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Review

Status of carbapenem-resistant *Acinetobacter baumannii* harboring carbapenemase: First systematic review and meta-analysis from Iran

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ABSTRACT

Carbapenem-resistant *Acinetobacter baumannii* (CRAB) has been considered as an important pathogen causing hospital-acquired infections thought the world. Class A carbapenemases, class B (metallo-β- lactamases; MBLs) and class D (oxacillinases) are the most important enzymes that are able to hydrolyze carbapenems. There are various reports on the CRAB harboring carbapenemase genes in Iran; but, a comprehensive analysis on the prevalence of CRAB and carbapenemases has not yet been performed. We systematically searched different electronic databases including: Medline (via PubMed), Embase, Web of Science, and the Iranian Database from January 2000 to December 2018. Meta-analysis was performed using the Comprehensive Meta-Analysis (Biostat V2.2) software. Our analysis indicated that the pooled prevalence of resistance to imipenem and meropenem was 81.1% (95% CI 76.6–84.9) and 83.6% (95% CI 78.7–87.5), respectively. Among genes encoding class D carbapenemases OXA-23, OXA-24, and OXA-58 were found with the prevalence 73.7% (95% CI 66.5–79.8), 21.9% (95% CI 15.2–30.4), and 6.2% (95% CI 3.1–11.9), respectively. Among genes encoding class B carbapenemases, IMP, VIM and NDM genes were found with the prevalence 16.7% (95% CI 5–43.2) and 12.3% (95% CI 5.3–25.8) and 2.7% (95% CI 1.3–5.5), respectively. Genes encoding class A carbapenemases were not observed. The results of this study indicated that imipenem and meropenem resistance rates are high in Iran and these drugs are not recommended for *A. baumannii* infections. Thereby, antimicrobial stewardship and improvements in infection control practices are recommended strategies for prevention and spread of these strains.

1. Introduction

Acinetobacter baumannii has been considered as a notorious pathogen associated with hospital-acquired infections thought the world (Dijkshoorn et al., 2007). It is a common cause of nosocomial infections such as urinary tract infection, blood infection, meningitis, pneumonia, endocarditis, and skin infection (Dijkshoorn et al., 2007; Razavi Nikoo et al., 2017). Mortality due to *A. baumannii* infections varied between 8% to 23% in the hospital and between 10 and 43% in intensive care unit patients (Fishbain and Peleg, 2010). Currently, this organism has developed resistance to many antibiotics (quinolones, aminoglycosides and carbapenems) and multi-drug resistance (MDR) has been commonly documented (Dijkshoorn et al., 2007; Fishbain and Peleg, 2010). Carbapenems (imipenem, meropenem, or doripenem) have been established as the first-line drugs to treat infections caused by *A. baumannii* (Fishbain and Peleg, 2010; Razavi Nikoo et al., 2017). However, the increasing prevalence of carbapenem-resistant *A. baumannii* (CRAB) poses a therapeutic challenge for physicians in the management of infections caused by these strains (Soudeiha et al., 2017). One of the major mechanisms of carbapenem resistance is production of carbapenemase enzymes (Hsu et al., 2017). These enzymes are members of the classes A, B, and D based on molecular Ambler classification (Hsu et al., 2017). The members of class A carbapenemases are SME, IMI, NMC, GES, SFC and KPC families. Class B enzymes, also referred to as metallo-β- lactamases (MBLs), include IMP, VIM, SIM and NDM. Class D β-lactamases called OXA-type enzymes or oxacillinases are the most prevalent carbapenemases in *A. baumannii* (Jeon et al., 2015; Hsu et al., 2017). Currently, six subclasses of OXA related to *A. baumannii* have been identified ((i) OXA-23-like (OXA-23, OXA-27, OXA-49, and OXA-239), (ii) OXA-24-like (OXA-24, OXA-25, OXA-26, OXA-40, and OXA-72), (iii) OXA-51-like, (iv) OXA-58, (v) OXA-143-like (OXA-143 and OXA-231) and (vi) OXA-235-like (OXA-235, OXA-236, and OXA-237) (Jeon et al., 2015; Hsu et al., 2017). Studies published so far indicate that the percentage of carbapenem resistant isolates have been increased over the last ten years in Iran (Farshadzadeh et al., 2015; Saffari et al., 2017; Soudeiha et al., 2017). To date, the prevalence of

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carbapenemase genes among carbapenem-resistant *A. baumannii* has been documented in literatures and a comprehensive analysis from different areas of Iran has not carried out yet. This study was designed to determine the prevalence of CRAB and carbapenemase encoding genes in Iran, using a systematic review and meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

2. Materials and methods

2.1. Search strategies

We performed an extensive literature search of Medline (via pubmed), Embase, Web of Science, and Iranian Database from January 2000 to December 2018 using the following terms: "*Acinetobacter baumannii*" or "*A. baumannii*", "carbapenems", "carbapenem-resistant *A. baumannii*" or "CRAB", "class A carbapenemases", "class B carbapenemases" or "Metallo-β-lactamases" or "MBLs" and "class D carbapenemases" or "oxacillinases" in combination with Iran. Cross-sectional or cohort studies that reported the prevalence of CRAB, class A carbapenemases, MBLs and oxacillinases were considered. The titles and abstracts for possible inclusion in the reviews were screened by two researchers independently. The searching was restricted to in English and Persian language. Eligible articles were selected in three stage: firstly, based on the title, secondly, based on abstracts, and thirdly, based on the full-text publication. Studies that have the following characteristics were included: a standard method had to be used to detect *A. baumannii*, reported data on the number of CRAB and detection of class A, B and D carbapenemases by molecular methods such as polymerase chain reaction (PCR). Studies that have one or more of the following characteristics were excluded: studies did not report CRAB, class A, B and D carbapenemases prevalence, duplicate and overlapping studies, studies published in languages other than English or Persian, nonhuman studies, review articles, congress abstracts and meta-analyses or systematic reviews.

2.2. Data extraction and definitions

For all studies, the following details were extracted: first author, published time, sample size, study setting, prevalence of CRAB, class A, B and D carbapenemases. Additionally, to minimize the potential bias caused by an inadequate sample size, articles with < 50 subjects were excluded. Two investigators independently extracted all data from included studies and the results were reviewed by a third reviewer. Disagreements were resolved by consensus.

2.3. Quality assessment of studies

Two investigators using a checklist provided by the Joanna Briggs Institute assessed the study quality independently (Moher et al., 2009).

2.4. Statistical analysis

Meta-analyses were carried out using Comprehensive Meta-Analysis version 2.2 (Biostat, Englewood, NJ, USA). We used fixed or random effects models, based on statistical heterogeneity between studies. Statistical heterogeneity was assessed via Cochran's Q and I^2 statistics. The Begg rank correlation and Egger weighted regression methods in combination with a funnel plot were used to assess publication bias ($p < .05$ was regarded as statistically significant).

3. Results

Our literature search yielded 1066 studies, and of these, 63 articles based on the mentioned criteria were included in this meta- analysis, (Table 1). The pooled prevalence of resistance to imipenem and meropenem was 81.1% (95% CI 76.6–84.9) and 83.6% (95% CI 78.7–87.5), respectively as shown in Table 2. Study selection process and reasons for exclusion of studies are shown in Fig. 1, and the main characteristics of the selected studies are presented in Table 1. Among genes encoding class D carbapenemases, OXA-23, OXA-24, and OXA-58 were found with the prevalence 73.7% (95% CI 66.5–79.8), 21.9% (95% CI 15.2–30.4), and 6.2% (95% CI 3.1–11.9), respectively. Among genes encoding class B carbapenemases, IMP, VIM and NDM genes were found with the prevalence 16.7% (95% CI 5–43.2), 12.3% (95% CI 5.3–25.8) and 2.7% (95% CI 1.3–5.5), respectively. Genes encoding class A carbapenemases were not found. Heterogeneities between studies ($I^2 = 93$; $p = .001$ for imipenem, $I^2 = 92.8$; $p < .001$ for meropenem, $I^2 = 91.1$; $p < .001$ for OXA-23, $I^2 = 93.3$; $p < .001$ for OXA-24, $I^2 = 81.4$; $p < .001$ for OXA-58, $I^2 = 95.8$; $p < .001$ for IMP, $I^2 = 93.1$; $p < .001$ for VIM, and $I^2 = 90.2$; $p < .001$ for NDM) were found, so the random effect model was used to meta-analysis. Figs. 2 and 3 show forest plots for the prevalence rate of imipenem and meropenem resistance, respectively. As it is shown in Table 2, some evidence of publication bias was observed by Begg's and Egger's tests ($p < .05$ for imipenem and meropenem resistance, OXA-23 and OXA-24 genes), but was not observed for IMP and VIM genes (IMP: Begg test, $P = .2$; Egger test, $P = .4$. VIM: Begg test, $P = .3$; Egger test, $P = .2$. NDM: Begg test, $P = .1$; Egger test, P = .3). Publication bias was observed by Eegg's test for OXA-58 ($p = .008$), but was not observed by Egger's test ($p = .1$). Asymmetric shape of funnel plots (Figs. 3 and 4) suggests some evidence of publication bias among evaluated papers.

4. Discussion

To our knowledge, we provide the first systematic review and meta-analysis on the prevalence of the carbapenem-resistant *A. baumannii* harboring carbapenemase genes in Iran. According to this meta-analysis, 81.1% and 83.6% of *A. baumannii* isolates were resistant to imipenem and meropenem, respectively. The findings of this study highlight that carbapenems are not the drug of choice for treatment of *A. baumannii* infections in Iran. A higher prevalence of carbapenems resistance have been reported in neighboring countries, namely from Pakistan (100%), Turkey (98.9%) and United Arab Emirates (76.4%) (Begum et al., 2013; Sonnevend et al., 2013; Guven et al., 2014). However, the prevalence of carbapenem resistance in *A. baumannii* vary greatly among different countries in Seweden only 13% and 10% of *Acinetobacter* isolates were resistant to imipenem and meropenem, respectively (Fraenkel et al., 2006). Several factors may have contributed to the emergence of CRAB in developing countries such as Iran. First, the emergence of carbapenem resistance in *A. baumannii* is related to the misuse, overuse of antibiotics and this is exacerbated by lack of standard treatment guidelines (Jabalameli et al., 2018). Second, poor infection control practices by healthcare professionals and overcrowding of hospitals have played an important role in the emergence of CRAB in Iran (Alp et al., 2011; Alp and Damani, 2015; Emaneini et al., 2016). Third, implementation of antimicrobial stewardship programs was poor in Iran (Esfandiari et al., 2016). Appropriate antimicrobial stewardship involves selecting an appropriate drug, dose, and duration of treatment, along with control of antibiotic use that prevents the emergence of resistance isolates such as CRAB (Dyar et al., 2017). Fourth, being bordered by countries with high prevalence of CRAB such as Pakestan, Iraq and Turkey may lead to the dissemination of CRAB within Iran; but this theory requires typing of the isolates (Sohrabi et al., 2012; Xie et al., 2018). Fifth, hand hygiene among Iranian healthcare workers and sanitary conditions (contamination of the hospital environment) are poor; thereby this organism can spread to patients by direct contact with the environment and by the hands of personnel (Emaneini et al., 2016; Emaneini et al., 2017). Sixth, the poor education and training of HCWs concerning prevention of transmission, lack of isolation rooms, inadequate contact precautions, lack of a good microbiological laboratory capacity and personal protective equipment

Table 1
Characteristics of studies included in the meta-analysis.

Study	Published time	Source	Province	Sample size	No. of imipenem resistant	No. of meropenem resistant	MBLs[a]			Class D		
										β- actamase (oxacillinases)		
							IMP (n)	VIM (N)	NDM (N)	OXA-23(n)	OXA-24 (n)	OXA-58(n)
Pournajaf (Pournajaf et al., 2018)	2018	Burn wounds	Tehran	73	69	ND	ND	ND	ND	ND	ND	ND
Armin (Armin et al., 2018)	2018	Clinical samples	Tabriz & Mashhad	171	68	68	N	6	3	ND	ND	ND
Shokri (Shokri et al., 2017)	2017	Clinical samples	Isfahan	110	ND	ND	ND	ND	4	ND	ND	ND
Sarikhani (Sarikhani et al., 2017)	2017	Clinical samples	Qom	108	97	97	ND	ND	ND	ND	ND	ND
Khosroshahi (Khosroshahi et al., 2017)	2017	Clinical samples	Tabriz	100	62	63	ND	ND	ND	ND	ND	ND
Moosavian (Moosavian et al., 2017)	2017	Clinical samples	Ahvaz	151	138	142	ND	ND	N	ND	ND	ND
Mohammadi (Mohammadi et al., 2017b)	2017	Burn wounds	Tehran	103	93	96	ND	ND	ND	93	40	1
Khodaei (Khodaei and Eftekhar, 2017)	2017	Clinical samples	Tehran	50	50	50	ND	ND	ND	ND	ND	ND
Bardbari (Bardbari et al., 2017)	2017	Clinical samples	Hamadan	75	71	73	ND	ND	ND	64	23	N
Mohajeri (Mohajeri et al., 2017)	2017	Clinical samples	Kermanshah	75	62	57	ND	ND	ND	60	14	N
Zarifi (Zarifi et al., 2017)	2017	Clinical samples	Mashhad	140	137	138	ND	ND	ND	ND	ND	ND
Mirshekar (Mirshekar et al., 2018)	2017	Clinical samples	Tehran	72	55	ND	ND	ND	N	61	22	N
Mohajeri (Mohajeri et al., 2016)	2017	Clinical samples	Kermanshah	104	50	50	ND	ND	ND	ND	ND	ND
Sarhaddi (Sarhaddi et al., 2017)	2017	Burn wounds	Mashhad	54	54	ND	38	38	ND	36	37	N
Madadi-Goli (Madadi-Goli et al., 2017)	2017	Clinical samples	Kashan	124	ND	ND	124	ND	ND	ND	ND	ND
Saffari (Saffari et al., 2017)	2017	Clinical samples	Bandar Abbas	64	ND	ND	ND	ND	ND	63	2	N
Mohammadi (Mohammadi et al., 2017a)	2017	Burn wounds	Tehran	100	94	89	ND	ND	ND	100	74	N
Salimizand (Salimizand et al., 2016)	2017	Clinical samples	Kurdistan	54	16	37	ND	ND	ND	28	N	N
Goudarzi (Goudarzi and Azimi, 2017)	2017	Clinical samples	Tehran	105	65	48	ND	ND	ND	ND	ND	ND
Azizi (Azizi et al., 2016)	2016	Clinical samples	Kerman	65	53	ND	ND	ND	ND	ND	ND	ND
Goudarzi (Goudarzi et al., 2016)	2016	Clinical samples	Tehran	120	112	75	ND	ND	ND	ND	ND	ND
Asadolah-Malayeri (Ostad Asadolah-Malayeri et al., 2016)	2016	Clinical samples	Tehran	60	52	58	ND	ND	ND	57	N	N
Maspi (Maspi et al., 2016)	2016	Clinical samples	Tehran	86	63	78	13	2	N	ND	ND	ND
Shoja (Shoja et al., 2016)	2016	Clinical samples	Ahvaz	124	97	91	ND	ND	ND	83	6	N
Tarashi (Tarashi et al., 2016)	2016	Clinical samples	Tehran	189	187	189	10	34	N	N	N	N
Alaei (Alaei et al., 2016)	2016	Clinical samples	Shiraz	85	73	79	ND	ND	ND	44	13	N
Moghadam (Moghadam et al., 2016)	2016	Clinical samples	Shiraz	98	94	95	23	14	ND	ND	ND	ND
Pourabbas (Pourabbas et al., 2016)	2016	Blood	Shiraz	59	59	59	N	1	ND	46	18	5
Davoodi (Davoodi et al., 2015)	2015	Clinical samples	Tehran	104	70	ND	ND	ND	ND	ND	ND	ND
Bagheri Josheghani (Bagheri Josheghani et al., 2015)	2015	Clinical samples	Kashan	124	106	108	ND	ND	ND	99	31	4
Farshadzadeh (Farshadzadeh et al., 2015)	2015	Burn wounds	Tehran	92	69	ND	ND	ND	N	ND	ND	ND
Kooti (Kooti et al., 2015)	2015	Clinical samples	Shiraz	200	197	199	ND	ND	ND	80	14	1
Goudarzi (Goudarzi et al., 2015)	2015	Clinical samples	Tehran	128	116	ND	5	9	N	ND	ND	ND
Zanganeh (Zanganeh and Eftekhar, 2015)	2015	Burn wounds, clinical isolates	Tehran	58	58	ND	ND	ND	ND	47	12	N
Bahador (Bahador et al., 2015)	2015	Burn wounds	Tehran	62	38	ND	ND	1	N	39	N	N
Safari (Safari et al., 2015)	2015	Clinical samples	Hamadan	100	87	95	N	30	ND	ND	ND	ND
Azimi (Azimi et al., 2015)	2015	Clinical samples	Tehran	126	108	ND	ND	ND	ND	ND	ND	ND
Karbasizadeh (Karbasizade et al., 2015)	2015	Clinical samples	Isfahan	50	25	25	ND	ND	ND	ND	ND	ND
Fallah (Fallah et al., 2014)	2014	Clinical samples	Tehran	108	99	99	ND	ND	ND	ND	ND	ND
Hojabri (Hojabri et al., 2014)	2014	Burn wounds, clinical isolates	Tehran & Tabriz	71	60	60	ND	ND	ND	47	24	N
Nasrolahei (Nasrolahei et al., 2014)	2014	Clinical samples	Tehran & Sari	100	67	74	ND	ND	ND	ND	ND	ND
Norozi (Norozi et al., 2014)	2014	Clinical samples	Kermanshah	84	68	63	ND	ND	ND	56	24	N
Fazeli (Fazeli et al., 2014)	2014	Clinical samples	Isfahan	121	ND	121	ND	ND	ND	ND	ND	ND
Peerayeh (Peerayeh et al., 2014)	2014	Clinical samples	Tehran & Bandar-Abbas	157	76	ND	ND	ND	ND	ND	ND	ND

(*continued on next page*)

Table 1 (*continued*)

Study	Published time	Source	Province	Sample size	No. of imipenem resistant	No. of meropenem resistant	MBLs[a]			Class D		
										β- actamase (oxacillinases)		
							IMP (n)	VIM (N)	NDM (N)	OXA-23(n)	OXA-24 (n)	OXA-58(n)
Mohajeri (Mohajeri et al., 2014)	2014	Clinical samples	Kermanshah	84	43	39	ND	ND	ND	ND	ND	ND
Sharif (Sharif et al., 2014)	2014	Clinical samples	Tehran	200	171	164	ND	ND	ND	ND	ND	ND
Abdi (Abdi-Ali et al., 2014)	2014	Clinical samples	Tehran	75	51	ND	ND	ND	ND	ND	ND	ND
Pajand (Pajand et al., 2013)	2013	Burn wounds, clinical isolates	Tehran	75	64	64	ND	ND	ND	51	36	N
Mohajeri (Mohajeri et al., 2013)	2013	Clinical samples	Kermanshah	104	83	78	ND	ND	ND	81	20	N
Azimi (Azimi et al., 2013)	2013	Burn wounds	Tehran	93	80	ND	ND	ND	ND	ND	ND	ND
Safari (Safari et al., 2013)	2013	Clinical samples	Hamadan	100	85	94	ND	ND	ND	ND	ND	ND
Peerayeh (Najar Peerayeh et al., 2013)	2013	Clinical samples	Tehran	123	83	104	ND	ND	ND	ND	ND	ND
Shoja (Shoja et al., 2013)	2013	Tracheal tube discharges	Ahvaz	206	198	198	ND	ND	N	175	18	N
Haeli (Haeili et al., 2013)	2013	Clinical samples	Tehran	136	102	ND	ND	ND	ND	ND	ND	ND
Vafaei (Vafaei et al., 2013)	2013	Clinical samples	Tehran	100	76	69	ND	ND	ND	ND	ND	ND
Goudarzi (Goudarzi et al., 2013)	2013	Clinical samples	Tehran	221	202	219	ND	ND	ND	123	3	28
Owlia (Owlia et al., 2012)	2012	Exudates of wounds	Tehran	126	107	ND	ND	ND	ND	ND	ND	ND
Farajnia (Farajnia et al., 2013)	2012	Clinical samples	Tabriz	100	62	63	ND	ND	ND	ND	ND	ND
Sohrabi (Sohrabi et al., 2012)	2012	Clinical samples	Tabriz	100	62	62	ND	ND	ND	ND	ND	ND
Mirnejad (Mirnejad et al., 2011)	2011	Clinical samples	Tehran	50	39	22	ND	ND	ND	ND	ND	ND
Peymani (Peymani et al., 2011)	2011	Clinical samples	Tabriz	100	53	56	ND	ND	ND	ND	ND	ND
Japoni (Japoni et al., 2011)	2011	Clinical samples	Shiraz	79	18	22	ND	ND	ND	ND	ND	ND
Taherikalani (Taherikalani et al., 2009)	2009	Clinical samples	Tehran	80	66	66	ND	ND	ND	20	12	17
Boroumand (Boroumand et al., 2009)	2009	Clinical samples	Tehran	191	47	ND	ND	ND	ND	ND	ND	ND
Feizabadi (Feizabadi et al., 2008)	2008	Clinical samples	Tehran	108	55	56	ND	ND	ND	ND	ND	ND

[a] MBLs: Metallo-β- lactamases, ND: Not detected, N: Negative.

Table 2
Meta-analysis of CRAB and carbapenemase genes.

Subgroups		No of study	Prevalence (95% CI)	n/N*	Heterogeneity test, I2 (%)	Heterogeneity test, *p* value	Begg's test	Egger's test
Imipenem resistance		60	81.1 (76.6–84.9)	4899/6281	93	< 0.001	0.00000	0.00000
Meropenem resistance		45	83.6 (78.7–87.5)	3889/4790	92.8	< 0.001	0.00007	0.00003
Class D	OXA-23	23	73.7 (66.5–79.8)	1649/2342	91.1	< 0.001	0.00471	0.00119
β- Actamases	OXA-24	20	21.9 (15.2–30.4)	472/2086	93.3	< 0.001	0.00368	0.00597
	OXA-58	6	6.2 (3.1–11.9)	66/920	81.4	< 0.001	0.1	0.008
MBLs*	IMP	6	16.7 (5–43.2)	89/555	95.8	< 0.001	0.2	0.4
	VIM	8	12.3 (5.3–25.8)	129/776	93.1	< 0.001	0.3	0.2
	NDM	2	2.7 (1.3–5.5)	7/281	90.2	< 0.001	0.1	0.3

n = number of events, N = total number of *A. baumannii* isolated from patient, MBLs: Metallo-β- lactamases

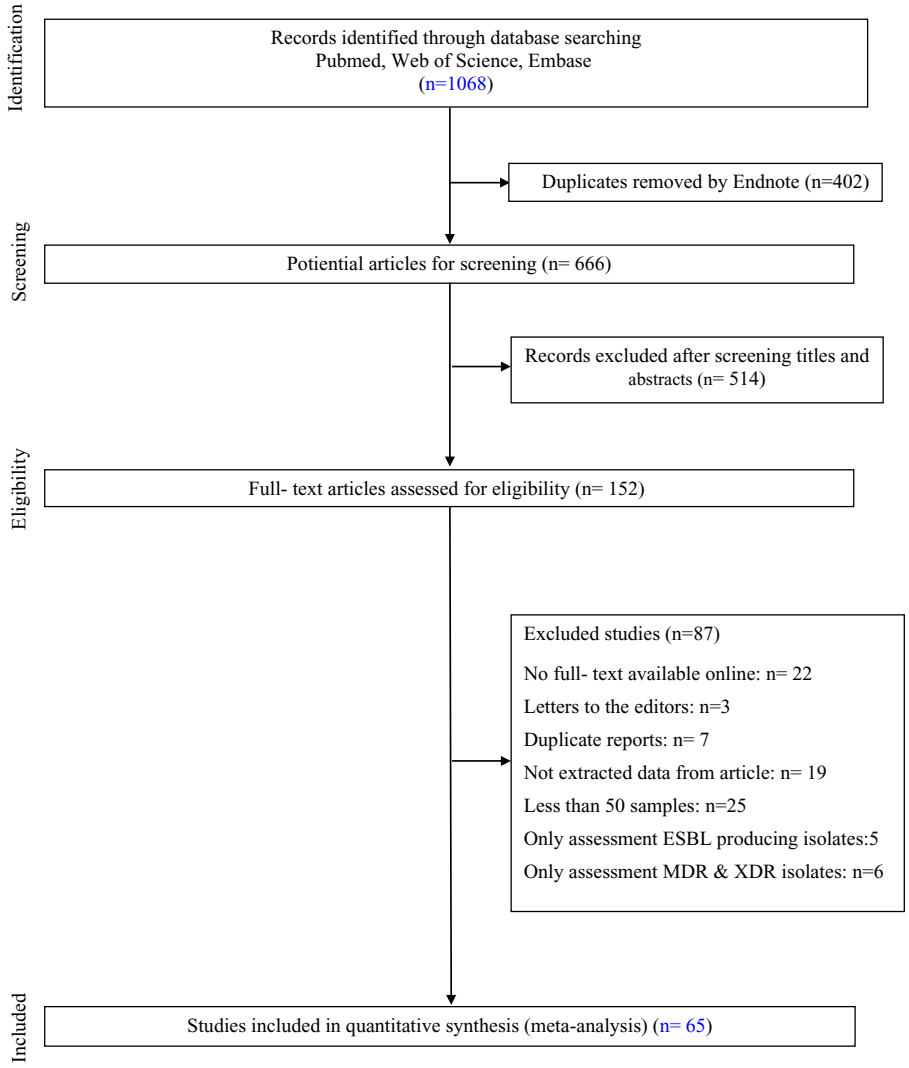
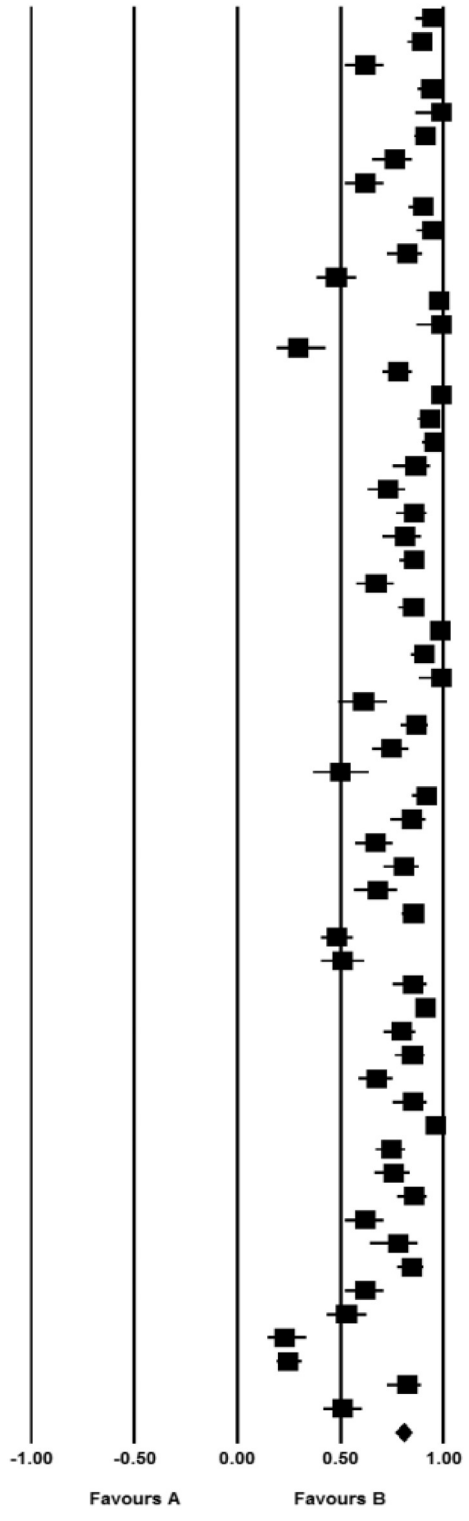


Fig. 1. Summary of the literature search and study selection.

have remained as a major challenge in Iranian hospitals (Alp et al., 2011; Alp and Damani, 2015; Emaneini et al., 2016; Esfandiari et al., 2016; Emaneini et al., 2017; Jabalameli et al., 2018). Based on our findings, the main cause of carbapenem resistance in *A. baumannii* is the expression of the class D (OXA) carbapenemases and, to a lesser extent, MBLs. The OXA-23 (73.7%) gene was the predominant carbapenemases in the Iranian *A. baumannii* isolates. This is not surprising, since OXA-23 has been found around the world (Hasan et al., 2014; Chang et al., 2015; Kamolvit et al., 2015; Mohd Rani et al., 2017). In our study, the prevalence of OXA-24 and OXA-58 was 21.9% and 6.2% respectively. In contrast to our findings, Villalón et al. from Spain, reported that 20.3% of *A. baumannii* harbored OXA-58 (Villalon et al., 2013). In other studies conducted in Nepal, Joshi et al. observed that none of the *A. baumannii* isolates harbored OXA-24 and OXA-58 (Joshi et al., 2017). In Saudi Arabia, El-Mahdy et al. revealed that 100% of *A. baumannii* harbored OXA-23, but OXA-24 and OXA-58 genes do not have role in resistance to carbapenem (El-Mahdy et al., 2017). In Egypt, Al-Agamy et al. reported that 7.5%, and 5% of *A. baumannii* harbored OXA-24 and OXA-58, respectively (Al-Agamy et al., 2014). Nemec et al. from Czech Republic reported that the major cause of carbapenem resistance in *A. baumannii* is the up-regulation of the chromosomal OXA-51-like β-lactamase, neither class D carbapenemases nor MBLs (Nemec et al., 2008).

Study name	Total	Event rate	Lower limit	Upper limit	Z-Value	p-Value
Pournajaf	69 / 73	0.945	0.863	0.979	5.537	0.000
Sarikhani	97 / 108	0.898	0.825	0.943	6.842	0.000
Khosroshahi	62 / 100	0.620	0.521	0.710	2.376	0.017
Mohammadi	94 / 100	0.940	0.873	0.973	6.535	0.000
Khodaei	50 / 50	0.990	0.862	0.999	3.247	0.001
Moosavian	138 / 151	0.914	0.857	0.949	8.143	0.000
Mirshekar	55 / 72	0.764	0.653	0.848	4.231	0.000
Goudarzi	65 / 105	0.619	0.523	0.707	2.416	0.016
Mohammadii	93 / 103	0.903	0.829	0.947	6.701	0.000
Bardbari	71 / 75	0.947	0.866	0.980	5.597	0.000
Mohajeri	62 / 75	0.827	0.724	0.897	5.121	0.000
Mohajei	50 / 104	0.481	0.387	0.576	-0.392	0.695
Zarifi	137 / 140	0.979	0.936	0.993	6.548	0.000
Sarhaddi	54 / 54	0.991	0.871	0.999	3.302	0.001
Salimizand	16 / 54	0.296	0.190	0.430	-2.902	0.004
Shoja	97 / 124	0.782	0.701	0.846	5.877	0.000
Tarashi	187 / 189	0.989	0.959	0.997	6.384	0.000
Goudarzii	112 / 120	0.933	0.872	0.966	7.211	0.000
Moghadam	94 / 98	0.959	0.896	0.985	6.184	0.000
Asadolah-Malayeri	52 / 60	0.867	0.755	0.932	4.929	0.000
Maspi	63 / 86	0.733	0.630	0.815	4.136	0.000
Alaei	73 / 85	0.859	0.768	0.918	5.796	0.000
Azizi	53 / 65	0.815	0.702	0.892	4.646	0.000
Azimi	108 / 126	0.857	0.785	0.908	7.038	0.000
Davoodi	70 / 104	0.673	0.577	0.756	3.455	0.001
Bagheri Josheghani	106 / 124	0.855	0.781	0.907	6.955	0.000
Kooti	197 / 200	0.985	0.955	0.995	7.193	0.000
Goudarz	116 / 128	0.906	0.842	0.946	7.481	0.000
Zanganeh	58 / 58	0.992	0.879	0.999	3.353	0.001
Bahador	38 / 62	0.613	0.487	0.725	1.762	0.078
Safari	87 / 100	0.870	0.789	0.923	6.393	0.000
Farshadzadeh	69 / 92	0.750	0.652	0.828	4.563	0.000
Karbasizadeh	25 / 50	0.500	0.365	0.635	0.000	1.000
Fallah	99 / 108	0.917	0.848	0.956	6.887	0.000
Hojabri	60 / 71	0.845	0.741	0.912	5.172	0.000
Nasrolahei	67 / 100	0.670	0.572	0.755	3.330	0.001
Norozi	68 / 84	0.810	0.711	0.880	5.207	0.000
Abdi-Ali	51 / 75	0.680	0.567	0.775	3.045	0.002
Sharif	171 / 200	0.855	0.799	0.897	8.835	0.000
Peerayeh	76 / 157	0.484	0.407	0.562	-0.399	0.690
Mohajri	43 / 84	0.512	0.406	0.617	0.218	0.827
Pajand	64 / 75	0.853	0.754	0.917	5.395	0.000
Godarzi	202 / 221	0.914	0.869	0.944	9.851	0.000
Mohajerii	83 / 104	0.798	0.710	0.864	5.626	0.000
Safarii	85 / 100	0.850	0.766	0.908	6.194	0.000
Karmostaji	83 / 123	0.675	0.587	0.752	3.792	0.000
Rezaee	64 / 75	0.853	0.754	0.917	5.395	0.000
Shojaa	198 / 206	0.961	0.924	0.980	8.898	0.000
Haeli	102 / 136	0.750	0.671	0.816	5.548	0.000
Vafaei	76 / 100	0.760	0.667	0.834	4.923	0.000
Azimii	80 / 93	0.860	0.774	0.917	6.076	0.000
Sohrabi	62 / 100	0.620	0.521	0.710	2.376	0.017
Mirnejad	39 / 50	0.780	0.645	0.874	3.707	0.000
Owlia	107 / 126	0.849	0.776	0.902	6.943	0.000
Farajnia	62 / 100	0.620	0.521	0.710	2.376	0.017
Peymani	53 / 100	0.530	0.432	0.625	0.600	0.549
Japoni	18 / 79	0.228	0.149	0.333	-4.550	0.000
Boroumand	47 / 191	0.246	0.190	0.312	-6.665	0.000
Taherikalani	66 / 80	0.825	0.726	0.894	5.270	0.000
Feizabadi	55 / 108	0.509	0.416	0.602	0.192	0.847
		0.811	0.766	0.849	10.564	0.000



Meta Analysis

Fig. 2. Forest plot of prevalence of imipenem-resistant *A. baumannii.*

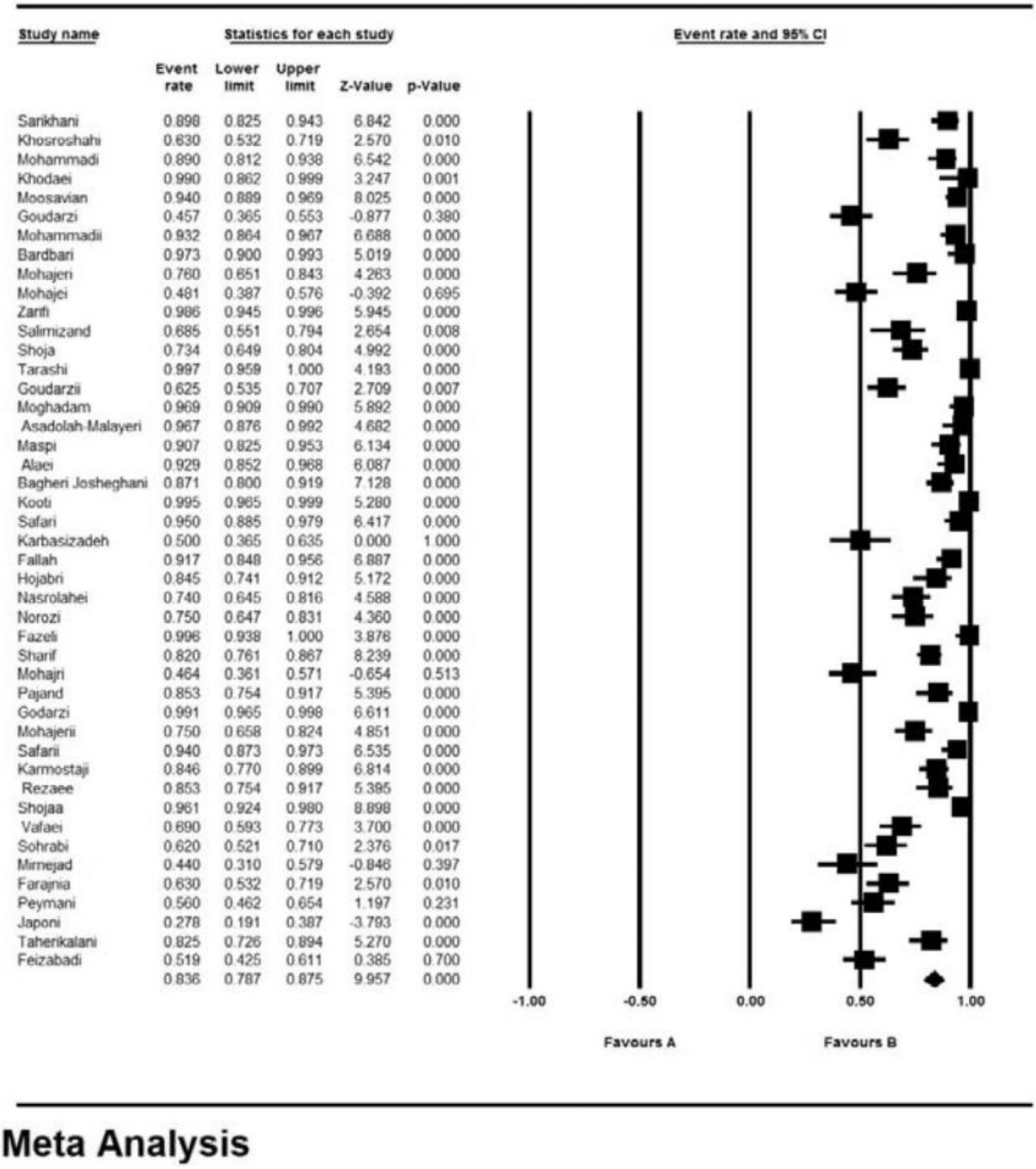


Fig. 3. Forest plot of prevalence of meropenem-resistant *A. baumannii.*

Our analyses also revealed that the most common types of MBLs are IMP, VIM and NDM genes, with the prevalence of 16.7%, 12.3% and 2.7%, respectively. IMP and VIM producing CRAB strains have been reported worldwide (Lee et al., 2005; Poirel and Nordmann, 2006; Loli et al., 2008). In contrast to our findings, Alkasaby et al. from Egypt reported that 95.7%, 7.1% and 42.9% of *A. baumannii* harbored IMP, VIM and GIM, respectively (Alkasaby and El Sayed Zaki, 2017). In the other report from Egypt, Gomaa et al. reported that 86.4% and 68% of *A. baumannii* harbored VIM and NDM genes, respectively (Gomaa et al., 2017). In Nepal, Joshi et al. reported that 13.6% of *A. baumannii* harbored NDM gene (Joshi et al., 2017). These great differences in oxacillinases and MBLs prevalence between different countries are probably due to antimicrobial selection pressure, horizontal transfer of carbapenemase genes by mobile genetic elements (plasmids) between different species, spread of particular clones carrying these genes, and the number of isolates examined (Bourafa et al., 2018). The current review has some limitations. First, the studies could not fully indicate the prevalence of carbapenem resistance and carbapenemase genes in Iran because the magnitude of the issue is not yet determined in different areas of the country. Second, only published articles were considered in the current meta-analysis; exactly like any other meta-analysis, the potential for publication bias should be considered. Third, heterogeneity was observed among the studies included. Fourth, lack of information concerning the epidemiological data (sex, age and wards) should be considered. In conclusion, this current systematic review indicated that carbapenem resistance rates are high in Iran and this class of drug is not recommended for treating infections due to *A. baumannii*. Thereby, improvements in infection control practices and

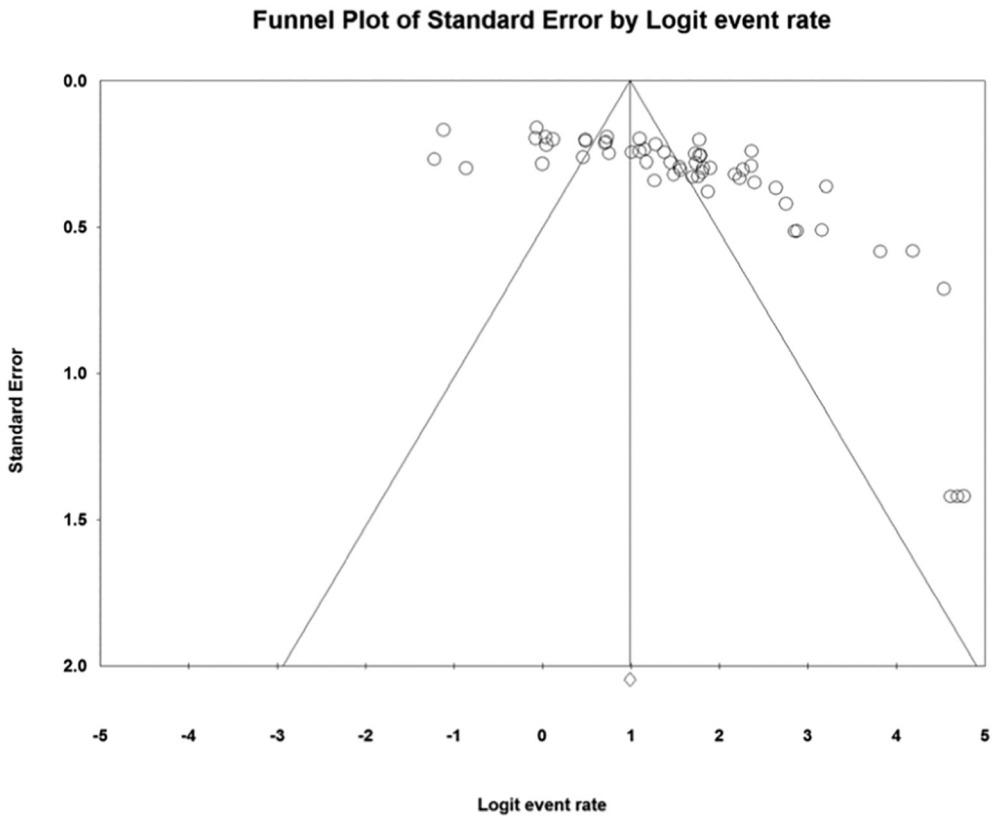


Fig. 4. Funnel plot of prevalence of imipenem -resistant *A. baumannii* (Asymmetric shape of funnel plot indicates bias in this meta-analysis) indicates.

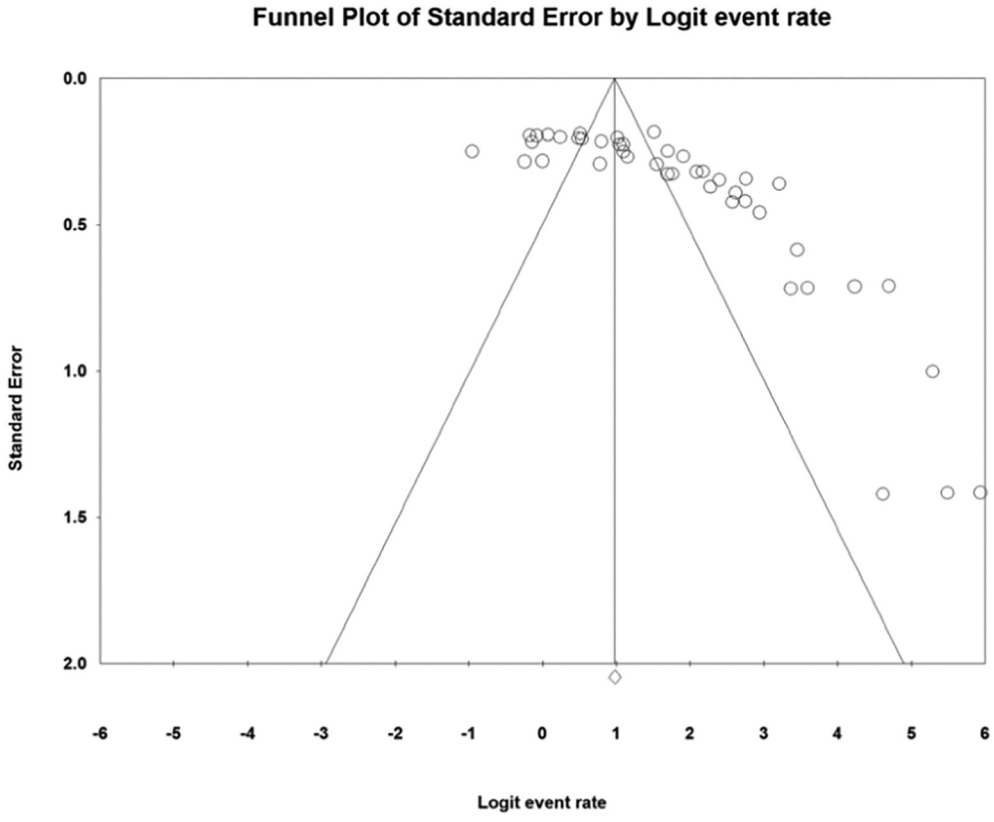


Fig. 5. Funnel plot of prevalence of meropenem -resistant *A. baumannii* (Asymmetric shape of funnel plot indicates bias in this meta-analysis) indicates.

antimicrobial stewardship are recommended strategies for prevention and spread of these strains (Fig. 5).

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Conflict of interests

None declared.

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