ScienceDirect

Journal of Global Antimicrobial Resistance

Volume 22, September 2020, Pages 152-160

Prevalence of β-lactamase and antibiotic-resistant *Pseudomonas aeruginosa* in the Arab region

Mahfouz Nasser [a], Samarpita Gayen [a], Arun S. Kharat [a b]

Show more

https://doi.org/10.1016/j.jgar.2020.01.011

Get rights and content

Highlights

- Scanty information available on *Pseudomonas aeruginosa* antimicrobial sensitisation from the Arab region.
- *P. aeruginosa* is a growing wound and hospital infection havoc-creating pathogen.
- Classification of *P. aeruginosa* as antibiotic resistant, multi-drug resistant, extremely drug-resistant, totally drug-resistant yet to be popularised among the Arab countries.
- Summary of various antibiotic resistance genes in *P. aeruginosa* from Arab region.
- Help researchers understand significance of antibiotic resistance studies and create awareness and curb development of antibiotic resistance in *P. aeruginosa* in Arab region.

Abstract

Background

Several studies in the Arab region have recognised the rate of nosocomial infections caused by *Pseudomonas aeruginosa* (*P. aeruginosa*), which produce β-lactamase, and identified their emergence and prevalence in the region. This article reviewed molecular studies on these β-lactamase-producing *P. aeruginosa* during 2010–2018 in several countries of the Arab region in order to analyse the trend of rising prevalence of disease causing drug-resistant *P. aeruginosa* in the Arab region.

Methods

Data from selected clinical studies during 2010–2018 on β-lactamase-producing *P. aeruginosa* in the Arab region were obtained from reliable scientific databases for analysis and evaluation.

Results

Significant changes were found in resistance of *P. aeruginosa* towards certain antibiotics of the β-lactam class. There was an increasing trend in the occurrence of resistance genes in β-lactamase-producing *P. aeruginosa*.

Conclusion

This review showed that there is an increasing prevalence of β-lactamase-producing *P. aeruginosa* in some countries in the Arab region. This is a major cause of concern as this implies that more and more instances of multidrug resistance are emerging in this area. This leads to an overall negative impact on health concerns and amounts to increasing difficulty in combating disease. It is recommended that awareness about antibiotic use and abuse be made a priority and measures to curb unchecked use of prescription antibiotics be put into place. Effective screening methods to detect cases of resistance at their onset may be developed.

Previous Next

Keywords

Molecular; β-lactamase; *Pseudomonas aeruginosa*; Arab region

1. Introduction

The spread of multidrug-resistant (MDR) pathogenic bacteria is a major cause of global concern. Being a nosocomial infection, β-lactamase-producing *Pseudomonas aeruginosa* (*P. aeruginosa*) is one that the human population is more vulnerable to. Characterised by their ability to hydrolyse β-lactams, β-lactamase-producing *P. aeruginosa* is multiresistant to a wide range of antimicrobials such as penicillin, cephalosporin, cephamycin and carbapenem. *P. aeruginosa* is an opportunistic, non-spore forming, Gram-negative bacillus measuring 0.5–0.8 μm by 1.5–3.0 μm. Almost all strains are motile by means of a single polar flagellum [1]. Although it rarely causes infection in healthy people, it may cause serious infections in immunocompromised hosts such as acquired immuno-deficiency syndrome (AIDS) patients [2]. *P. aeruginosa* is one of the important reasons for healthcare-associated infections amongst hospitalised patients. This bacterium can simply develop resistance to all conventional anti-pseudomonas antimicrobials through one-of-a-kind intrinsic and acquired resistance mechanisms. This bacterium commonly demonstrates multiple resistant isolates, which represent a serious threat to public health due to their limited therapy and leads to morbidity and mortality [3].

The rate of nosocomial infections caused by β-lactamase-producing *P. aeruginosa* in the Arab region has increased and several studies have identified their prevalence in the region. Several publications have appeared in recent years documenting the prevalence of antimicrobial resistance. New surveillance data released on 29 January 2018 by the World Health Organization (WHO) revealed widespread and, in some cases, excessive levels of antimicrobial resistance across the globe in the most common bacterial infections caused by bacteria, among them *P. aeruginosa*

(Global Antimicrobial Resistance Surveillance System (GLASS) Report Early Implementation, 2017) [30].

Growing rates of antimicrobial resistance among this bacterium are a major issue worldwide and the most common mechanisms of this resistance are the production of β-lactamases, including four Ambler classification classes A, D, B, and C. β-lactamases are encoded genes that are a part of the bacterial chromosome or genes acquired by transfer of mobile genetic elements [5]. Previous studies have indicated that among the β-lactamases recognised in *P. aeruginosa*, extended-spectrum β-lactamases (ESBLs), metallo-β-lactamases (MBLs) and Amp-C are the most clinically important. The β-lactamases classified under the Ambler classification are divided into four classes: Class A ESBLs, Class B MBLs, Class C AmpC, and Class D (OXA type). Two of them – Class A ESBLs and Class B MBLs – are reported as quickly developing enzymes in clinical isolates of *P. aeruginosa.* ESBLs are capable of hydrolysing penicillins, cephalosporins and aztreonam (with the exception of cephamycin or carbapenem). ESBLs are inhibited by β-lactamase inhibitors such as clavulanic acid [6], [7], [8], [9].

The Arab region is a geographical term that indicates an area located in the middle of the old world continents (Asia, Africa and Europe) and occupies a large area on two continents: Asia and Africa. It contains 22 countries, of which 12 are located in south-western Asia and 10 located in northern Africa. The Arab region is bordered by the Mediterranean Sea and Turkey in the north; the Indian Ocean, Arabian Sea and Great Sahara in the south; Iran, the Arabian Gulf and Gulf of Oman in the east; and the Atlantic Ocean in the west. Clinical studies from countries in this region that documented the prevalence of disease causing *P. aeruginosa* were evaluated to find out the status and peculiarities of the spread of infection and the impact on the global scenario. The present review systematically analysed previous studies that reported β-lactamase-producing *P. aeruginosa* with molecular mechanisms, available in PubMed, PMC, and Scopus databases from 2010–2018 from most countries in the Arab region (Saudi Arabia, Jordan, Iraq, Iran, Kuwait, Palestine, Lebanon, Qatar, Morocco, Egypt, Libya, Algeria, Tunisia, and Morocco). It primarily analysed the trend of rising prevalence of disease causing drug-resistant *P. aeruginosa* in the Arab region and determined the challenges and potential risk factors that may contribute to the transmission of β-lactamase genes in this region. This knowledge could lead to the improvement of strategies to overcome or reduce their prevalence in the near future.

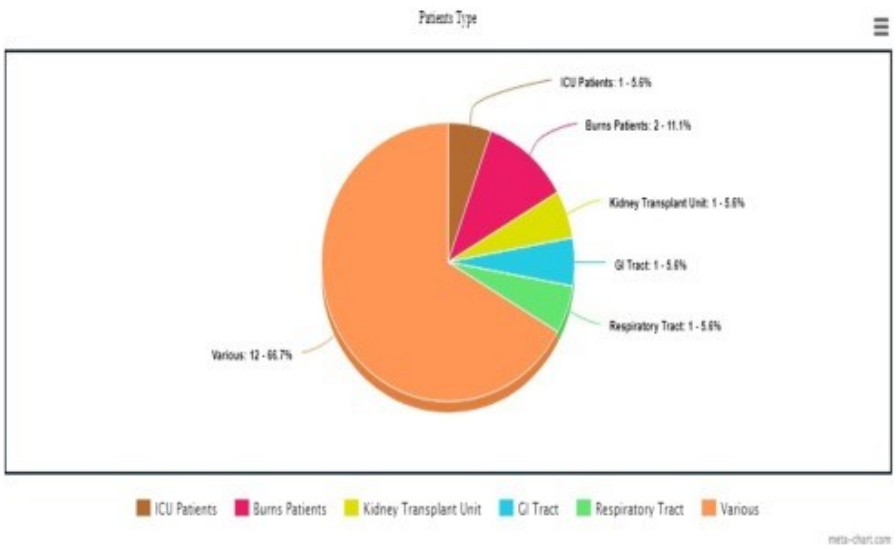
2. Methods

The data of percentages of resistant *P. aeruginosa* for a total of 35 antibiotics tested in 18 studies over the period 2011–2018 from different countries in the Arab region were used to calculate the mean percentage of the period. Statistical analysis paired *t*-test was performed for each antibiotic and/or combination of antibiotics as described in the research articles. The types of patients from where the samples were collected are shown in Fig. 1. The types of studies that were the basis of this review are shown in Fig. 2. The following hypotheses were tested for:

- **Null hypothesis:** There has been **no change** in resistance over the years for the particular

antibiotic and/or combination of antibiotic.

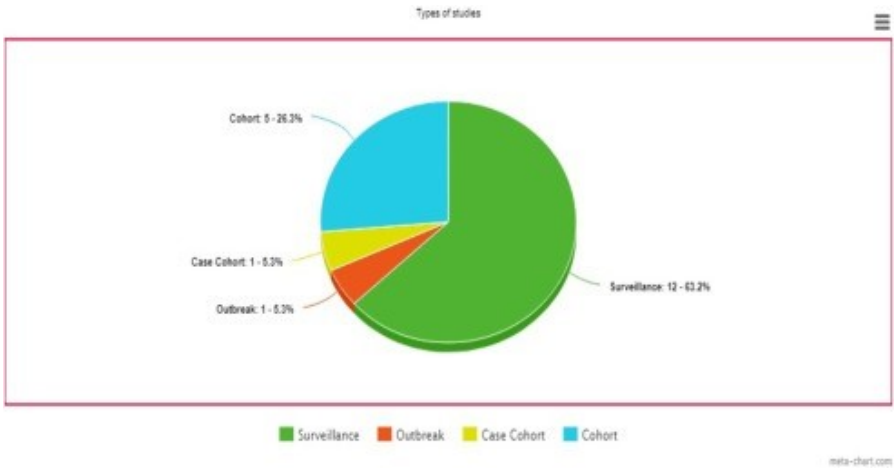
- **Alternate hypothesis:** There has been a **change** in resistance over the years for the particular antibiotic and/or combination of antibiotic.



Download : Download high-res image (126KB)

Download : Download full-size image

Fig. 1. The distribution of the types of patients from whom *Pseudomonas aeruginosa* were isolated in the various selected studies in the Arab region 2011–2018.



Download : Download high-res image (98KB)

Download : Download full-size image

Fig. 2. The distribution of the types of studies selected from the Arab region published during 2011–2018 for understanding the molecular prevalence of β-lactamase-producing *Pseudomonas aeruginosa* in the Arab region.

The percentages of β-lactamases that were found were tabulated and the trend that was seen was averaged over 2011–2018.

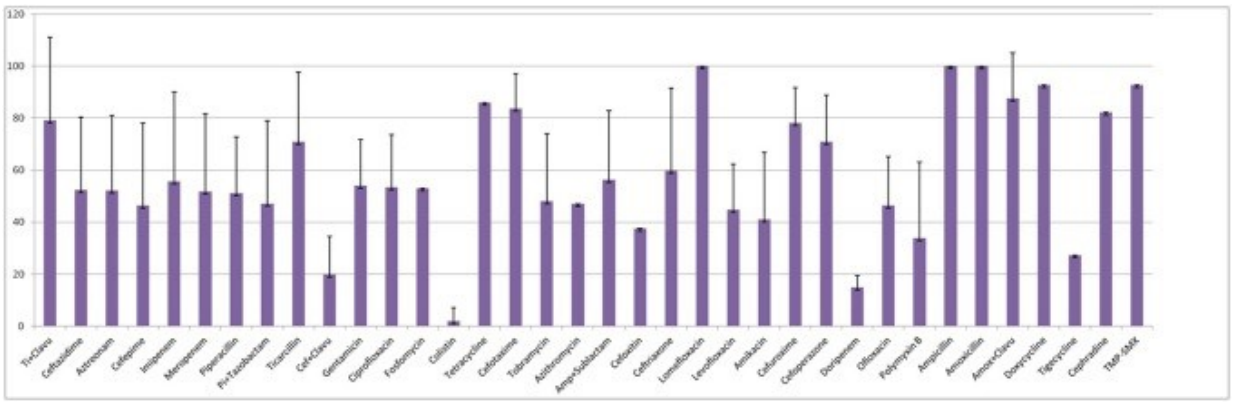
3. Results

3.1. Change in resistance levels to antibiotics

The antibiotics in which a significant change in resistance by *P. aeruginosa* during 2011–2018 are ceftazidime, aztreonam, cefepime, imipenem, piperacillin + tazobactam, ticarcillin, ciprofloxacin, and cefotaxime. Thus, it can be seen that the β-lactam class of antibiotics and fluoroquinolones are the classes against which the resistance profile of *P. aeruginosa* is seen to have changed over the studied period.

3.2. Percentage distribution of resistance to antibiotics averaged over 2011–2018

Fig. 3 represents the percentage distribution of resistance to antibiotics averaged over the period 2011–2018. Tables 1a and 1b show the percentage distribution of resistance to antibiotics used in the studies during 2011–2018.



Download : Download high-res image (258KB)

Download : Download full-size image

Fig. 3. Percentage distribution of resistance to antibiotics averaged over 2011–2018.

Graph showing the distribution of average percentage of *Pseudomonas aeruginosa* showing resistance to mentioned antibiotics, as shown by selected studies from the Arab region published during 2011–2018.

Abbreviations: Ti, Ticarcillin; Clavu, Clavulanic acid; Pi, Piperacillin; Cef, Ceftazidim; Amp: Ampicillin; Amox, Amoxicillin; TMP-SMX, Sulphamethoxazole + Trimethoprim.

Table 1a. Percentage distribution of resistance during 2011–2018 (Part 1).

Author	Year	Ti + Clavul	Ceftazidime	Aztreonam	Cefepime	Imipenem	Meropenem	Piperacillin	Pi + Tazol
Hammami	2011	100	75	100	100	95.8	70.8		
Al-Agamy	2012	25	19.5	16.5	20.5	16		32.5	22.5
Tawfik	2012								
Touati	2013	100	100						100
Aghamiri	2014		47			47		54	
Al-Bayssari	2014								
Al-Charrakh	2014		37.5		25	37.5	25		37.5
Sjolander	2014	100	50	100	50	100			100
Zafer	2014		60.6	45.1		39.34			25.4
Maroui	2015	54.5	3	39.4	21.2			27.3	15.2
Mathlouthi	2015	95	66	37	70	87.5	79	62	37
Zafer	2015		51.51		30.3	93.93			36.36
Abdalhamid	2016		92.3		92.3	100	92.3		
Al-Agamy	2016		67.64	35.29		17.64	11.76		
Abaza	2017		60	73.3	70	73.3	66.7	80	70
El-Domany	2017		50			12.2			
Al Dawodeyah	2018		18	42.7	18	19.7	21.3		37.8
El-Shouny	2018		82.2			71.4	71.4		75
Ismail	2018		9.09	31.81	13.63	22.72	27.27		9.09

Abbreviations: Ti, ticarcillin; Pi, piperacillin; Cef, Ceftazidime; Clavu, clavulanic acid.

Table 1b. Percentage distribution of resistance during 2011–2018 (Part 2).

Author	Year	Azithromycin	Amp+Sulbactam	Cefoxitin	Ceftriaxone	Lomefloxacin	Levofloxacin	Ar

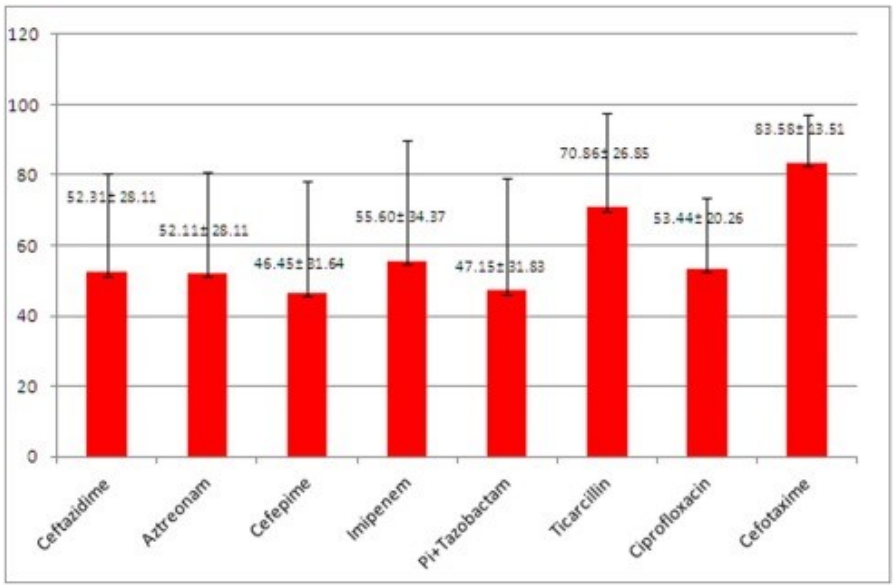
Author	Year	Azithromycin	Amp+Sulbactam	Cefoxitin	Ceftriaxone	Lomefloxacin	Levofloxacin	Ar
Hammami	2011							
Al-Agamy	2012							
Tawfik	2012							
Touati	2013							
Aghamiri	2014	47						
Al-Bayssari	2014							
Al-Charrakh	2014		37.5	37.5	37.5			
Sjolander	2014					100	50	50
Zafer	2014							
Maroui	2015							12
Mathlouthi	2015							79
Zafer	2015							30
Abdalhamid	2016							53
Al-Agamy	2016							8.8
Abaza	2017							86
El-Domany	2017							25
Al Dawodeyah	2018							50
El-Shouny	2018		75		82.2		25	35
Ismail	2018						59.09	18

Abbreviations: Amp, ampicillin; Amox, amoxycillin; Clavu, clavulanic acid.

3.3. Percentage distribution of resistance to noteworthy antibiotics during 2011–2018

Fig. 4 represents the percentage distribution of resistance to noteworthy antibiotics averaged during 2011–2018. Table 2 shows the percentage distribution of resistance in *P. aeruginosa* to noteworthy antibiotics averaged over 2011–2018 along with their standard deviation, namely:

ceftazidime (52.31%), aztreonam (52.11%), cefepime (46.45%), imipenem (55.56%), piperacillin + tazobactam (47.15%), ticarcillin (70.86%), ciprofloxacin (53.44%), and cefotaxime (83.58%).



Download : Download high-res image (167KB)

Download : Download full-size image

Fig. 4. Percentage distribution of resistance to noteworthy antibiotics 2011–2018.

Graph showing the distribution of percentages of resistant *Pseudomonas aeruginosa*, which have been seen to show significant changes in antibiotic resistance (2011–2018) towards noteworthy antibiotics as calculated from the data from selected studies from the Arab region during 2011–2018.

Abbreviations: Pi, Piperacillin.

Table 2. Summary of the frequency of β-lactamase-producing *Pseudomonas aeruginosa* in the Arab region (percentage of gene types of β-lactamase).

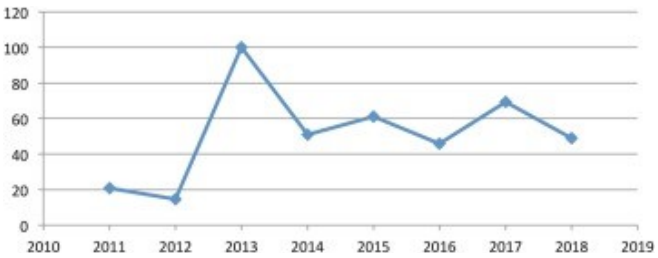
Author	Country	Year	Isolates	SHV	TEM	CTX-M	VEB	GES	OXA-2	OXA-10	OXA-50	NDM	VIM-2	I
Al-Agamy [12]	Saudi Arabia	2012	200	0	0	0	20	5	0	0	0	0	16	0
Tawfik [15]	Saudi Arabia	2012	156	0	0	0	106	31	0	87	0	0	0	0
Touati [16]	Algeria	2013	17	0	0	0	0	0	0	0	0	0	14	0
Al-Bayssari	Lebanon	2014	35	0	0	0	0	0	0	0	0	0	16	2

Author	Country	Year	Isolates	SHV	TEM	CTX-M	VEB	GES	OXA-2	OXA-10	OXA-50	NDM	VIM-2	I
[18]														
Al-Charrakh [24]	Egypt	2014	122	0	0	0	12	0	0	51	0	5	71	3
Zafer [19]	Egypt	2015	48	0	0	0	0	0	0	0	0	2	28	1
Maroui [21]	Libya	2015	24	0	0	0	0	0	0	0	0	0	19	0
Mathlouthi [7]	Morocco	2015	123	0	0	0	0	0	0	0	0	0	2	0
Zafer [20]	Saudi Arabia	2016	13	0	0	0	0	0	0	0	0	4	1	0
Abdalhamid [2]	Saudi Arabia	2016	34	0	0	0	16	0	0	14	0	0	0	0
Al-Agamy [22]	Iraq	2016	75	0	0	0	0	0	0	0	0	0	0	6
Abaza [25]	Egypt	2017	114	0	0	0	0	0	0	0	0	4	8	5
El-Domany [11]	Egypt	2017	30	0	0	0	0	0	0	0	0	0	0	1
Al Dawodeyah [6]		2018	50	0	0	0	0	0	17	0	12	0	0	1
El-Shouni [4]	Jordan	2018	32	4	6	22	6	5	0	0	0	0	3	0
Ismail SJ [26]	Iraq	2018	100	0	0	0	0	0	0	0	0	6	0	0

Abbreviations: SHV, Sulfhydryl reagent variable resistance gene; TEM, Temoniera resistance gene; CTX-M, active against Cefotaxime beta lactamase; VEB, Vietnamese extended spectrum beta lactamase; GES, Guiana extended spectrum beta lactamase; OXA, oxacillinases extended spectrum beta lactamase; NDM, New Delhi metallo beta lactamase; VIM, verona integron encoded metabollo beta lactamase; IMP, active on imipenem carpapenem; SPM, Sao Paulo metallo beta lactamase; PCR, polymerase chain reaction.

3.4. Average percentage of β-lactamase gene types during 2011–2018

Fig. 5 shows the average percentage of β-lactamase gene types during 2011–2018.



Download : Download high-res image (68KB)

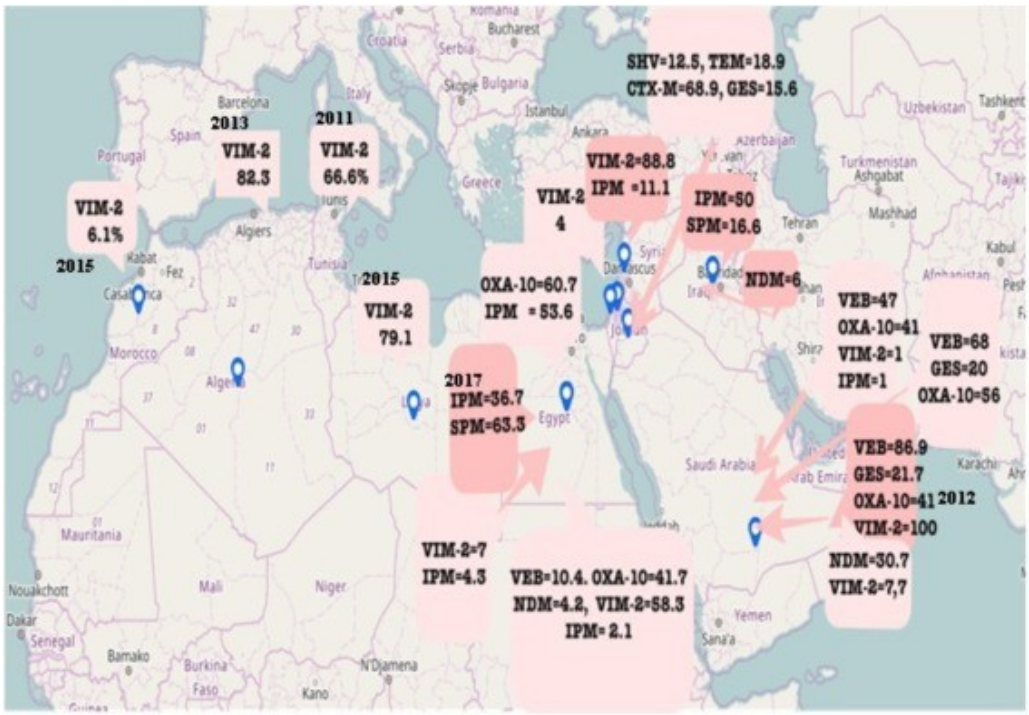
Download : Download full-size image

Fig. 5. Average percentage of β-lactamase gene types during 2011–2018.

Data collected from selected studies from the Arab region published during 2011–2018

3.5. Mapping of the frequency of β-lactamase-producing *P. aeruginosa* in the Arab region (percentage of gene types of β-lactamase)

Fig. 6 shows the distribution of percentage of gene types of β-lactamase-producing *P. aeruginosa* in the Arab region according to the studies.



Download : Download high-res image (545KB)

Download : Download full-size image

Fig. 6. Map of the frequency of β-lactamase-producing *Pseudomonas aeruginosa* in the Arab region (percentage of gene types of β-lactamase) as reported in selected studies from the Arab region published during 2011–2018.

4. Discussion

This study found significant changes in resistance of *P. aeruginosa* to a handful of antibiotics among several antibiotics used in the studies carried out in various parts of the Arab region during 2011–2018. Hence, the Null Hypothesis is rejected and the Alternate Hypothesis is accepted i.e there is change in resistance over the years for particular antibiotic and/or combination of antibiotic and discussed here. Three of eight significant drugs belong to the cephalosporin class, which work by disrupting synthesis of the bacterial cell wall by inhibiting the formation of the peptidoglycan layer. Although their working is similar to the penicillin class of drugs, they are widely known to be less susceptible to β-lactamases. Two of these eight significant drugs belong to the extended-spectrum class penicillin and work by the mechanism of competitive inhibition. One of the eight is a carbapenem, another one is a fluoroquinolone and another one is a monobactam. Compared with cephalosporins and penicillins, carbapenems have a broader spectrum of activity, although they also work by inhibiting bacterial cell wall synthesis. Fluoroquinolones work by inhibiting cell division by affecting DNA gyrase, which is required for bacterial DNA separation during the cell division process. Monobactam is similar to penicillin and works by inhibiting cell wall synthesis by blocking peptidoglycan cross linking. With the exception of fluoroquinolones, all other types of the

mentioned classes of antibiotics exhibit the β-lactam structure against which the β-lactamase-producing *P. aeruginosa* have emerging resistance.

This review focused on studies conducted in countries in the Arab region to determine whether the emergence of disease resistance and spread is on the rise in a generally impoverished region with lack of access to standard healthcare, exposure to war or warlike scenarios, hot and dusty climatic factors, unsanitary living conditions, and population factors. Extended-spectrum β-lactamases in nosocomial isolates of *P. aeruginosa* have been identified as early as 2001 in Kuwait [34]. Blagui et al. reported the first OXA-18-type ESBL in *P. aeruginosa* in 2007 in Tunisia in a nosocomial outbreak [35]. In a study published in 2011, Hammami et al. studied 24 non-replicate imipenem-resistant *P. aeruginosa* in a kidney transplantation unit in Tunisia, so as to establish an epidemiological relationship among them and identify the enzymatic mechanism involved in imipenem resistance [10]. An outbreak of VIM-2-producing *P. aeruginosa* in a kidney transplantation unit was described in their study. Disease outbreak is a result of disease facilitating factors such as no effective treatment and/or containment options available [11]. A 4-year study (2001–2005) showed a gradual increase in resistance to various anti-pseudomonal drugs by *P. aeruginosa* and suggested selection of resistant mutants [36]. The ESBLs and MBLs among *P. aeruginosa* isolates in Saudi Arabia were investigated and revealed that 39 (19.5%) *P. aeruginosa* isolates were ceftazidime-resistant; there was also considerable resistance to other antibiotics except colistin [12].

An important point to note in the dominance of acquired ceftazidime-inactivating β-lactamases is that it was in contrast to the situation in Europe and the USA, where most ceftazidime resistance in *P. aeruginosa* is attributable to AmpC and efflux [13], [14]. The *blaVEB*, and *blaGES* genes were found in 20 (86.95%) and five (21.74%) of 23 ESBL-positive isolates, respectively, whilst *blaVIM* was detected in all 16 MBL-producers. *blaOXA*-10-like is often accompanied *blaVEB*, *blaVIM* or *blaGES*. The frequent combination of *blaOXA*-10-like genes with *blaVIM* and *blaVEB* was noteworthy and could be because all these genes are often carried as cassettes within class 1 integrons, which facilitates their association [13]. The rate of prevalence of class A, class B and class D β-lactamases among clinical isolates of extended-spectrum cephalosporin (ESC)-non-susceptible *P. aeruginosa* from Riyadh, Saudi Arabia, was determined in 2012 [15]. The prevalence of ESBL was 69.44% and MBL was 42.85% in ESC-non-susceptible *P. aeruginosa*. The prevalence of structural genes for VEB-1 was 68%, OXA-10 56% and GES 20% as ESBLs in *P. aeruginosa*. In MBL-producing isolates, the VIM gene was detected in 15 (100%) isolates. The *blaOXA*-10 like gene was concomitant with *blaVEB*, *blaGES* and/or *blaVIM*. The *blaVEB*-1 and *blaOXA*-10 genes were the predominant ESBL genes and $bla_{VIM}$was the dominant MBL gene in ESC-non-sensitive *P. aeruginosa* isolates in Saudi Arabia [15].

In a study from Algeria in 2013, Touati et al. reported the first molecular characterisation of VIM-2-producing *P. aeruginosa* clinical isolates that harboured a novel class I integron, which also contained two gene cassettes encoding resistance to aminoglycosides (*aadB* and *aacA4*) [16]. In 2015, in their effort to identify and characterise carbapenem-resistant Gram-negative bacilli in hospital patients, Bouraffa et al. revealed OprD mutations in two *P. aeruginosa* isolates among other

isolated carbapenem-resistant Gram-negative bacilli showing reduced susceptibility to carbapenems [37]. Adding to this, Zowawi et al. first reported the novel ESBL PME-1-producing *P. aeruginosa* in Qatar in 2015, suggesting that the 'high-risk clone' contributes to the global spread of MDR mechanisms [38]. In Palestine in 2014, Sjölander et al. showed VIM-producing *P. aeruginosa* whose resistance properties could be explained by carbapenemases and other possible mutational resistance mechanisms, which influences the loss of the OprD outer membrane porin channel [17]. The OprD product along with de-repressed chromosomal AmpC is a major pathway of imipenem and/or increased efflux pump excretion of carbapenems. It was the first report of *blaVIM*-producing *P. aeruginosa* from Palestine [17]. In 2014, Al Bayssari et al. reported the emergence of *blaVIM-2* and *blaIMP-15* carbapenemases in a series of clinical isolates of carbapenem-resistant *P. aeruginosa* in Lebanon, which re-emphasised a rapid dissemination of the *blaVIM-2* carbapenemase-encoding gene in the Mediterranean basin [18]. In 2014, Zafer et al. reported the first occurrence of New Delhi MBL-producing *P. aeruginosa* in Egypt and the presence of more than one *blaMBL* gene in carbapenem-resistant *P. aeruginosa* [39]. In further studies in Egypt, Zafer et al. reported *bla*VIM-2, *bla*IMP-1, *bla*NDM, and *bla*OXA-10 in *P. aeruginosa* while screening for ESBLs and MBLs in 122 *P. aeruginosa* isolates. The prevalence of *bla*VIM-2 was found to be 58.3%, *bla*OXA-10 was 41.7%, *bla*VEB-1 was 10.4%, *bla*NDM was 4.2%, and *bla*IMP-1-like gene was 2.1% [19]. In a subsequent study in 2015, Zafer et al. examined the genetic relatedness between MBL-producing carbapenem-resistant clinical isolates of *P. aeruginosa* collected from Egypt and found that the high prevalence of *blaVIM-2* producers was not due to the spread of a single clone [20]. They also reported a unique ST233 clone producing VIM-2 documented in *P. aeruginosa* strains isolated from Cairo university hospitals [20]. The study by Mathlouthi et al. in 2015 in Libya first reported describing imipenem-resistant *P. aeruginosa* as the first case of co-occurrence of *blaVIM*-2 with loss of OprD porin in identical isolates of *P. aeruginosa*, which demonstrated that such mutations in OprD can be used as a tool to study clonal propagation in *P. aeruginosa* isolates [7].

In 2015, Maroui et al. reported the first isolation of *blaVIM* genes in clinical isolates of *P. aeruginosa* in Morocco [21]. This work was performed to establish the resistance profile and detect carbapenemase-producing in 123 *P. aeruginosa* isolates. Carbapenem resistance was observed in 33 *P. aeruginosa* isolates, where 33.3% of them were found to be MDR, and 12% of isolates were found to be susceptible to all tested antibiotics. Among the carbapenem-resistant strains, two (6.1%) were shown to be positive for both carbapenemases and MBLs [19].

In a 2016 study to detect the prevalence of gastrointestinal tract colonisation of carbapenem-resistant *P. aeruginosa* in patients admitted to intensive care units in Saudi Arabia, Abdalhamid et al. detected *blaNDM* type and *blaVIM* type in isolates and AmpC overexpression [2]. This discovery of *blaNDM* and *blaVIM* in colonising carbapenem-resistant *P. aeruginosa* strains is a major cause for concern for infection control. Al Agamy et al. clearly demonstrated a high level of resistance to carbapenems in the isolates in their study in Riyadh, Saudi Arabia, in 2016 [12]. Diverse resistance mechanisms were observed in these isolates, which revealed the various ways in which drug resistance is acquired by *P. aeruginosa.* Twelve of the 34 carbapenem-resistant isolates (35.3%)

expressed MBLs, either *blaVIM* or *blaIMP*. Interestingly, it was found that while 11 of 39 carbapenem-resistant *P. aeruginosa* isolates carried carbapenemase genes (*blaVIM* and *blaGES-5*), the rest (i.e. 72%) had no genes that explained the observed resistance [12]. It was seen that 13 of the 34 carbapenem-resistant strains (38%) harboured *blaVEB*-1 alone or with *blaOXA-10* or harboured *blaGES-6* alone but did not reveal any known resistance mechanism that could explain their resistance, as these are not carbapenemase-encoding genes. These results are also consistent with a negative outcome of MBL phenotypic test and, hence, go on to suggest other mechanisms of resistance that were not tested for in this study. A high level of resistance to carbapenems in the isolates was clearly demonstrated. The diversity of the resistance mechanisms seen in the isolates revealed the different ways by which *P. aeruginosa* could acquire drug resistance. Interestingly, it was found that 11 of 39 carbapenem-resistant *P. aeruginosa* isolates carried carbapenemase genes (*blaVIM* and *blaGES-5*), while the rest (28/39, 72%) had no genes to explain the resistance that was seen. These strains also produced negative results in the phenotypic test for MBL, thereby suggesting other mechanisms responsible for their carbapenem resistance [22]. The urgent need for more investigative studies on the unknown mechanisms of resistance in *P. aeruginosa* is emphasised by the finding that 38% of these isolates revealed no resistance mechanism, which could explain carbapenem resistance [23].

In 2016, Al Charrakh et al. concluded in their study on *P. aeruginosa* isolates, from Baghdad, producing MBLs by using phenotypic and molecular methods that antibiotic resistance was increased against all third-generation cephalosporins [24]. Although carbapenem was the drug of choice for the *P. aeruginosa* isolates producing ESBL, the emergence of MBLs producing bacteria posed a major threat to the treatment of bacterial infection in Baghdad hospitals. In their study, they found that *blaIMP* was the predominant gene amongst the MBL genes of *P. aeruginosa.* The *blaIMP* gene was seen to be encoded by chromosomal DNA, whereas the *blaSPM-1* was encoded by plasmid and seemingly this mechanism of resistance can cause nosocomial outbreaks [24].

In 2017, in a study on 114 *P. aeruginosa* isolates from Egypt, El-Domany et al. found through antimicrobial susceptibility testing that 50 isolates (43.8%) exhibited an MDR phenotype, and 14 of them (12.2%) were imipenem (IPM)-resistant [11]. Of these 14 isolates, 13 (11.4%) exhibited MBL phenotype. PCR was used to identify the MBLs encoding genes, *blaVIM* and *blaIMP*. The results revealed that four isolates harboured only the *blaVIM* gene, one isolate harboured only the *blaIMP* gene, and four isolates harboured both genes together. This was the first report of *blaIMP* carbapenemase-encoding gene in Africa and also the first report of the emergence of *P. aeruginosa* coproducing *blaVIM* and *blaIMP* genes in Egypt [11]. Abaza et al. studied the occurrence of MBL-producing *P. aeruginosa* in Alexandria, Egypt in 2017 [25]. All of the 30 (100%) selected *P. aeruginosa* isolates that were tested for MBL production were found to be positive; where 19 (63.3%) revealed *bla* gene and 11 (36.7%) had *bla* gene. It was seen that 26 (86.7%) of the isolates of the MBL-producing *P. aeruginosa* were found to be highly susceptible to polymyxin B and 26 (86.7%) were highly resistant to amikacin [25]. In 2018,

El-Shouny et al. identified 50 non-duplicated *P. aeruginosa* isolates from Egypt and found a high prevalence of MDR and pan-drug resistance (PDR) in 38 (76%) isolates obtained from 10 clusters, whereas 21 (42%) were identified as ESBL-producing MDR or PDR *P. aeruginosa* isolates. The *blaOXA-2* gene (60.7%) was found to be the most prevalent ESBL-encoding gene, followed by *blaIMP-7* (53.6%) and *blaOXA-50* (42.8%) [4].

In a study in Jordan in 2018, Al Dawodeyah et al. recovered 61 of 284 (21.5%) *P. aeruginosa* isolates and it was seen that 52.5% of *P. aeruginosa* isolates were MDR and all of the isolates were susceptible to colistin, while they had lower susceptibility to other tested antibiotics [6]. Positive results for *blaCTX-M* were seen in 68.9%, *blaVEB* in 18.9%, *blaTEM* in 18.9%, *bla*GES in 15.6%, and *blaSHV* in 12.5% of isolates. They found no specific link between the resistance to antibiotics, occurrence of virulence genes and their genotypes amongst these MDR isolates. They highlighted the fact that the presence of ESBL-producing bacteria can drive caregivers into increased use of carbapenems as a treatment option, which in return would increase the selection of carbapenem-producing infection causing organisms through evolution and lead to more resistant organisms [6].

In 2018, Ismail et al. reported the emergence of *bla*NDM-variant carrying *P. aeruginosa* for the first time in Iraq. They showed that this variant was exhibiting resistance to meropenem and imipenem [26]. This review showed that there has been a change in the resistance pattern of *P. aeruginosa* towards several β-lactam class antibiotics over the years. The indiscriminate use of these antibiotics drives selection pressure to allow for more and more resistant strains to develop, and a word of caution in their use is required. Since the production of β-lactamases is often plasmid-mediated, the resultant carbapenem resistance has a potential for rapid dissemination [40]. The antibiotics found to be significant in this review are prescription medicines and should only be used as prescribed. It may be that there is a lack of awareness about proper dosage and not sticking to the schedule; overuse or use according to personal convenience may be some of the issues that impact the emergence of resistance, while hygiene conditions and proper patient handling and care may have an impact on the spread of the resistance genes into the environment. Moreover, initial screening methods to detect resistant strains need to be developed to identify and isolate cases, so as to curtail spread of infection and fuel further resistance.

In developed nations, the emergence of previously undetected resistant strains and genes in disease outbreaks have been linked to endemic variants [27] in developing areas such as the Arab nation, as reported by Nordmann et al. in 2014. This is reportedly due to tourism and unscreened travel into and out of countries [28]. This shows the need for screening at the entry point, so that this spread and integration may be curtailed at its onset. Moreover, reports by Al Bayssari et al. in 2014 of horizontal spread of the β-lactamase genes have been reported from countries similar to those in the Arab region (such as India, Japan and China) where previously non-resistance strains developed resistance due to recombination between bacteria [18]. High ESBL resistance rates highlight the need for surveillance systems for monitoring antimicrobial resistance at local and national levels in hospital settings [41]. The 2016 report by the European Centre for Disease Prevention and Control

showed that in Europe, 33.9% of *P. aeruginosa* were resistant to at least one of the antimicrobial combinations (piperacillin ± tazobactam, fluoroquinolones, ceftazidime, aminoglycosides, and carbapenems) that were under surveillance [29], [30]. Thus, this report showed great variation in antimicrobials in inter-country percentages of resistance, where there was a higher percentage of resistance in southern and eastern Europe compared with northern Europe. Fallah et al. and Shahcheraghi et al. also reported increasing resistant strains of *P. aeruginosa* in the Arab region [31], [32], [33].

Studies in the Arab region affirm the need for more clinical studies to be undertaken to define the actual status of disease prevalence causing *P. aeruginosa*, so that measures may be taken for their containment, treatment using effective prescribed medications, and to prevent antibiotic abuse. Further studies are also required in the Arab region to investigate the unknown mechanisms of resistance and to devise a treatment plan that can optimise infection control and prevent emergence of modified drug-resistant strains.

Funding

No funding.

Competing interests

Authors have no conflict of interest to declare.

Ethical approval

Not required.

Acknowledgements

The authors would like to express sincere gratitude towards an anonymous reviewer, whose input helped to improve the presentation and message quality of this article. Laboratory members for their critical discussions are also acknowledged.

Recommended articles

References

[1] S. Baron (Ed.), Medical Microbiology (4th edition), University of Texas Medical Branch at Galveston, Galveston (TX) (1996)

Google Scholar ↗

[2] B. Abdalhamid, N. Elhadi, N. Alabdulqader, K. Alsamman, R. Aljindan

Rates of gastrointestinal tract colonization of carbapenem-resistant Enterobacteriaceae and *Pseudomonas aeruginosa* in hospitals in Saudi Arabia

New Microbes New Infect, 10 (2016), pp. 77-83, 10.1016/j.nmni.2016.01.014 ↗

PMID: 26933499

View PDF View article View in Scopus ↗ Google Scholar ↗

[3] E. Paramythiotou, C. Routsi

Association between infections caused by multidrug-resistant Gram-negative bacteria and mortality in critically ill patients

World J Crit Care Med, 5 (2) (2016), pp. 111-120, 10.5492/wjccm.v5.i2.111 ↗

PMID: 27152254

Google Scholar ↗

[4] W.A. El-Shouny, S.S. Ali, J. Sun, S.M. Samy, A. Ali

Drug resistance profile and molecular characterization of extended spectrum β-lactamase (ESβL)-producing *Pseudomonas aeruginosa* isolated from burn wound infections. Essential oils and their potential for utilization

Microb Pathog, 116 (2018), pp. 301-312, 10.1016/j.micpath.2018.02.005 ↗

PMID: 29407236

View PDF View article View in Scopus ↗ Google Scholar ↗

[5] T.R. Walsh, M.A. Toleman, L. Poirel, P. Nordmann

Metallo-β-lactamases: the quiet before the storm?

Clin Microbiol Rev, 18 (2) (2005), pp. 306-325, 10.1128/CMR.18.2.306-325.2005 ↗

PMID: 15831827

View in Scopus ↗ Google Scholar ↗

[6] H.Y. Al Dawodeyah, N. Obeidat, L.F. Abu-Qatouseh, A.A. Shehabi

Antimicrobial resistance and putative virulence genes of *Pseudomonas aeruginosa* isolates from patients with respiratory tract infection

Germs, 8 (1) (2018), pp. 31-40, 10.18683/germs.2018.1130 ↗

PMID: 29564246

View in Scopus ↗ Google Scholar ↗

[7] N. Mathlouthi, Z. Areig, C. Al-Bayssari, S. Bakour, A. Ali El Salabi, S. Ben Gwierif, *et al.*

Emergence of carbapenem-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii* clinical isolates collected from some Libyan hospitals

Microb Drug Resist, 21 (3) (2015), pp. 335-341, 10.1089/mdr.2014.0235 ↗

PMID: 25587875

View in Scopus ↗ Google Scholar ↗

[8] K. Bush, G.A. Jacoby, A.A. Medeiros
A functional classification scheme for β-lactamases and its correlation with molecular structure
Antimicrob Agents Chemother, 39 (6) (1995), pp. 1211-1233
PMID: 7574506
View in Scopus ↗ Google Scholar ↗

[9] D.L. Paterson, R.A. Bonomo
Extended-spectrum β-lactamases a clinical update
Clin Microbiol Rev, 18 (4) (2005), pp. 657-686, 10.1128/CMR.18.4.657-686.2005 ↗
PMID: 16223952
View in Scopus ↗ Google Scholar ↗

[10] S. Hammami, I. Boutiba-Ben Boubaker, R. Ghozzi, M. Saidani, S. Amine, S. Ben Redjeb
Nosocomial outbreak of imipenem-resistant *Pseudomonas aeruginosa* producing VIM-2 metallo-β-lactamase in a kidney transplantation unit
Diagnost Pathol, 6 (1) (2011), p. 106, 10.1186/1746-1596-6-106 ↗
PMID: 22035284
View in Scopus ↗ Google Scholar ↗

[11] R.A. El-Domany, M. Emara, M.A. El-Magd, W.H. Moustafa, N.M. Abdeltwab
Emergence of Imipenem-Resistant *Pseudomonas aeruginosa* clinical isolates from Egypt Coharboring *VIM* and *IMP* Carbapenemases
Microb Drug Resist, 23 (2) (2017), pp. 682-686, 10.1089/mdr.2016.0234 ↗
PMID: 28085553
View in Scopus ↗ Google Scholar ↗

[12] M.H. Al-Agamy, A.M. Shibl, A.F. Tawfik, N.A. Elkhizzi, D.M. Livermore
Extended-spectrum and metallo-β-lactamase among ceftazidime-resistant *Pseudomonas aeruginosa* in Riyadh, Saudi Arabia
J Chemother, 24 (2) (2012), pp. 97-100, 10.1179/1120009X12Z.00000000015 ↗
PMID: 22546765
View in Scopus ↗ Google Scholar ↗

[13] M. Gomila, M. Del Carmen Gallegos, V. Fernndez-Baca, A. Pareja, M. Pascual, P. Daz-Antoln, *et al.*
Genetic diversity of clinical *Pseudomonas aeruginosa* isolates in a public hospital in Spain
BMC Microbiol, 13 (1) (2013), p. 138, 10.1186/1471-2180-13-138 ↗
PMID: 23773707
View in Scopus ↗ Google Scholar ↗

[14] V.I. Siarkou, D. Vitti, E. Protonotariou, A. Ikonomidis, D. Sofianou
Molecular epidemiology of outbreak-related *pseudomonas aeruginosa* strains carrying the novel variant blaVIM-17 metallo-β-lactamase gene
Antimicrob Agents Chemother, 53 (4) (2009), pp. 1325-1330, 10.1128/AAC.01230-08
PMID: 19164147
View in Scopus Google Scholar

[15] A.F. Tawfik, A.M. Shibl, M.A. Aljohi, M.A. Altammami, M.H. Al-Agamy
Distribution of Ambler class A, B and D β-lactamases among *Pseudomonas aeruginosa* isolates
Burns, 38 (6) (2012), pp. 855-860, 10.1016/j.burns.2012.01.005
PMID: 22348803
View PDF View article View in Scopus Google Scholar

[16] M. Touati, S.M. Diene, M. Dekhil, A. Djahoudi, A. Racherache, J.M. Rolain
Dissemination of a class 1 integron carrying VIM-2 carbapenemase in *Pseudomonas aeruginosa* clinical isolates from a hospital intensive care unit in Annaba, Algeria
Antimicrob Agents Chemother, 57 (5) (2013), pp. 2426-2427, 10.1128/AAC.00032-13
PMID: 23459493
View in Scopus Google Scholar

[17] I. Sjölander, F. Hansen, A. Elmanama, R. Khayyat, A. Abu-Zant, A. Hussein, *et al.*
Detection of NDM-2-producing acinetobacter baumannii and VIM-producing *Pseudomonas aeruginosa* in Palestine
J Glob Antimicrob Res, 2 (2) (2014), pp. 93-97, 10.1016/j.jgar.2013.11.002
PMID: 27873597
View PDF View article View in Scopus Google Scholar

[18] C. Al-Bayssari, S.M. Diene, L. Loucif, S.K. Gupta, F. Dabboussi, H. Mallat, *et al.*
Emergence of VIM-2 and IMP-15 carbapenemases and inactivation of oprD gene in carbapenem-resistant *Pseudomonas aeruginosa* clinical isolates from Lebanon
Antimicrob Agents Chemother, 58 (8) (2014), pp. 4966-4970, 10.1128/AAC.02523-13
PMID: 24913164
View in Scopus Google Scholar

[19] M.M. Zafer, M.H. Al-Agamy, H.A. El-Mahallawy, M.A. Amin, M.S.E.D. Ashour
Antimicrobial resistance pattern and their β-lactamase encoding genes among *Pseudomonas aeruginosa* strains isolated from cancer patients
Biomed Res Int, 101635 (2014), 10.1155/2014/101635

PMID: 24707471

Google Scholar

[20] M.M. Zafer, M.H. Al-Agamy, H.A. El-Mahallawy, M.A. Amin, S. El Din Ashour
Dissemination of VIM-2 producing *Pseudomonas aeruginosa* ST233 at tertiary care hospitals in Egypt
BMC Infect Dis, 15 (1) (2015), pp. 1-7, 10.1186/s12879-015-0861-8
PMID: 25880997

Google Scholar

[21] I. Maroui, A. Barguigua, A. Aboulkacem, K. Ouarrak, M. Sbiti, H. Louzi, *et al.*
First report of VIM-2 metallo-β-lactamases producing *Pseudomonas aeruginosa* isolates in Morocco
J Infect Chemother, 22 (3) (2016), pp. 127-132, 10.1016/j.jiac.2015.11.008
PMID: 26711231

View PDF View article View in Scopus Google Scholar

[22] M.H. Al-Agamy, K. Jeannot, T.S. El-Mahdy, H.A. Samaha, A.M. Shibl, P. Plésiat, *et al.*
Diversity of molecular mechanisms conferring carbapenem resistance to *Pseudomonas aeruginosa* Isolates from Saudi Arabia
Can J Infect Dis Med Microbiol (2016), pp. 1-7, 10.1155/2016/4379686
PMID: 27597874

Google Scholar

[23] R. Viau, K.M. Frank, M.R. Jacobs, B. Wilson, K. Kaye, C.J. Donskey, *et al.*
Intestinal carriage of Carbapenemase-producing organisms: current status of surveillance methods
Clin Microbiol Rev, 29 (1) (2015), pp. 1-27, 10.1128/CMR.00108-14

Google Scholar

[24] A.H. Al-Charrakh, S.J. Al-Awadi, A.S. Mohammed
Detection of metallo-β-lactamase producing *Pseudomonas aeruginosa* isolated from public and private hospitals in Baghdad, Iraq
Acta Medica Iranica, 54 (2) (2016), pp. 107-113
PMID: 26997597

View in Scopus Google Scholar

[25] A.F. Abaza, S.A. El Shazly, H.A.S. Selim, G.S.A. Aly
Metallo-β-lactamase producing *Pseudomonas aeruginosa* in a Healthcare Setting in Alexandria, Egypt
Pol J Microbiol, 66 (3) (2017), pp. 297-308, 10.5604/01.3001.0010.4855

PMID: 29319510

View in Scopus Google Scholar

[26] S.J. Ismail, S.S. Mahmoud

First detection of New Delhi metallo-β-lactamases variants (NDM-1, NDM-2) among *Pseudomonas aeruginosa* isolated from Iraqi hospitals

Iran J Microbiol, 10 (2) (2018), pp. 98-103

PMID: 29997749

View in Scopus Google Scholar

[27] D. Rankin, L. Caicedo, N. Dotson, P. Gable, A. Chu

Notes from the Field: verona integron-encoded metallo-β-lactamase-producing *Pseudomonas aeruginosa* outbreak in a long-term acute care hospital — Orange County, Florida, 2017

MMWR, 67 (21) (2018), pp. 611-612

PMID: 29851944 PMCID: PMC6038905 DOI: 10.15585/mmwr.mm6721a6

View in Scopus Google Scholar

[28] P. Nordmann, L. Poirel

The difficult-to-control spread of carbapenemase producers in *Enterobacteriaceae* worldwide

Clin Microbiol Infect, 20 (2014), pp. 821-830, 10.1111/1469-0691.12719

View PDF View article View in Scopus Google Scholar

[29] Surveillance Report: antimicrobial resistance surveillance in Europe

(2015)

[accessed 19 July 2019]

https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/antimicrobial-resistance-europe-2015.pdf

Google Scholar

[30] Global antimicrobial resistance surveillance system (GLASS) report early implementation

(2017)

[accessed 19 July 2019]

Google Scholar

[31] F. Fallah, R.S. Borhan, A. Hashemi

Detection of bla(IMP) and bla(VIM) metallo-beta-lactamases genes among *Pseudomonas aeruginosa* strains

Int J Burns Trauma, 3 (2013), pp. 122-124

Google Scholar ↗

[32] F. Shahcheraghi, M. Abbasalipour, M. Feizabadi, G. Ebrahimipour, N. Akbari
Isolation and genetic characterization of metallo-beta-lactamase and carbapenemase producing strains of *Acinetobacter baumannii* from patients at Tehran hospitals
Iran J Microbiol, 3 (2011), pp. 68-74
View in Scopus ↗ Google Scholar ↗

[33] S. Aghamiri, N. Amirmozafari, J. Fallah Mehrabadi, B. Fouladtan, H. Samadi Kafil
Antibiotic resistance pattern and evaluation of metallo-β-lactamase genes including bla-IMP and bla-VIM Types in *Pseudomonas aeruginosa* Isolated from Patients in Tehran Hospitals
Int Sch Res Notices Microbiol, 941507 (2014), 10.1155/2014/941507 ↗
PMID: 24944839 DOI
Google Scholar ↗

[34] L. Poirel, V.O. Rotimi, E.M. Mokaddas, A. Karim, P. Nordmann
VEB-1-like extended-spectrum beta-lactamases in *Pseudomonas aeruginosa*, Kuwait
Emerg Infect Dis, 7 (3) (2001), pp. 468-470, 10.3201/eid0703.010322 ↗
View in Scopus ↗ Google Scholar ↗

[35] S. Kalai Blagui, W. Achour, M.S. Abbassi, M. Bejaoui, A. Abdeladhim, A. Ben Hassen
Nosocomial outbreak of OXA-18-producing *Pseudomonas aeruginosa* in Tunisia
Clin Microbiol Infect, 13 (2007), pp. 794-800
View PDF View article CrossRef ↗ View in Scopus ↗ Google Scholar ↗

[36] H.A. Babay
Antimicrobial resistance among clinical isolates of *Pseudomonas aeruginosa* from patients in a teaching hospital, Riyadh, Saudi Arabia, 2001–2005
Jpn J Infect Dis, 60 (2007), pp. 123-125
CrossRef ↗ Google Scholar ↗

[37] N. Bourafa, W. Chaalal, S. Bakour, R. Lalaoui, N. Boutefnouchet, S.M. Diene, *et al.*
Molecular characterization of carbapenem-resistant Gram-negative bacilli clinical isolates in Algeria
Infect Drug Resist, 11 (2018), pp. 735-742, 10.2147/IDR.S150005 ↗
View in Scopus ↗ Google Scholar ↗

[38] H.M. Zowawi, E. Ibrahim, M.W. Syrmis, A.M. Wailan, A. AbdulWahab, D.L. Paterson

PME-1-producing *Pseudomonas aeruginosa* in Qatar

Antimicrob Agents Chemother, 59 (6) (2015), pp. 3692-3693, 10.1128/AAC.00424-15 ↗

View in Scopus ↗ Google Scholar ↗

[39] Z. Mai Mahmoud, M. Amin, H. El Mahallawy, M.S. El-Din Ashour, M. Al Agamy

First report of NDM-1-producing *Pseudomonas aeruginosa* in Egypt

Int J Infect Dis, 29 (2014), pp. 80-81

Google Scholar ↗

[40] H.M. Zowawi, H.H. Balkhy, T.R. Walsh, D.L. Paterson

β-lactamase production in key Gram-negative pathogen isolates from the Arabian Peninsula

Clin Microbiol Rev, 26 (3) (2013), pp. 361-380

View in Scopus ↗ Google Scholar ↗

[41] A. Peymani, T. Naserpour-Farivar, E. Zare, K.H. Azarhoosh

Distribution of bla_{TEM}, bla_{SHV}, and bla_{CTX-M} genes among ESBL-producing *P. aeruginosa* isolated from Qazvin and Tehran hospitals, Iran

J Prev Med Hyg, 58 (2) (2017), pp. E155-60

View in Scopus ↗ Google Scholar ↗

Cited by (23)

Detection of ESBLs types bla<inf>CTX-M</inf>, bla<inf>SHV</inf> and bla<inf>TEM</inf> resistance genes among clinical isolates of Pseudomonas aeruginosa

2022, Gene Reports

> *Citation Excerpt :*
>
> …Data from another study in our area in 2014 showed that the production of ESBLs was observed in 58.25 % of clinical isolates of P. aeruginosa (Dohmen et al., 2015) which was almost in line with our results (66 %). As new data emerge, there is an increasing β-lactamase-producing P. aeruginosa strains in the Arab region (Nasser et al., 2020). Many country-specific studies support the notion that ESBLs are widespread in P. aeruginosa not only in Iran but also worldwide (Pragasam et al., 2017; Mushtaq et al., 2021; Farhan et al., 2019)….

Show abstract

Biomimetically synthesized Physalis minima fruit extract-based zinc oxide nanoparticles as eco-friendly biomaterials for biological applications

2022, Journal of Drug Delivery Science and Technology

Citation Excerpt :

...E. faecalis resistant to vancomycin is commonly a urinary tract infectious pathogen that infects the endocardium, bloodstream, biliary tract, abdomen and burns wounds [4–6]. Similarly, Pseudomonas aeruginosa, a Gram-negative bacterium, is an opportunistic infectious disease in immunocompromised people and causes nosocomial infections that are resistant to various medications, such as cephalosporins and penicillin carbapenems, cephamycins and cefepime [7–10]. Hence, an urge to design a bactericide against these two dangerous MDR pathogens is essential....

Show abstract

Pharmacokinetics of meropenem in critically ill patients in Saudi Arabia

2021, Saudi Pharmaceutical Journal

Citation Excerpt :

...Optimizing the dosing of antibiotics is crucially important due to the increasing rate of drug resistance, limited number of new antibiotics and high mortality associated with hospital-acquired infections especially with gram-negative bacteria (Abdul-Aziz et al., 2020). Several studies in Saudi Arabia have reported over the last 20 years an increased prevalence of multi-drug resistant gram-negative bacteria especially carbapenem-resistant gram-negative bacteria (Al Johani et al., 2010, Balkhy et al., 2012, Yezli et al., 2014, Al-Obeid et al., 2015, Elabd et al., 2015, Zowawi et al., 2015, Zowawi 2016, Zowawi et al., 2018, Alotaibi 2019, Alhifany et al., 2020, Nasser et al., 2020). For example, the susceptibility of Acinetobacter baumannii to meropenem decreased from ~70% in 2006 to ~10% in 2012 (Al-Obeid et al., 2015)....

Show abstract

Molecular Analysis of Antibiotic Resistance in Carbapenem-Resistant Pseudomonas aeruginosa Isolates Isolated from Clinical Samples ↗

2024, Mikrobiyoloji Bulteni

Characterization of β-lactamase and virulence genes in Pseudomonas aeruginosa isolated from clinical, environmental and poultry sources in Bangladesh ↗

2024, PLoS ONE

Characterization of β-lactamase and virulence genes in Pseudomonas aeruginosa isolated from clinical, environmental and poultry sources in Bangladesh ↗

2023, bioRxiv

View all citing articles on Scopus ↗