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Original Article

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Evaluation of resistance to aminoglycosides among clinical isolates of *Acinetobacter baumannii*: A systematic review and meta-analysis

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ABSTRACT

In past decades, aminoglycosides have been commonly used to treat gram-negative infections as well as multi-drug resistant tuberculosis strains. However, in recent years, intrinsic, adaptive and acquired resistances have been raised against aminoglycosides which limits the uptake of these antibiotics. Acquired resistance to *Acinetobacter baumannii* responsible for nosocomial infection against aminoglycosides, has been led to a medical dilemma. In the present study, we aimed to investigate the prevalence rate of *A. baumannii* resistance to aminoglycosides using a meta-analysis and systematic review. International databases of Scopus, PubMed, Web of Science and Google Scholar, as well as national databases, include SID, Magiran, IranDoc, and IranMedex, were searched carefully and 62 articles published during years 1993 and 2016 were selected. After data extraction, random-effects model was used for analysis. Also, data heterogeneity was assessed using the I2 index and the final statistical analysis was done using STATA and R software. The total sample size of 28,055 extracted from the chosen articles and entered the meta-analysis process. The drug resistance value of *A. baumannii* isolates to various antibiotics was determined as follows: Amikacin 69% (57% to 81%), Tobramycin61% (52% to 71%), Netilmicin 35% (11% to 59%) and Gentamicin 68% (57% to 80%). The highest and lowest sensitivity of *A. baumannii* was considered against Netilmicin 57% (32% to 82%) and Gentamicin 26% (12% to 39%), respectively. According to our findings, the drug-resistance rate of *A. baumannii* clinical isolates to aminoglycosides, especially Amikacin, Tobramycin, and Gentamicin are relatively high. So, Gentamicin and Amikacin are not recommended as first-line treatment of *A. baumannii* isolates.

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Keywords
Drug- resistance,
Aminoglycosides,
Acinetobacter baumannii,
Meta-analysis

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INTRODUCTION

Acinetobacter baumannii is a gram-negative, non-fermentative and immobile bacilli which could lead to opportunistic nosocomial infections, especially in hospital intensive care units [1, 2]. Acinetobacter related organisms

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are almost ubiquitous in the nature; however, *A. baumannii* targets are exposed areas of the skin as well as mucosal membranes or moist tissues. These bacteria have low dietary requirements for growth and can survive a long time in adverse conditions, dry surfaces and the also aquatic environment. Also, this bacteria has not been identified as normal flora and can cause severe infections in immunocompromised individuals [3, 4]. *A. baumannii* is primarily associated with hospital-borne infections and pose a great threat to those patients who are hospitalized in the intensive care unit [5] or who had a prolonged hospital stay and are receiving wide spectrum antimicrobial treatment or anti-cancer therapy. Various hospital-acquired infections such as bacteremia, urinary tract infection, secondary meningitis, as well as upper respiratory tract pneumonia has been reported to be associated with *A. baumannii*. It is also one of the most common bacterial cause of sepsis in immunodeficient patients [6] and has been evidenced as the most common bacterial species isolated from blood, sputum, skin, pleural fluid and urine of hospital admitted patients [7, 8]. Many studies have been conducted to investigate the mortality rate associated with *A. baumannii* infection; however, there is still debate to actual impact of this infection on patient's mortality. In this regard, the result of some studies indicated that *A. baumannii* infection has a detrimental effect on patient's outcome.

Family of aminoglycoside antibiotics (such as Gentamicin, Amikacin, Netilmicin, Tobramycin) is prescribed as the first-line therapy against *A.baumannii* isolates. The bactericidal activity of AGs are almost because of their ability to disrupt mRNA reading frame which results in incomplete protein production [9]. It has been reported that microorganisms can cause treatment associated problems by obtaining the multi-faceted resistance to a wide range of antibiotics [4]. Accordingly, many studies have suggested that *A.baumannii* could acquire drug resistance against aminoglycoside antibiotics. Considering this, it is difficult to control the infection, and as a result, patients with *A. baumannii* infection may face critical problems [10]. Nowadays, a global concern is related with nosocomial infections which are of considerable importance especially in intensive-care units of hospitals. Acquired drug resistance by *A.baumannii* could pose a major threat to patients with prolonged hospital stays. Several studies have been conducted worldwide to investigate the prevalence of antibiotic resistance in the clinical isolates of *A. baumannii*. Soroush and colleagues in 2010 found 81% of *A.baumannii* isolates with multi-drug resistance pattern at Children's Medical Center in Tehran [11]. Zerrily and colleagues (Aril et al. 2008) in Lebanon, found 50% of *A.baumannii* isolates with drug-resistance to at least 64 mg/l and 125 mg /l concentrations of Amikacin and Gentamicin, respectively [12]. Kooti et al. 2015 (Kooti et al. 2015) also showed 84.5% and 86.5% of *A.baumannii* isolates are resistant to Gentamicin and Amikacin, respectively [13]. Carretto and colleagues (Italy, 2011) investigated 277 species of *A.baumannii* in which sensitivity and resistance to Amikacin was determined to be 18.9% and 80.3%, respectively [14]. Given to that, the prevalence of antibiotics resistance in *A. baumannii* isolates are gr owing up and are associated with patient's mortality. Therefore, considering the prevalence of *A. baumannii* resistance to AGs is a global necessity. Here in the present study, we have tried to investigate the prevalence rate of *A. baumannii* resistance to aminoglycosides using a meta-analysis and systematic literature review. The data of such study could definitely help decision makers to take appropriate measurements in order to prevent the increasing spread of antibiotic resistance.

MATERIALS AND METHODS

The current study is a systematic review and meta-analysis aimed to review, collect, analyze, and interpret information on the prevalence rate of aminoglycoside antibiotic resistance among *A. baumannii* clinical isolates between the years 1993 and 2016 in Iran and other countries in the world. To this end, international and national databases, including Google Scholar, PubMed, Web of Science, Scopus, SID, Magiran, IranDoc, and IranMedex were searched carefully and the studies pertaining to antibiotic resistance of *A.baumannii* to aminoglycosides were obtained.

The titles, abstracts and full texts of the selected articles were examined thoroughly to exclude unrelated works and maintain possible related articles. Searching was mainly performed using the systematic search keywords such as prevalence of drug resistance, antibiotics, antibiotic resistance, aminoglycosides, and *A.baumannii* with all possible combinations keywords, original and sensitive. In addition, relevant studies which were referenced or listed in the selected articles were also evaluated for further inclusions in this study.

Inclusion and exclusion criteria

Herein, all cross-sectional studies or studies in relation to the "prevalence of antibiotic resistance in clinical isolates of *Acinetobacter baumannii*" were considered carefully. To enter the study, selected articles were examined in three stages: title, abstract and full text and the studies related to the prevalence of antibiotic resistance in *A.baumannii* isolates were included in present study.

Also some articles were excluded from the meta-analysis because of the following criteria; articles with insufficient information, articles without epidemiological methodologies, studies which was not cross-sectional, studies that related to other Acinetobacter isolates, the studies were related to antibiotic resistance other than the aminoglycoside group, review articles, abstracts of congresses, studies published in languages other than Persian and Latin, as well as meta-analysis studies and repetitive publications.

Data Extraction

Initially, 112 articles including phrases "the prevalence of resistance "and "Acinetobacter baumannii" and "aminoglycosides" in their titles were listed based on their

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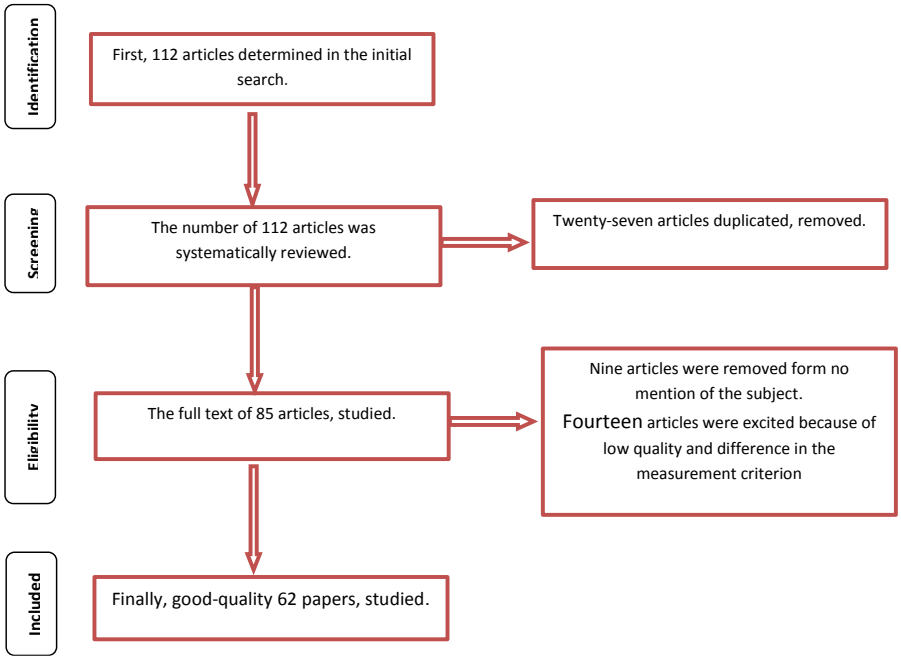

Figure 1. Data flowchart entered to the meta-analysis

abstracts**.** The primary list was assessed and 27 out 112 articles that were found to be duplicated, were excluded. Also, 23 out of the remaining 85 studies were further excluded due to lack of relevance to subjected matter or different measurement criteria (Fig. 1). Finally, 62 were found to be appropriate to enter the meta-analysis. A checklist consisting of multiple sections with necessary information of each study (researcher name, the year of study, study location, the number of samples, the prevalence of resistance to any aminoglycoside antibiotics, sensitivity rate for each of antibiotics, method of resistance and sensitivity measurement to antibiotics) was prepared. General specifications and main data needed to investigate are shown in Table 1.

Statistical analysis

The prevalence of antibiotic resistance and number of samples were collected from each study. For calculating the variance of each study, the weighted average values of the binomial distribution and the prevalence rate reported in the considered studies were obtained. Due to the differences in the prevalence rate reported in each study (heterogeneity of studies), heterogeneity index (I^2) of random-effects model was used.

RESULTS

In the present study, a number of 62 articles on the prevalence of aminoglycoside antibiotics resistance among *A.baumannii* clinical isolates between that are reported between the years 1993 and 2016 were collected and examined in detail. General features of all included articles in this meta-analysis are summarized in Table 1. The total

Table 1. General features and data of selected articles in the meta-analysis, the prevalence of resistance to aminoglycoside antibiotics in clinical isolates of *A. baumannii*

Author	*Year*	*Location*	*Sample Number*	*Amikacin*		*Tobramycin*		*Netilmicin*		*Gentamicin*	
				Sensitivity	*Resistance*	*Sensitivity*	*Resistance*	*Sensitivity*	*Resistance*	*Sensitivity*	*Resistance*
Kooti.S[11]	2015	Iran	200	8.5	86.5	-	-	-	-	-	-
Kwan. S.K[13]	2007	Korea	214	-	30.2	-	-	-	-	-	-
Aygun.G[14]	2002	France	170	45.5	54.5	36.4	63.6	95.2	4.8	4.8	95.2
Gur. D[40]	2008	Turkey	321		-	43.9		-	-	-	25.6
Hamez[42]	2012	Syria	260	21.7	-			-	-	-	17.3
Elabd. F.M[20]	2014	Saudi Arabia	108	-	75	-	79.6	-	-	-	81.5
Chen.C.M[21]	2014	Taiwan	87	44	87	-	-	-	-	50	98
Mohamed.H.A[43]	2014	Egypt	40	32.5	45	-	-	-	-	-	-
Carretto.E[22]	2011	Italy	277	18.9	80.3	-	-	-	-	-	-
Livermore.D.M[44]	2010	London	166	15.5		13.9	-	-	-	4.9	-
Vafaii.S[45]	2014	Iran	130	-	95	-	56	-	-	-	63
Mirzaii.E[46]	2015	Iran	100	-	95	-	56	-	-	-	63
Farahani.N[47]	2013	Iran	50	10	90	28	28	-	-	30	64

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Table 1. Cntd

Caroline.J.H[37]	2002	UK	443		21	-	-	-	-	-	7.5
Mostofi.S[48]	2011	Iran	50	10	85	72	26	-	-	36	61
Hashemizadeh. Z[49]	2010	Iran	147		81	-	-	-	-	-	78
Anguti.G[50]	2015	Iran	61	50	38	50		-	-	-	77
Cisneros.J.M[23]	2016	Spanish	79	20	80	10	60	61	39	2	97
Scheetz.M.H[51]	2007	USA	93	38	-	-	-	-	-	-	-
Song.J.Y[52]	2007	Korea	43		-	-	-	-	-	-	-
Noormohamady .Z[15]	2014	Iran	100	21	66	30	67	-	-	9	89
Karlowsky.JA[38]	2003	USA	7394	80.2	13.8			-	-	49.3	47.9
Liu.JY[53]	2015	Taiwan	378	4	96	5	94	-	-	0	100
Reguero.MT[24]	2013	Columbia	51	-	68			-	-		82
Dinh Van.T[30]	2014	Vietnam	66	-		31.7	42.9	-	-	17.5	1
Aliakbarzade.K[54]	2014	Iran	103	17	81	37	63	-	-	11	86
Karbasizadeh.V[18]	2013	Iran	456		64			-	-	-	-
HernandezTorres. A[29]	2012	France	77	57	13	57	31	-	-	-	-
Talebi Taher.M[19]	2013	Iran	51	38	65	-	-	-	-	5	94.2
Vila.J[55]	1993	Spain	54	72		50		66		33	-
Sadeqifard.N[56]	2007	Iran	66	44	56	48.5	50	18.2	78.8		-
Nazari Monazam.A[57]	2014	Iran	100	30	95	10	56	-	-	-	63
Sinirtas.M[58]	2009	Europe	100	-	100	-	100	-	-	-	100
Higgins.PG[59]	2010	Europe	515	35.7	-	-	-	-	-	-	-
Dizbay.M[25]	2008	Turkey	66	30.3	63.6	-	-	51.5	30.3	-	-
Yau.W[26]	2009	Africa	30	20	80	26.7	73.3	-	-	6.7	93.3
Saderi.H[60]	2016	Iran	106	2.8	96.2	22.6	73.6	-	-	-	79.2
Jasemi.S[7]	2016	Iran	2382	53.4	40	-	-	-	-	60	33.4
Japooninejad.AR[61]	2014	Iran	56	-	77	-	-	-	-	-	85.5
Mirnejad.R[62]	2012	Iran	500	-	90	-	28	-	-	-	64
Hosainijazani.N[63]	2010	Iran	48	-	52	-	-	-	-	-	70.8
McGowan.JE[41]	2006	USA	433	56	14	-	-	-	-	-	-
Shrestha.S[64]	2015	Nepal	122	-	98	-	-	-	-	-	-
Amin Shahidi.M[65]	2015	Iran	86	-	66.3	-	72.1	-	-	-	-
Shokri.D[36]	2015	Iran	43	65.7	28.6	-	-	-	-	34.3	62.8
Lowings. M[66]	2015	Africa	100	-	7	-	-	-	-	-	-
Fazeli. H[67]	2014	Iran	121	-	87.6	-	86.8	-	-	-	-
Ahmadi. KH[68]	2014	Iran	43	14	86	-	-	-	-	-	-
Shahcheragi.F[69]	2009	Iran	95	-	75.7	-	-	-	-	-	-
Kalaatbari Farahani.R[70]	2008	Iran	48	6.7	80	10	68.3	-	-	58.3	30
Afshar Yavari.SH[31]	2016	Turkey	150	22	72	48	52	46	54	32	62
Alaee. N[33]	2013	Iran	84	-	-	52	43	41	36	-	-
Ardebili.A[71]	2012	Iran	65	-	94		62	-	-	-	86
Mirnejad. R[72]	2013	Iran	400	5	95	37	56	-	-	27	63
Farshadzadeh. Z[73]	2015	Iran	92		86		66	-	-	-	93
Moammadi.F[28]	2014	Iran	100	5.1	85.6	19.6	80.4	-	-	10.3	89.7
Baran. G[32]	2008	Turkey	1100	54.4	86.4	35.1	74.2	36.8	32.1	73.7	78.8
Nasrolahei M[74]	2014	Iran	100	-		-	83	-	-		83
Bayram Y[75]	2013	Turkey	377	-	64	-	-	-	-		94
Morkel G[76]	2014	Africa	14	14	86	-	-	-	-	14	86
Noreen H[77]	2011	USA	-	-	-	-	33.9	-	-	-	-
Kumar A[78]	2014	India	65	32.4	-	-	-	-	-	20.3	-

sample size 28,055 was obtained. Drug-resistant rate of *A. baumannii* was obtained to Amikacin (69%), Tobramycin (61%), Netilmicin (35%) and Gentamicin (68%). Clinical isolates of *A.baumannii* showed the most and least sensitivity to Netilmicin antibiotic (57%) and Gentamicin (26%), respectively.

According to Tables 2 and 3, the mean value of prevalence rate of drug resistance to Amikacin in world obtained to be 69% (0.57%-81%) and the highest intercontinental drug-resistance rates of *A. baumannii* to Amikacin were observed in Asia (76%), Tobramycin in Africa (73%), and Gentamicin in Africa (93%). However, the lowest rates of resistance were reported to Amikacin in America (14%), to Tobramycin in Europe (63%) and to Gentamycin in America (48%). Considering Iran, *A. baumannii* drug resistance to Amikacin in Iran was reported

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Table 2. The total rate of resistance and sensitivity *of A. baumannii* to aminoglycosides, according to the studies were included in the meta-analysis.

P for Heterogeneity	*Homogeneity Index I^2 (%)*	*Confidence interval 95% (CI%95)*	*Prevalence*	*Study number*	*Sensitivity or Resistance*	*Aminoglycoside antibiotics*
0.000	99.9	0.57 – 0.81	0.69	49	R	Amikacin
0.000	99.7	0.18 – 0.43	0.30	36	S	
0.000	98.3	0.52 – 0.71	0.61	30	R	Tobramycin
0.000	96.8	0.25 – 0.40	0.33	23	S	
0.00	99.2	0.11 – 0.59	0.35	7	R	Netilmicin
0.000	99.2	0.32 – 0.82	0.57	8	S	
0.000	99.8	0.57 – 0.80	0.68	38	R	Gentamicin
0.000	99.8	0.12 – 0.39	0.26	23	S	

Table 3. The frequency distribution of *A. baumannii* resistance to aminoglycosides according to the study location and continent in the meta-analysis.

P value	*Homogeneity index I^2(%)*	*Confidence interval 95% (CI%95)*	*Prevalence*	*Sensitivity or Resistance*	*Continent*	*Aminoglycoside antibiotics*
0.000	98.0	-0.03 - 0.90	0.44	R	Africa	Amikacin
0.252	27.4	0.12 - 0.34	0.23	S		
0.907	0.00	0.13 - 0.15	0.14	R	America	
0.000	98.8	0.36 - 0.81	0.58	S		
0.000	98.9	0.69 - 0.83	0.76	R	Asia	
0.000	99.1	0.16 - 0.36	0.26	S		
0.001	99.8	0.19 - 0.98	0.59	R	Europe	
0.000	96.1	0.22 - 0.49	0.36	S		
–	0	0.57 - 0.89	0.73	R	Africa	Tobramycin
–	0	0.11- 0.43	0.27	S		
–	–	–	–	R	America	
–	–	–	–	S		
0.000	97.2	0.53 - 0.72	0.63	R	Asia	
0.000	97.3	0.24 - 0.42	0.33	S		
0.000	99.1	0.18 - 1.10	0.64	R	Europe	
0.000	96.1	0.12 - 0.53	0.32	S		
0.000	99.5	0.84 - 1.02	0.93	R	Africa	
	0	-0.02 - 0.16	0.07	S		
0.000	0.00	0.47 - 0.49	0.48	R	America	
–	0	0.48 - 0.50	0.49	S		Gentamicin
0.000	99.8	0.57 - 0.84	0.70	R	Asia	
0.000	99.0	0.18 - 0.47	0.32	S		
0.000	99.7	0.00 -1.00	0.50	R	Europe	
0.000	86.6	0.02 - 0.13	0.07	S		

to be 77% (68% to 85%) which is very high in comparison to other studied countries. Also, according to the results, the highest sensitivity to Amikacin has been recorded in America, while the lowest sensitivity to Gentamicin was obtained in Europe and Africa.

DISCUSSION

The objective of this work was to determine the prevalence rate of antibiotic resistance among clinical isolates of *A. baumannii* to the group of aminoglycoside antibiotics in Iran and rest of the world using a systematic review method and meta-analysis. According to our results, the drug resistance rate of *A. baumannii* to Amikacin was obtained to be high (69%), which was almost similar in Iran and other countries (Table 1). The results of different studies conducted in Iran are as follows: Noormohammady (66%) [15], Kooti (86.5%) [11], Vafaee (95%) [16], Farahani (90%) [17], Karbasizadeh (64%) [18], Talebi Taher (65%) [19]). Also, the similar results were obtained in countries other than Iran as follows: Aygün in Turkey (54.4%) [14], Elebd in Saudi Arabia (75%) [20] Chen in Taiwan (87%) [21], Carretto in Italy (80.3%) [22], Cisnoros in Spain (80%) [23], Reguero in Colombia (68%) [24], Dizbay in (63.6 %) [25], Yau in Africa (80%) [26] (Diagram 1). In addition, the rate of antibiotic resistance to Amikacin in Iran (77%) compared to developed countries in America (28%), was obtained to be considerably high. Different factors may influence such a difference such as self-medication by patients, incomplete period of treatment, uncontrolled prescribing of antibiotics by physicians and health providers, receiving high or inadequate drug doses, unavailability of high quality drugs, reliance on empirical treatment, poor

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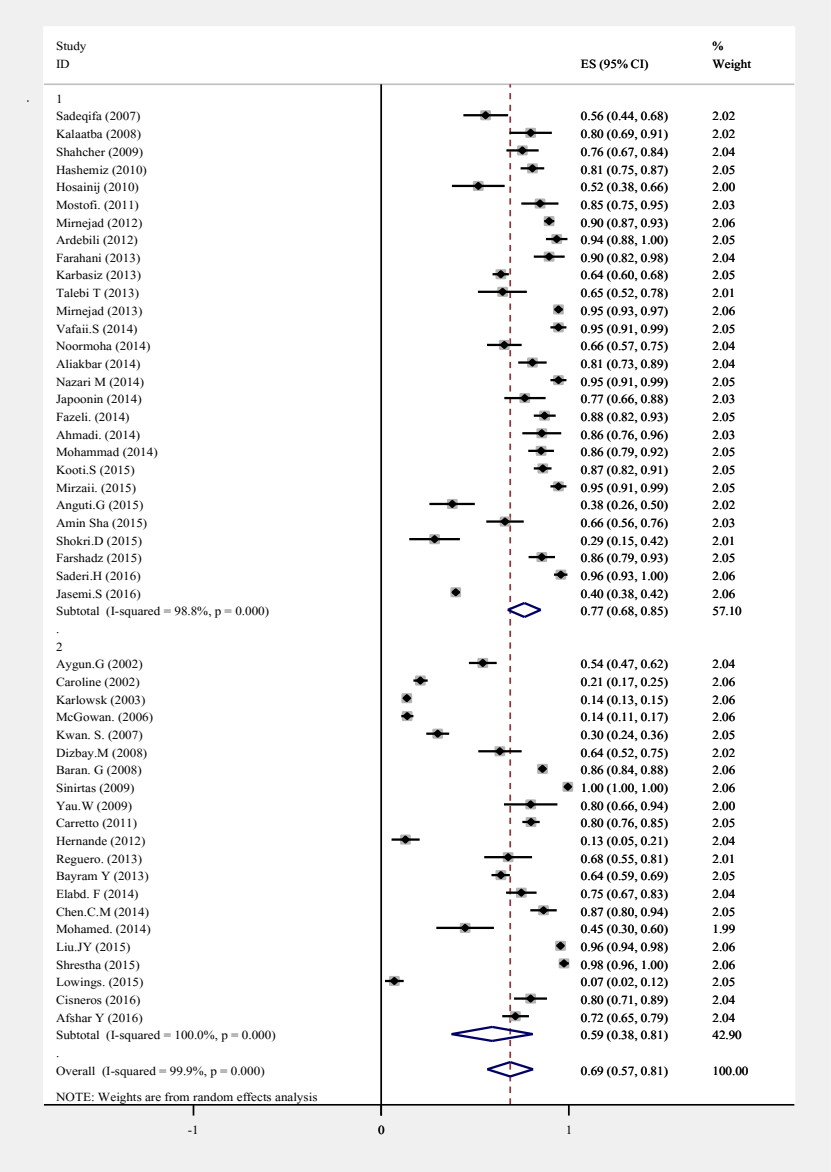

Diagram 1. Prevalence of resistance to Amikacin in clinical isolates of *A. baumannii* according to the location study (code 1: Iran and code 2: other parts of the world) based on the random-effects model. The midpoint of each line segment represents the estimate of the prevalence. The length of the segment indicates the 15% confidence interval in each study. Rhombic mark indicates the prevalence rate for all the studies.

hygiene conditions, low socioeconomic level and etc. which are most prevalent in developing countries. Given to these results it seems that the rate of *A. baumannii* resistance to aminoglycosides is rapidly increasing. Thus, it is necessary to take strict measurements in order to prevent and combat drug-resistance. Our findings also show that the drug-resistant rate of *A.baumannii* to Tobramycin (Diagram 2) was 61% worldwide, while this rate in Iran was obtained to be 59%. Accordingly the finding of studies in Iran were reported by Vafaii (56%) [16], Mizrahi (56%) [27], Noor Mohammady (67%) [15] and Mohammad (80.4%) [28], and in other countries the results of the studies are as follows: Amgun in Turkey (63.6%) [14], Hernandez Torres in France (31%) (31%) [29], Cisnoros in Spain (60%) [23], Dinah Van in Vietnam (42.9%) [30], Afsharyavari in Turkey (52%) [31]. The drug resistance rate of *A.baumannii* to Netilmicin was found to be 35% worldwide, while this rate is estimated to be 27% in Iran Similar results were obtained in other studies by Baran in Turkey (62.1 %) [32], Alaei in Iran (36%) [33], Afsharyavari in Turkey (54%) [31], Dizbay in Turkey (30.3%) [25] and Cisnoros in Spain (39%) [23].

The drug resistance rate of *A.baumannii* clinical isolates in terms of Gentamicin is reported to be 68.5% (57%-80%) in worlwide), which is similar to those reported in Iran and rest of the world (Diagram 4). These results were obtained from the studies from Vafaii (63%) [16], Mirzaii (63%)

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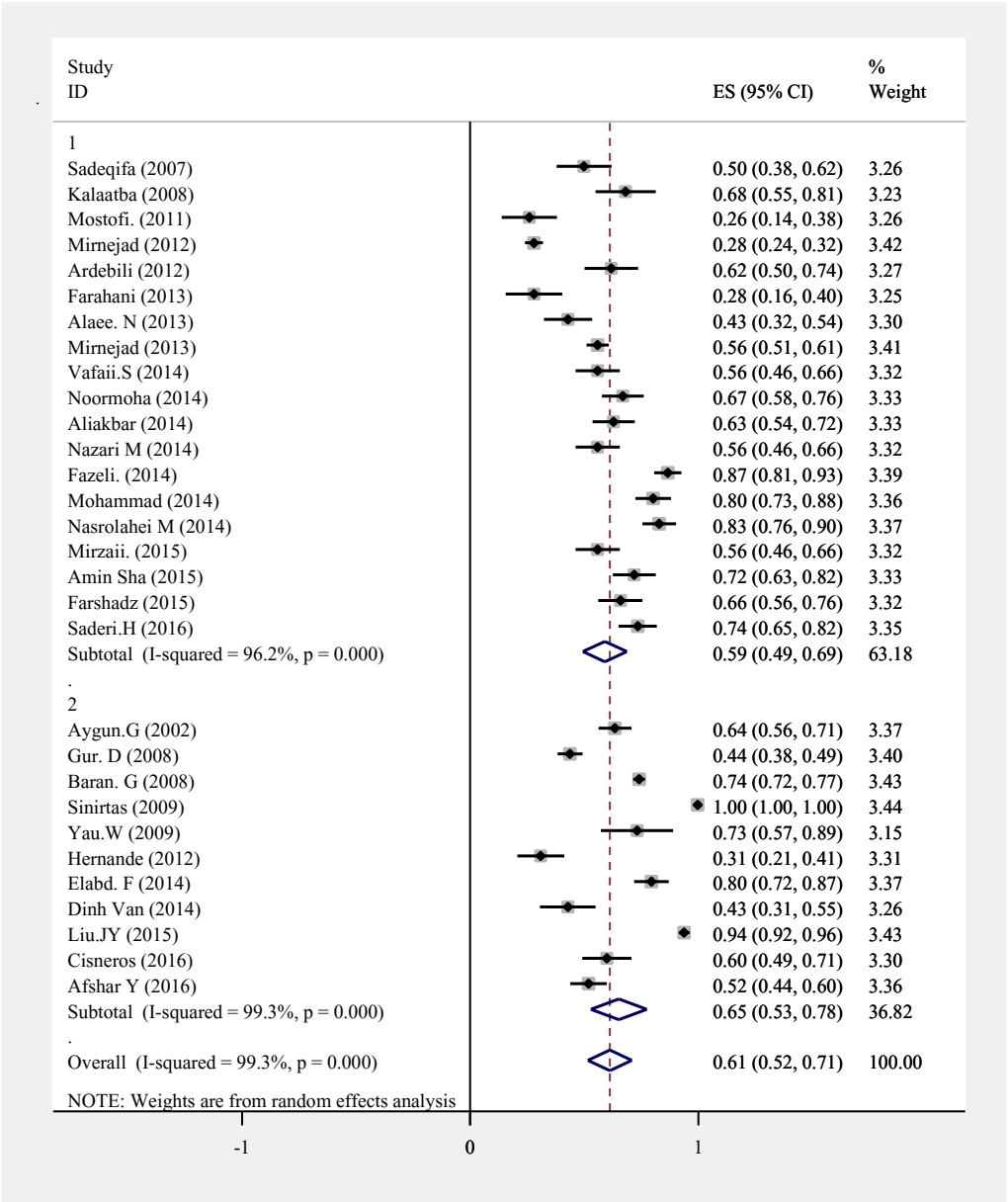

Diagram 2. Prevalence of resistance to Tobramycin in clinical isolates of *A. baumannii* according to the location study (code 1: Iran and code 2: other parts of the world) based on the random-effects model. The midpoint of each line segment represents the estimate of the prevalence. The length of the segment indicates the 15% confidence interval in each study. Rhombic mark indicates the prevalence rate for all the studies.

[27], Farahani (64%) [17], Saderi (79.2%) [34], Hosseini jazani (70.8%) [35] and Shokri in Iran (62.5%) [36], and Caroline in America (43%) [37], Karlowsky in America (47.9%) [38], Yau in Africa (93.3%) [26], Aygün in Turkey (95.2%) [14], Afsharyavari (62%) [31], Baran in Turkey (78.8%) [32], Reguero in Colombia (82%) [24], and Elebd in Saudi Arabia (81.5%) [20]. Due to high resistance of *A.baumannii* to Amikacin, Tobramycin, and Gentamicin, prescribing these antibiotics to treat *A. baumannii* is not recommended. Although, studies by Khalat Barry Farahani in Iran [39] and Gur Goor in Turkey [40] reported this rate 30% and 25.6% respectively, but the resistance rate is still high.

According to the results, clinical isolates of *A. baumannii* showed the highest sensitivity to Netilmicin (57%), while this sensitivity was the least to Gentamicin (26%) (Diagram 3). In addition, the highest and lowest resistance to Amikacin was observed in countries from Asia (77%) and America (28%), respectively. Considering Tobramycin, the highest resistance rate was reported in Africa (73%) and Europe (41%), respectively, while the lowest resistance rate are found to be Gentamicin in Africa (93%) and Europe

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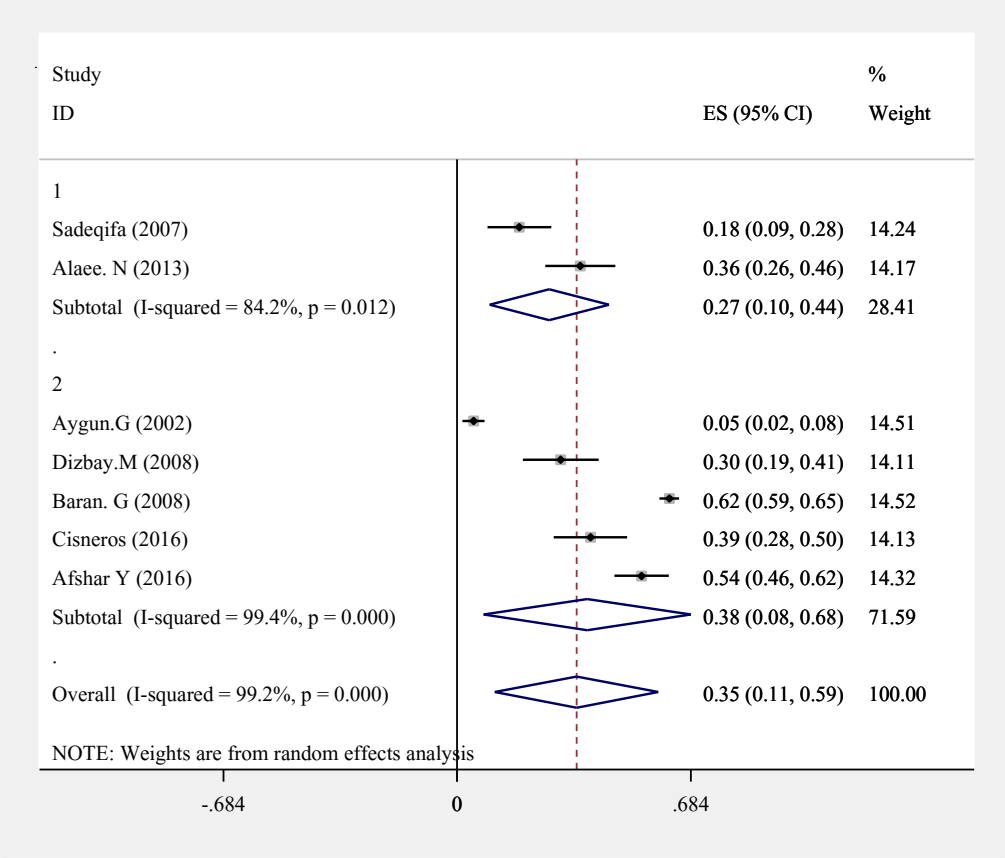

Diagram 3. Prevalence of resistance to Netilmicin in clinical isolates of *A. baumannii* according to the location study (code 1: Iran and code 2: other parts of the world) based on the random-effects model. The midpoint of each line segment represents the estimate of the prevalence. The length of the segment indicates the 15% confidence interval in each study. Rhombic mark indicates the prevalence rate for all the studies.

(61%), respectively. Putting the results together, the highest drug sensitivity is reported for Amikacin in clinical isolates from America continent and the least sensitivity to Gentamicin in Europe and Africa continents. In contrast to the results obtained by most of the studies, low resistance rate of *A. baumannii* to Netilmicin, Amikacin, Tobramycin, and Gentamicin have been reported only in few studies of Kwan in Korea [13], Caroline in the Kingham State [37], Karlwosky in America [38], Mc Gowan in America [41] and Herna´ndez-Torres in France [29]. We assume that this low resistance rate may be due to low consuming amount and minor amount prescription of these antibiotics and/or because of the few numbers of studies has been conducted in these regions.

CONCLUSION

Altogether, in all conducted studies the resistance rate of A. baumannii to aminoglycosides have been reported to be high all around the world. Thus, our findings strongly suggest that new strategies should be implemented in order to prevent acquiring drug resistance by *A. baumannii*. Also, prescription of aminoglycosides to treat this infection should be revisited.

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CONFLICT OF INTEREST

Authors want to declare that they have no conflict of interests.

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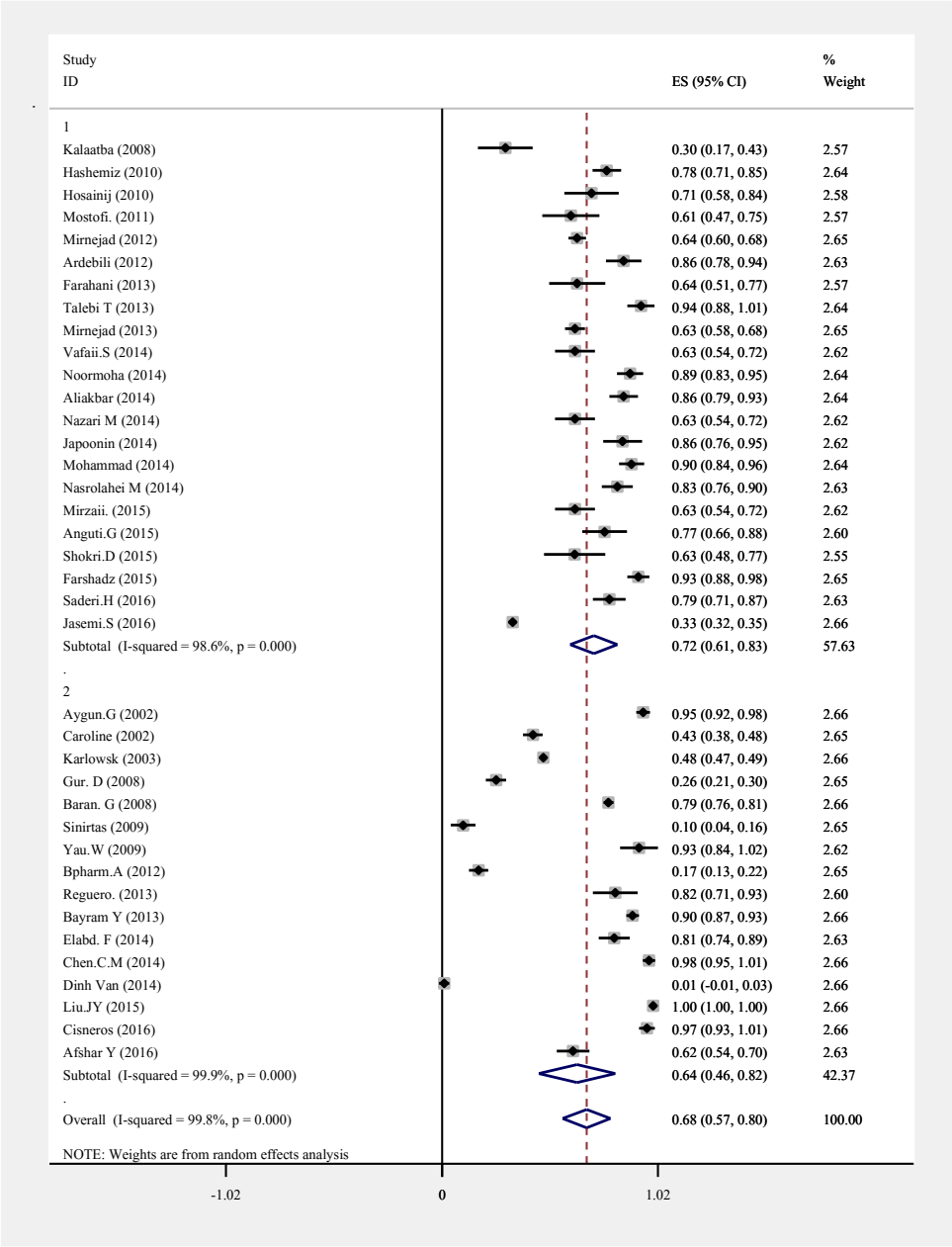

Diagram 4. Prevalence of resistance to Gentamicin in clinical isolates of *A. baumannii* according to the location study (code 1: Iran and code 2: other parts of the world) based on the random-effects model. The midpoint of each line segment represents the estimate of the prevalence. The length of the segment indicates the 15% confidence interval in each study. Rhombic mark indicates the prevalence rate for all the studies.

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