,    | 2015 | Mashhad              | 36          | 32                                | 88.88| Different wards of a teaching hospital                                           | [91]|
| Salimizand et al.,   | 2016 | 30                    | NR          | NR                                |      | patients and environmental specimens                                           | [92]|
| Sarhaddi et al.,     | 2017 | 54                    | 54          | 100                               |      | Burn wounds                                                                    | [93]|
| Alaei et al.,        | 2013 | Shiraz                | 85          | 43                                | 50.58| ICU patients                                                                   | [94]|
| Alaei et al.,        | 2016 | 85                    | 79          | 92.94                             |      | Isolates from patients in a tertiary care hospital                              | [95]|
| Japoni et al.,       | 2011 | 79                    | 18          | 22.78                             |      | Blood, urine wound and sputum                                                   | [96]|
| Pourabbas et al.,    | 2016 | 61                    | NR          | NR                                |      | patients with blood infections                                                 | [97]|
| Moghadam et al.,     | 2016 | 96                    | 95          | 98.95                             |      | Clinical specimens                                                              | [98]|
| Jafari et al.,       | 2013 | 63                    | 26          | 41.27                             |      | Clinical specimens                                                              | [99]|
| Kooti et al.,        | 2015 | 200                   | 199         | 99.50                             |      | Urine, wound, blood, sputum, ETT, body fluid, nose, throat and eye              | [100]|
| Sarikhani et al.,    | 2017 | Qom                   | 108         | 97                                | 89.81| Tracheal aspirate, urine, blood, wounds and CSF                                | [101]|
| Shoja et al.,        | 2013 | Ahvaz                 | 206         | 198                               | 96.11| Clinical specimen                                                               | [102]|
Studies included on resistance of *A. baumannii* to imipenem in Iran.

| Author            | Year | City            | Sample size | No. of Imipenem resistant isolates | %     | Isolated from                                                                 | Ref  |
|-------------------|------|-----------------|-------------|-----------------------------------|-------|-------------------------------------------------------------------------------|------|
| Shoja et al.,     | 2016 |                 | 124         | 97                                | 78.22 | Clinical specimen                                                              | [103]|
| Shoja et al.,     | 2017 |                 | 40          | 36                                | 90.00 | Wound, skin biopsy, blood                                                     | [9]  |
| Moosavian et al., | 2017 |                 | 151         | 142                               | 94.04 | Clinical specimens                                                            | [104]|
| Amin et al.,      | 2019 |                 | 85          | 69                                |       | Burn wounds; tracheal secretion, blood, bronchial lavage, urine               | [105]|
| Salimizand et al.,| 2014 | Kerman          | 40          | 13                                | 32.50 | Tracheal, urine, wound, Blood, CSF                                           | [106]|
| Saffari et al.,   | 2017 |                 | 64          | NR                                | NR    | Clinical Isolates                                                             | [107]|
| Azizi et al.,     | 2015 |                 | 65          | NR                                | NR    | Blood, lung of the patient with ventilator and URI                            | [108]|
| Mohajeri et al.,  | 2014 | Kermanshah      | 104         | 83                                | 79.80 | Sputum, blood, urine clinical specimens                                       | [109]|
| Mohajeri et al.,  | 2017 |                 | 75          | 62                                | 82.66 | Blood, sputum, wounds, urine, abdominal abscesses, synovia                   | [110]|
| Mohajeri et al.,  | 2015 |                 | 42          | 38                                | 90.47 | Clinical specimens                                                            | [111]|
| Noroozi et al.,   | 2014 | Kurdistan       | 84          | 67                                | 79.76 | Sputum, blood and urine                                                       | [112]|
| Salimizande et al.,| 2014 | Kurdistan       | 54          | 28                                | 51.85 | Environmental specimens                                                       | [106]|
| Karbasizade et al.| 2012 | Isfahan         | 50          | 26                                | 52    | ICU patients                                                                  | [113]|
| Rezaei et al.,    | 2018 |                 | 153         | 153                               | 100   | Various clinical sources                                                     | [114]|
| Ghaelebi et al.,  | 2017 |                 | 40          | 40                                | 100   | ICU patients                                                                  | [115]|
| Ghajavand et al., | 2014 |                 | 43          | 40                                | 93.02 | ICU specimens                                                                 | [116]|
| Vazirzadeh et al.,| 2015 |                 | 100         | 96                                | 96.00 | Clinical samples                                                              | [117]|
| Shamsizadeh et al.,| 2017 |                 | 40          | 34                                | 85.00 | ICU, surgery wards (SW), and internal medicine wards (IM)                    | [118]|
| Shokri et al.,    | 2017 |                 | 31          | 28                                | 90.33 | Different clinical specimens                                                 | [119]|
| Safari et al.,    | 2013 | Hamedan         | 100         | 85                                | 85.00 | Trachea, blood, urine, sputum and wound samples of patients bedridden in ICU  | [120]|

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Data Extraction, Synthesis and Analysis:
We reported our data in the following way: first author, city, sample size, the status and prevalence of resistance to imipenem. Statistical analysis was performed by Comprehensive Meta-Analysis Software Version 2.0 (Biostat, Englewood, NJ). The prevalence was reported with 95% confidence intervals (CIs). Random effects models were used. To assess the potential risk of publication bias, Begg rank correlation regression methods were used (P<0.05) and were considered indicative of a statistically significant publication bias.

Findings
The result of the search strategies yielded 122 articles that reported the prevalence of imipenem-resistant *A. baumannii* in Iran (Table 1). Most of the studies were performed in central Iran (e.g. Tehran, n=71). Figure 2 shows the forest plot from the meta-analysis of antimicrobial resistance of *A. baumannii* to imipenem, resulting in prevalence of 74.2% (95% CI, 69.7–78.2). As shown in Figure 3, based on the funnel plot of meta-analysis, some evidence for the publication bias was observed. The estimated ranks of correlation coefficients of Begg were 0.742. Figure 4 also shows genes responsible for imipenem-resistant *A. baumannii* associated with their prevalence. Figure 5 also displays the prevalence of imipenem-resistant clinical isolates of in different cities of Iran.
Fig. 2) Forest plot of the meta-analysis of imipenem resistance in A. baumannii. CI: confidence interval.
Discussion

A. baumannii is a multidrug-resistant nosocomial pathogen that causes severe infections among patients especially in ICU and can hydrolyze various β-lactam antibiotics by different enzymes such as carbapenemases [131, 132]. Among bacteria, resistance to carbapenems, especially imipenem, has been reported from various countries as well as in Iran [133-135]. Recently due to resistance of A. baumannii to a wide range of antimicrobial agents, raise a concern on controlling life-threatening infections worldwide [136]. Our meta-analysis declared a pooled frequency resistance rate to imipenem (74.2%), which is lower when compared with some studies in Iran [137]. One strategy for preventing the spread of carbapenem resistance from our neighboring countries e.g. Pakistan and Iraq, which has a high prevalence of multidrug resistance A. baumannii, is implementation of typing methods [138]. In recent years carbapenem resistance in A. baumannii isolates are increasing in the world. Various factors have been mentioned to contribute to this outbreak, for example, inadequate implementation of treatment instructions and protocols, excessive use of antimicrobial agents in health care systems or the community [139, 140]. It is suggested that controlling policy including standard administration guidelines together with the suitable drug, dosage as well as the duration of treatment should meticulously be monitored in order to prevent the emergence of resistance among bacteria. Our current study has evaluated the prevalence of imipenem-resistant in A. baumannii strains in different cities of Iran. The results showed that this resistance has increased in recent decades and there is a need for more prevention and monitoring to overcome infections caused by the bacterium. Our findings also declared that imipenem-resistant A. baumannii isolates harboring bla\(_{OXA-23}\) are the most among the strains. Similar to other studies, our study indicated a sporadic distribution of MBL genes of A. baumannii in Iran. However, bla\(_{OXA-23}\) has the highest prevalence distribution gene in Iran that is responsible for carbapenem-resistant A. baumannii as well as several others.
Asian countries [9, 141]. Other reports have indicated the prevalence of MBL gene among carbapenem-resistant isolates, which were significant at the second level. Sometimes phenotypic tests in the evaluation of antibiotic resistance may be reported as false negative or low-level resistance.

To date, several mechanisms have been implicated in carbapenem-resistant isolates, including modification of PBPs, reduction of outer membrane purines, low permeability, and degradation of AmpC β-lactamase. However, the reason for this requires further studies to more accurately assess the mechanisms of resistance among bacteria, especially imipenem-resistant *A. baumannii* [9, 142]. In this study, we focused on *bla* _OXA-23_ , *bla* _OXA-24_ , *bla* _OXA-58_ , and MBL genes and the distribution of them among nosocomial isolates of *A. baumannii*. Treatment of imipenem-resistant *A. baumannii* gets complicated due to location of carbapenemase on mobile elements and high level of abuse clinically prescribing carbapenem antibiotic and this lead to the high activity of OXA genes as well as high carbapenem-resistant isolates [141].

It should be said the main gene involved in this resistance was *OXA23*, which was present in all reviewed articles, while *OXA24* and *OXA58* were reported sporadically. Statistics also showed the highest prevalence of imipenem resistance was in Zanjan and Bandar-Abbas provinces was in the second level. Kerman showed the least prevalence among cities. It seems that sufficient study or the size of non-uniform samples can be effective in statistical analysis. As the statistics confirmed the distribution of OXA genes especially *OXA23* among isolates, it seems that the gene plays a critical role in imipenem resistance of *A. baumannii*. MBL genes are also important in resistance characteristics of *A. baumannii* to imipenem but at a lower level in comparison to OXA genes. However, this issue needs more studies. The distribution and transmission of OXA and MBL genes by plasmids, integrons, or other mobile elements should be also investigated. As a result, resistance to imipenem, VIM, and NDM has been increasing in recent years, and this could be a warning sign for the overuse of antibiotics to treat *A. baumannii* infections.

**Conclusion**

All in all, it can be said *A. baumannii* is an important global pathogen with the ability to resistant to different antibiotics and this can be an alarm for health care causing high mortality and morbidity and is a problematic microorganism during recent decades. Our study demonstrated the rapid spread of β-lactamase genes of OXA and MBL in hospitals of Iran between “2006 to 2020” and declares the significant role of them in resistance to carbapenems especially imipenem. Overall, prescription antibiotics in Iran should be frequently monitored and evaluated, resulting in a limited transfer of antibiotic resistance genes among multidrug-resistant *A. baumannii*.

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