Reviews in Clinical Medicine

Colistin resistance burden among clinical isolates of gram-negative rods: A systematic review and meta-analysis

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ABSTRACT

Introduction: In recent decades, the inappropriate use of antibiotics and the existence of transferable resistant elements have caused the emergence of multidrug-resistant (MDR) gram-negative organisms. Antimicrobial resistance is becoming one of the major challenges to public health and has caused morbidity and mortality worldwide. The purpose of this study was the assessment of the prevalence and frequency of colistin resistance among gram-negative bacilli (Enterobacteriaceae, Acinetobacter spp., and Pseudomonas spp.) in Iran and around the world.

Methods: For this systematic review and meta-analysis, we searched international and national databases, including PubMed, Google Scholar, SID, and Magiran, from 1998 to 2018 for articles and abstracts describing colistin resistance among gram-negative bacilli. We have included 92 studies that met our inclusion criteria, and the outcomes were combined using a random-effects model to derive the event rate of colistin resistance among gram-negative bacilli. Data were analyzed by the Comprehensive Meta-Analysis Software (V2), and the heterogeneity of the studies was assessed using the I2 index.

Results: Out of the 11050 papers identified, 92 studies met the strict inclusion criteria and were finally included. The overall event rate of colistin resistance among gram-negative bacilli (GNB) was about 6.6%, while the event rate of colistin resistance among Acinetobacter spp. (n = 18504) was 2.8% (summary: 95% confidence interval (CI): [0.02, 0.041], P = 0.001, I2 = 70, df (Q) = 36, Q-value = 121.924). The colistin resistance among Pseudomonas spp. (n = 15094) was 3% (95% CI: [0.022, 0.041], P = 0.001, I2 = 68.3, df (Q) = 25, Q-value = 85.648), and the colistin resistance among Enterobacteriaceae spp. (n = 44772) was 0.8% (95% CI: [0.004, 0.014], P = 0.001, I2 = 87.6, df (Q) = 15, Q-value = 71.291). Therefore, the event rate of resistance to colistin among GNB was relatively low (6.6%).

Conclusion: The event rate of resistance to colistin among GNB was low. Therefore, this antimicrobial agent can still be administered as a suitable option against GNB that are resistant to other antibiotics such as carbapenems.

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Introduction

Recently, the inappropriate use of antibiotics and the existence of transferable resistant elements have caused the emergence of multidrug-resistant (MDR) gram-negative organisms (i.e., resistant to ≥ 1 drug(s) in 3 or more antimicrobial drug classes) (1, 2). Antimicrobial resistance is becoming one of the major challenges to public health and has caused morbidity and mortality worldwide (3). Infections by MDR bacterial strain can cause treatment failure, increased medical costs, prolonged hospital stays, and heavy socioeconomic burdens (4). The prevalence of antibiotic resistance and the absence of effective antibiotics have gradually reduced the treatment options for infectious diseases (5). Especially, the MDR strains of Acinetobacter baumannii have been declared as a significant worldwide threat by the World Health Organization (WHO) (6). Colistin (Polymyxin E) has antimicrobial activity against gram-negative bacilli (GNB) such as Escherichia coli, Klebsiella pneumonia, Acinetobacter spp., and Pseudomonas aeruginosa (7). The increasing rate of MDR in gram-negative bacilli has led to the use of colistin as an effective agent against organisms, considered as the last resort treatment for infections caused by MDR gram-negative bacilli (8).

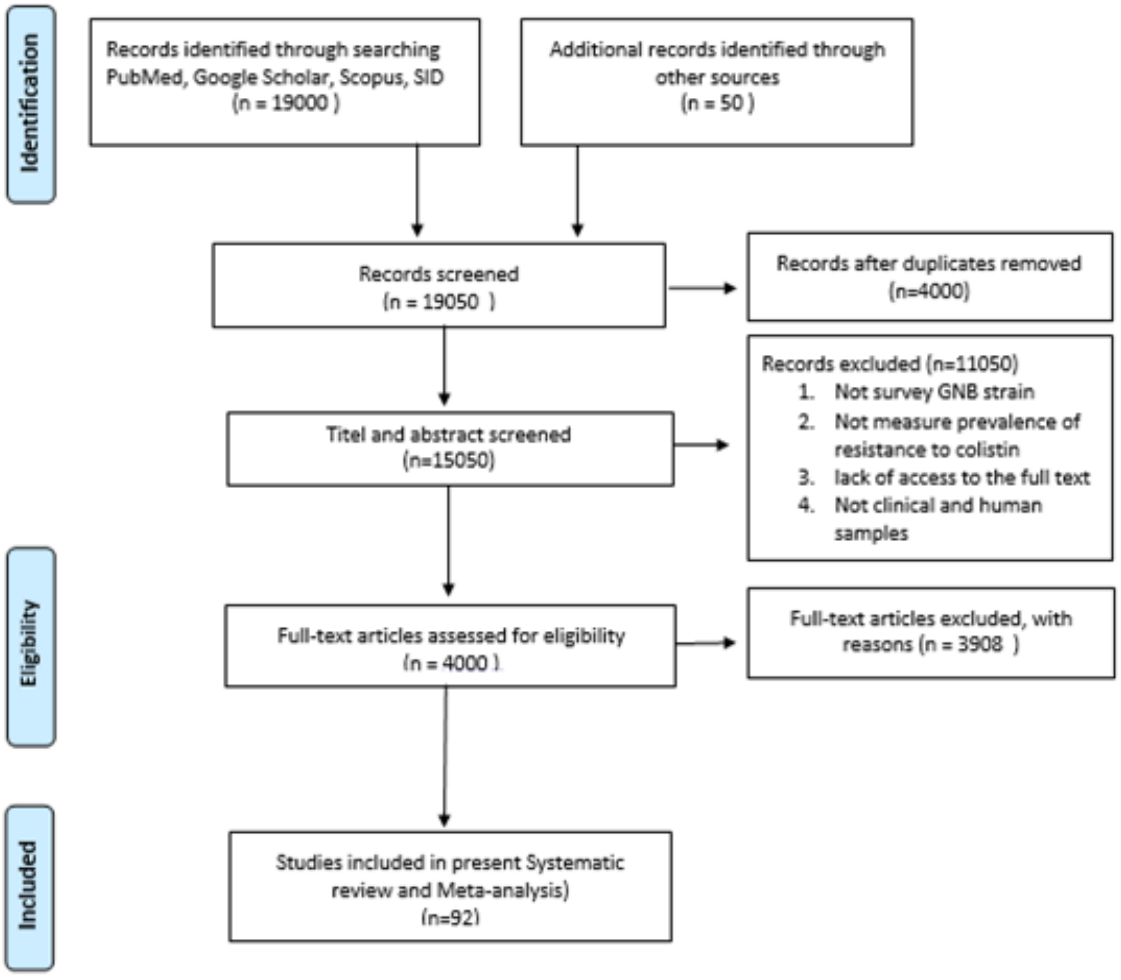
Colistin has a significant efficacy to prevent the dissemination of GNB infections and can also treat critical diseases such as ventilator-associated pneumonia (VAP), bacteremia caused by multidrug-resistant bacteria, and P. aeruginosa lung infections in the cystic fibrosis patients. It has thus become a suitable agent against GNB infections. Moreover, colistin is the only drug that is known to be universally active against multi-resistant clinical strains (9, 10). Therefore, to control the resistance of antimicrobial agents to colistin is of great importance. Unfortunately, in recent years, the inappropriate use of colistin has given rise to increased GNB strains resistant to colistin (11). The mechanisms of the resistance to colistin have not been completely understood; however, there are several hypotheses such as the alteration of the bacterial outer membrane, reduced levels of a specific outer membrane protein, decrease of Mg2+ and Ca2+ contents in the cell envelope, lipid alterations, efflux pumps (such as MexAB-OprM and MexXY-OprM), the elevation of the outer membrane protein H1 levels, and specific modifications of the lipid A component of the outer membrane lipopolysaccharide (LPS) (12-14). However, the prevalence of resistance to colistin is not very high (1, 15). Facing the challenge of increasing bacterial resistance, we cannot just expect the discovery of new powerful antibiotics; therefore, practical approaches to more efficiently use |existing antibiotics such as colistin should be considered (16). This study aimed to analyze the prevalence and frequency of colistin resistance among gram-negative bacilli in Iran and around the world.

Methods

Search strategy

This meta-analysis and systematic review has investigated the prevalence rate of resistance to colistin among clinical isolates of gram-negative bacilli in Iran

and around the world. We searched several well-known international biomedical databases including PubMed, Scopus, and Google Scholar along with Iranian databases such as Scientific Information Database (SID) and Magiran, from 1998 to 2018. We also searched for relevant articles that were presented in national and international congresses. Literature searches were done using these keywords (according to MeSH) and search terms: resistance, prevalence, colistin, and gram-negative bacilli, with all possible combinations. We selected articles after reading the abstracts. Then, we extracted the full text and removed any duplicate publication (e.g., published in both English and Persian) (Figure1).



SID- Iranian Scientific Information Data base

GNB- Gram Negative Bacilli

Figure1. Flowchart for literature search and study selection

Inclusion criteria

Among English and Persian articles/abstracts that were extracted, we included those with the following features: (i) Gram-negative bacilli were collected from clinical samples of the patients; (ii) research was conducted on human samples, not animals nor foods; (iii) studies that measured the prevalence of resistance to colistin in gram-negative bacilli were chosen to be included in this meta-analysis and systematic review. Phenotypic methods, such as the disc diffusion method or Kirby-Bauer and E-test according to the CLSI (clinical and laboratory standard institute), had been done to find colistin-resistant strains among gram-negative bacilli in most of the studies. We limited the search to original articles published in English or Persian. All original articles reporting on the prevalence of antimicrobial resistance to colistin in gram-negative bacilli were selected.

Exclusion criteria

The exclusion criteria were (i) not reporting the prevalence of resistance to colistin in clinical isolates of GNB; (ii) unrelated studies; (iii) low-quality articles; (iv) studies written in languages other than English and Persian; (v) samples that were not of human origin or were not clinical, or the origin of samples was not clear; (vi) meta-analyses and systematic reviews were also excluded.

Statistical analysis

The Comprehensive Meta-Analysis Software version 2 was used to calculate the pooled prevalence of resistance to colistin among gram-negative bacilli. Using the random-effects models, the summary effect estimates can determine an average of the study effect estimates which differ from one another.

Anywhere it was applicable, we applied the adjusted event rate. The crude effects estimates were used if adjusted estimates were not present. From the test of heterogeneity, the I_2 value and P-value were calculated to analyze whether there was evidence of between-study variation in the individual effect estimates, not due to random variation. The funnel plots were drawn, and we conducted the Egger's funnel plot asymmetry test to assess whether there was any publication bias.

Result

Our systematic and meta-analysis study has some limitations and publication biases, like other systematic reviews, which should be considered when interpreting the results. Due to differences in study design, the small sample size in some studies, and various approaches of data collection, the heterogeneity of data is visible. In addition, due to high heterogeneity in the results of our study, we had to eliminate some studies for each group of bacteria. Study heterogeneity may also be due to different patterns of taking antibiotics, based on the implications of the infectious disease in different geographic areas. Furthermore, the colistin resistance prevalence data were limited to a few countries and may not thus represent the worldwide trends. On the other hand, some studies had very different outcomes compared to others, which might be due to flaws in sampling or applying methods. Besides, since we were limited to English and Persian articles, studies written in other languages might have been missed. We had to also eliminate some studies from this review as their full text was not available. This systematic review and meta-analysis reveals weaknesses in the quality of colistin resistance data collected in different regions.

By assessing the titles and abstracts of different articles, 11050 out of 19050 articles were identified. About 4000 full-text papers

were reviewed, but only 92 studies met the strict inclusion criteria and were finally included. The characteristics of the included studies and data summaries are presented in Tables 1, 2, and 3. The colistin resistance among gram-negative bacilli was investigated in three main groups: *Acinetobacter* spp., *Pseudomonas* spp. and *Enterobacteriaceae* spp., where 63 studies provided information on the event rate of colistin resistance among *Acinetobacter* spp. (number of total samples (n) = 18504), 27 of them presented data for colistin resistance among *Pseudomonas* spp. (n = 15094), and 28 studies examined colistin resistance in *Enterobacteriaceae* spp. (n = 44772). The mean resistance to colistin among gram-negative bacilli was 6.6%.

Prevalence of colistin resistance among Acinetobacter spp.

As discussed, 63 studies reported colistin resistance among *Acinetobacter* spp. (n = 18504) (Figure 2). The most reported isolated resistant species were *A. baumannii* with the highest frequency in Iran and the world. The event rate of colistin resistance among *Acinetobacter* spp. was 2.8% (summary: 95% confidence interval (CI): [0.02, 0.041], P = 0.001, I_2 = 70, df (Q) = 36, Q-value = 121.924). Based on the funnel plot of the meta-analysis, we observed some evidence of publication bias, and a few studies with limited data were the source of this heterogeneity (Figure 3). A subgroup analysis in Iran revealed that the prevalence of colistin resistance was higher in Kerman, Mazandaran, Tabriz, and Isfahan, while the prevalence was the lowest in Tehran and Ahvaz (Table 1).

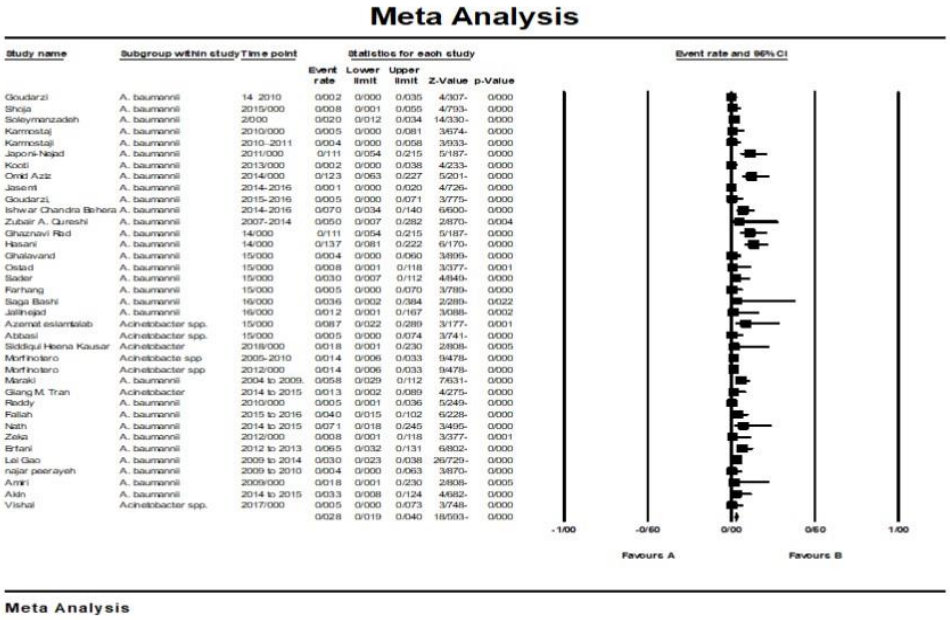


Figure 2. Forest plot,Acinetobacter

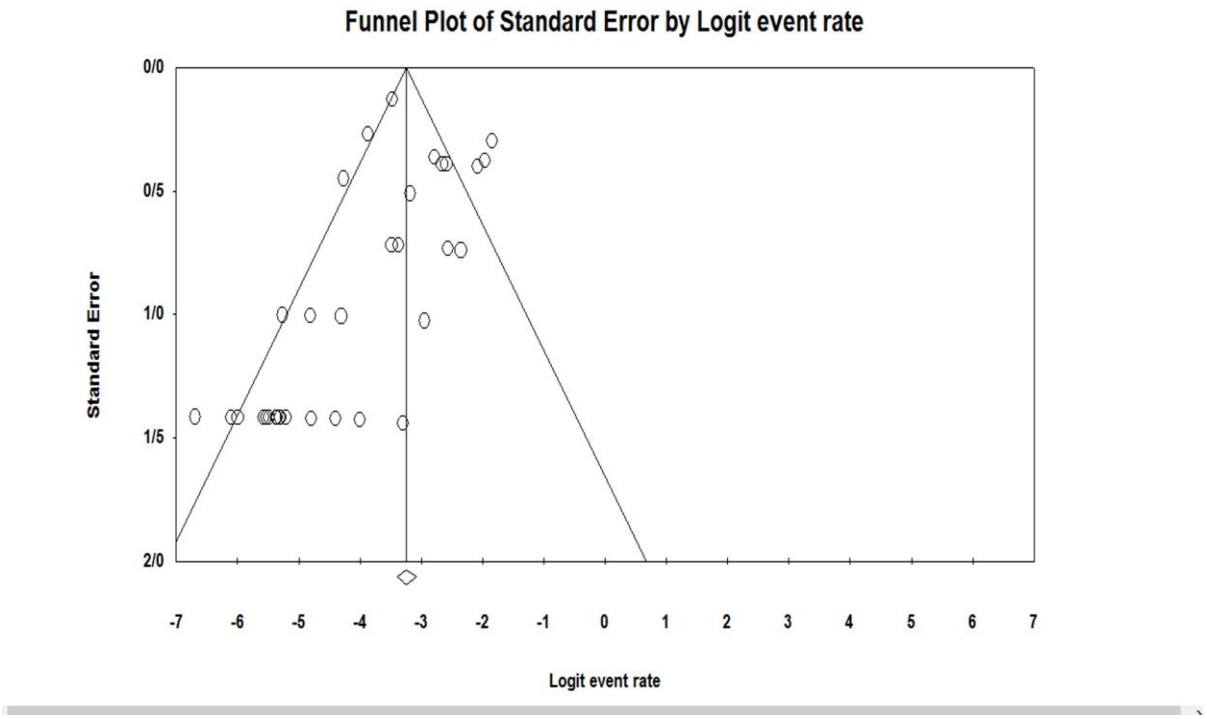


Figure 3. funnel plot, Acinetobacter

Table 1. Summary of studies regarding the prevalence of antimicrobial resistance to colistin in *Acinetobacter* spp.

First author publication Year Reference	Time of study	Country/City	Number of strains	Number of susceptible strains	Number of resistance strains
Maraki 2012 44	2004-2009	Greece	137	129	8
Amiri 2017 45	2009	Algeria and Tunisia	27	27	0
Moradi 2014 46	2009-2010	Tehran and Bandar Abbas	154	154	0
Soo Ko 2007 47	2002-2006	Korea	214	149	65
Hsieh 2014 48	2010	Northern Taiwan	557	557	0
Salimizand 2015 25	2012	Kerman	40	2	38
Reddy 2015 49	2010	South Africa	194	193	1
Goudarzi 2017 50	2015-2016	Tehran	105	105	0
Goudarzi 2013	2010	Tehran	221	221	0

51					
Mohammadi 2017 52	2013-2014	Tehran	100	100	0
Shoja 2016 53	2015	Ahvaz	124	123	1
Shoja 2017 54	2011-2012	Ahvaz	40	39	1
Kooti 2015 55	2012-2013	Shiraz	200	200	0
Izadi 2017 33	2014-2015	West of Iran	100	88	12
Karmostaj 2013 56	2010-2011	Tehran	131	131	0
Japoni-Nejad 2013 37	2011	Central part of Iran	63	56	7
Rahimzadeh 2012 57	2009-2010	Tabriz	100	77	23
Omid Aziz 2014 58	2013	Kerman	65	57	8
Shu-Chen Kuo 2012 59	2002-2010	Taiwan	1640	1637	3
Jasemi 2016 60	2014-2016	Tehran	401	401	0
Bagheri-Nesami 2017 61	2014-2015	Mazandaran	27	18	9
Khosroshahi 2017 62	2016	Tabriz	100	77	23
Behera 2017 38	2014-2016	India	100	93	7
Qureshi 2015 63	2007-2014	Pittsburgh	20	19	1
Ghaznavi Rad 2013 44	2011	Arak	63	56	7
Ghalavand 2014 64	2014	Tehran	125	125	0
Malayeri 2014 47	2013	Tehran	60	60	0
Soleymanzadeh 2015 65	2012-2013	Tehran	685	672	13

Rastegar Lari 2013 66	2010-2011	Tehran	68	68	0
Owlia 2012 67	2010-2011	Tehran	126	126	0
Farhang 2014 68	2014	Isfahan	107	107	0
Yousefian 2014 69	2014	Isfahan	96	45	51
Angoti 2014 70	2013-2014	Tabriz	61	7	54
Saga Bashi 2015 71	2015	Tabriz & Uremia	13	13	0
Kholdi 2014 72	2014	Sari	100	65	35
Eslamtalab 2015 73	2014	Kerman	23	21	2
Abbasi 2014 74	2014	Tehran	100	100	0
Kausar 2018 75	2015	Aurangabad, India	27	27	0
Morfin-otero 2012 76	2005-2010	Mexico	362	357	5
Rahimzadeh 2012 57	2009-2010	Tabriz	100	77	23
Jamil 2018 24	2014	Pakistan	23	23	0
Giang M. Tran 2017 61	2014-2015	Vietnam	75	74	1
Salimizand 2015 25	2012	Kerman	40	2	38
Owrang 2017 77	2014-2015	Tehran	105	104	1
Kapoor 2014 78	2010-2012	India	92	92	0
Fallah 2017 79	2015-2016	Tabriz	100	64	4
Lee 2014 80	2010	Taiwan	577	577	0
Nath 2016	2014-2015	India	28	26	2

81					
Zeka 2013 82	2013	Turkey	60	60	0
Erfani 2013 83	2012-2013	Tehran	107	100	7
Lei Gao 2017 84	2009-2014	China	2031	1970	61
Alaei 2015 85	2010-2011	Shiraz	85	72	13
Rossia 2017 86	2010-2014	Brazil	7446	7342	104
Khatun 2018 87	2016	India	115	115	0
AkIn 2018 88	2014-2015	Turkey	60	58	24
Khosroshahi 2017 62	2017	Tabriz	100	77	23
Tarashi 2016 89	2012-2015	Tehran	189	189	0
Gholami 2015 90	2013	Tehran	60	60	0
Farsiani 2015 91	2012	Mashhad	36	36	0
Vakili 2014 92	2011-2012	Isfahan	60	53	7
Fattouh 2014 93	2013-2014	Egypt	21	21	0
Mahdian 2015 94	2015	Tehran	37	37	0

Prevalence of colistin resistance among Pseudomonas spp.

Out of all studies with a focus on colistin resistance in *Pseudomonas* spp., 30 were included in this systematic review (Figure 4). The number of isolates from these articles was 15094 samples (Table 2). The colistin resistance among *Pseudomonas* spp. was 3% (95% CI: [0.022, 0.041], $P = 0.001$, $I_2 = 68.3$, df (Q) = 25, Q-value = 85.648). Based on the funnel plot of the meta-analysis, we observed some evidence of publication bias where this heterogeneity was due to some studies with limited data (Figure 5). It was seen that the event rate of colistin resistance in these bacteria in Iran was higher in Mazandaran and Tabriz.

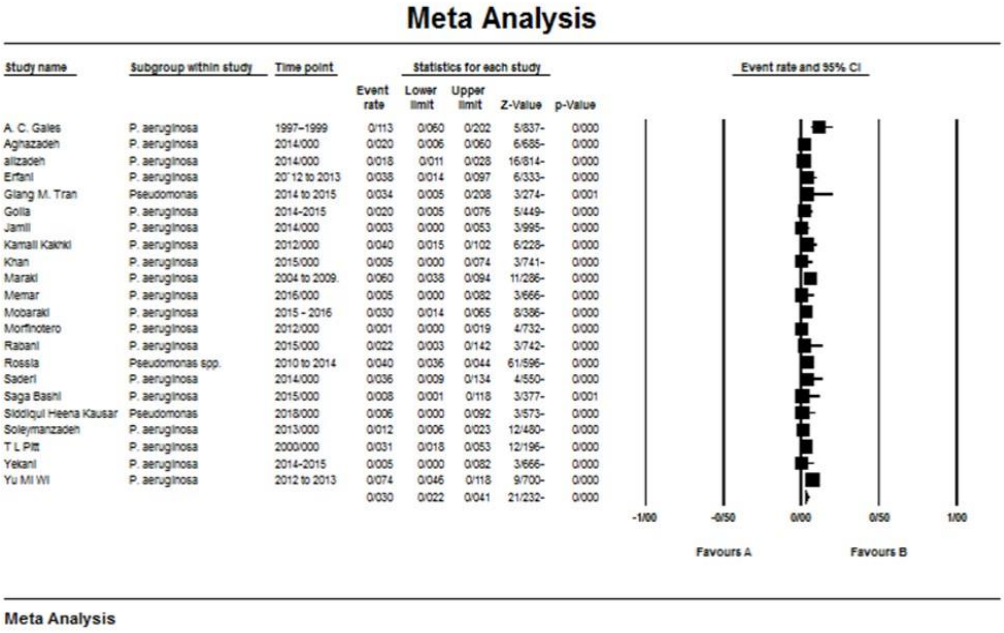


Figure 4. Forest plot, Pseudomonas

Table 2. Summary of studies on the prevalence of antimicrobial resistance to colistin in *Pseudomonas* Spp

First author publication Year Reference	Time of Study	Country/City	Number of strains	Number of susceptible strains	Number of resistance strains
Goli 2016 11	2014-2015	Tabriz	100	98	2
Aghazadeh 2016 95	2013-2014	Tabriz	151	148	3
Bagheri 2017 61	2015	Mazandaran	24	9	15
Rossi 2016 96	2010-2014	Brazil	9786	9395	391
Khan 2016 97	2015	India	100	100	0
Tran 2017 98	2014-2015	Vietnam	29	28	1
Wi YM 2017 1	2012-2013	South Korea	215	199	16
Pitt	2000	London	417	404	13

2003 99					
Jamil 2018 24	2014	Pakistan	143	143	0
Maraki 2012 100	2004 to 2009	Greece	298	280	18
Gales 2001 101	1998	Asia-Pacific, Europe, Latin America, and the United States/Canada.	80	80	0
Morfin-otero 2012 76	2005-2010	Mexico	404	404	0
Kausar 2018 75	2015	Aurangabad	79	79	0
Rabani 2015 102	2015	Shiraz	45	44	1
Saga Bashi 2015 103	2015	Tabriz	60	60	0
Ghotaslou 2016 104	2014-2015	Tabriz	90	90	0
Alizadeh 2014 81	2014	Tabriz	1000	982	18
Saderi 2014 105	2014	Tehran	55	53	2
Memar 2016 106	2016	Tabriz	90	90	0
Khorvash 2017 107	2012-2013	Isfahan	48	24	24
Nahaei 2007 27	2007	Tabriz	135	35	100
Mobaraki 2018 108	2015-2016	Tabriz	200	194	6
Khalil 2015 109	2010-2011	Egypt	104	42	62
Bagheri-Nesami 2017 61	2017	Mazandaran	21	8	13
Soleymanzadeh 2015 65	2012-2013	Tehran	685	678	7
Tarashi 2016 89	2012-2015	Tehran	309	309-306	0-3
Erfani	2012-2013	Tehran	105	101	4

2017 110					
Azimi 2016 111	2013-2014	Tabriz	160	160-157	0-3
Dawodeyah 2018 112	2018	Amman	61	61	0
Safari 2014 113	2012	Hamadan	100	96	4

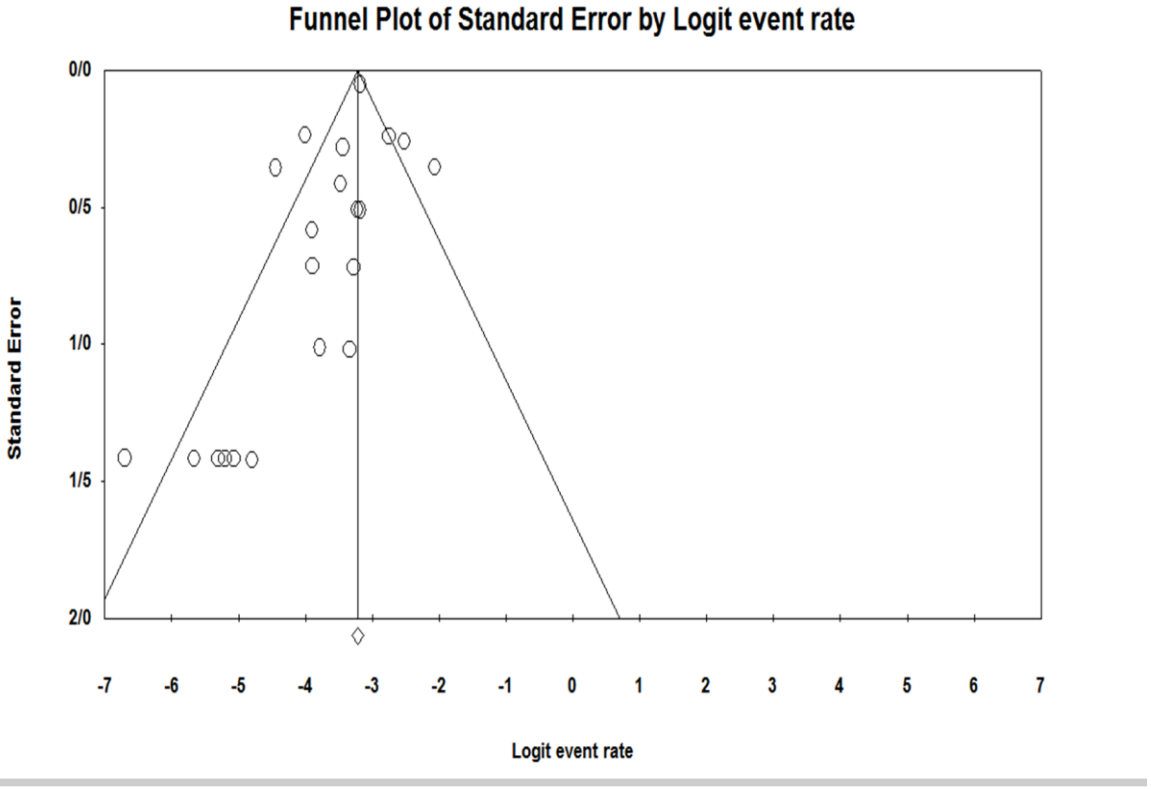


Figure 5. Funnel plot, Pseudomonas

Prevalence of colistin resistance among Enterobacteriaceae

Twenty-seven studies reported colistin resistance among *Enterobacteriaceae* spp. The number of isolates from these 27 articles were 44772 samples (Figure 6).

The prevalence of colistin resistance in *Enterobacteriaceae* was 0.8% (95% CI:

[0.004, 0.014], $P = 0.001$, $I_2 = 87.6$, df (Q) = 15, Q-value = 71.291). The funnel plot revealed some evidence of publication bias

due to a few studies with limited data (Figure 7).

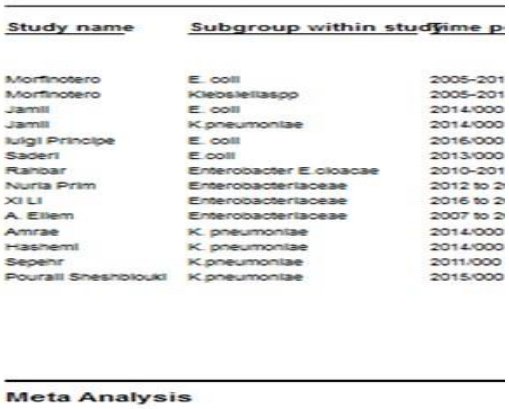


Figure 6. Forest plot, Enterobacteriacea

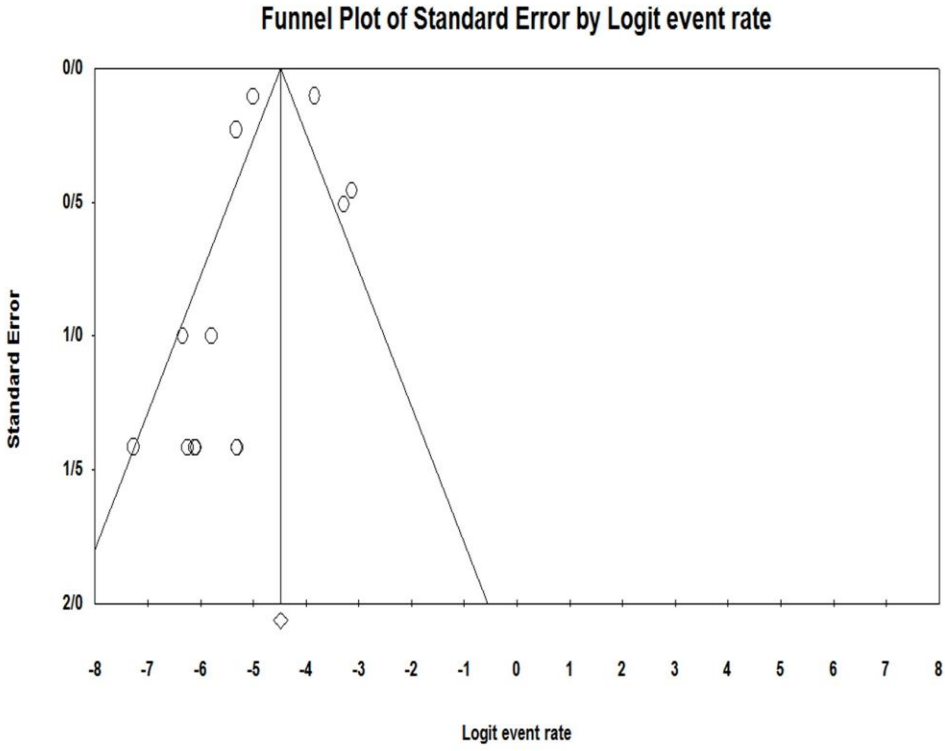


Figure 7. Funnel plot, Enterobacteriacea.

Table3. Summary of studies on the prevalence of antimicrobial resistance to colistin in *Enterobacteriaceae* spp.

First author publication Year Reference	Time of Study	Country/City	Strain	Number of strains	Number of susceptible strains	Number of resistance strains
Zakeri 2012 114	2012	Tabriz	*E. coli*	200	188	12
Liassine 2016 115	2016	Switzerland	*Enterobacteriaceae*	2049	2043	6
Hashemi 2014 116	2011-2012	Tehran	*K. pneumonia*	100	100	0
Marchaim 2014 117	2008-2009	Michigan	*Enterobacteriaceae*	92	77	15
Qamar 2017 39	2015-2016	Karachi, Pakistan	*Enterobacteriaceae*	251	211	40
Lübbert 2013 118	2010-2012	Germany	*K. pneumonia*	90	73	17
Marzi 2014 120	2012-2013	Turkey	*Enterobacteriaceae*	168	159	9
Maleki 2018 120	2015	Isfahan	*K. pneumonia*	100	100	0
Pourali 2015 121	2015	Shiraz	*K. pneumonia*	111	107	4
Saderi 2015 122	2015	Tehran	*E. coli*	715	715	0
Morfin-otero 2012 76	2005-2010	Mexico	*E. coli*	563	562	1
Morfin-otero 2012 76	2005-2010	Mexico	*Klebsiella spp.*	329	328	1
Lee 2011 123	2011	Korea	*Enterobacteriaceae*	344	313	31
Rahbar 2012 124	2010-2011	Tehran	*E. cloacae*	101	101	0
Toth 2010 26	2010	Hungary	*K. pneumonia*	9	1	8
Moubareck 2018 125	2015-2016	Dubai	*E. coli*	13	13	0
Jamil 2018 24	2014	Islamabad	*E. coli*	257	257	0
Principe	2016	Italy	*E. coli*	3902	3200	702

2018 126						
Prim 2017 127	2012-2015	Spain	*Enterobacteriaceae*	13579	13488	91
Li X 2018 128	2016-2017	Zhejiang, China	*Enterobacteriaceae*	224	224	0
Ellem 2017 129	2007-2016	Australia	*Enterobacteriaceae*	4555	4460	95
Rossi 2017 96	2010-2014	Brazil	*Enterobacteriaceae*	16533	15376	1157
Bathoorn 2016 28	2010 & 2013–14	Greece	*K. pneumoniae*	34	13	21
Moubareck 2018 125	2015-2016	Dubai	*K. pneumoniae*	70	48	22
AkIn 2018 88	2014-2015	Turkey	*Klebsiella spp.*	135	120	15
Jamil 2018 24	2014	Islamabad, Pakistan	*M. morganii*	28	0	28
Jamil 2018 24	2014	Islamabad, Pakistan	*K. pneumoniae*	220	220	0

Discussion

The widespread outbreak of multidrug-resistant gram-negative bacteria (MDR-GN bacteria) (i.e., resistant to ≥ 1 drug(s) in 3 or more classes of antimicrobial drugs) has raised concerns and promoted the use of polymyxins (colistin and polymyxin B) as the last-resort antibiotic option (17, 18). Furthermore, the occurrence of carbapenem resistance, extensively drug-resistant (XDR) organisms (i.e., resistant to all but two drug classes), and pandrug-resistant (PDR) (i.e., resistant to all drug classes) in infections caused by gram-negative bacilli has recently limited the effectiveness of antimicrobial agents or treatments (19, 20). The emergence of colistin-resistant strains is a critical problem as it limits the treatment options for infections caused by carbapenem-resistant gram-negative bacilli. Further, colistin should not be prescribed alone, and combination therapy should be considered (21). Moreover, this emerging intrinsic and gained antimicrobial resistance in gram-negative bacilli urges the appropriate use of colistin and the need for reliable susceptibility methods to predict the clinical response (5, 22, 23).

Despite the results of this study showing low resistance to colistin (6.6%), in some studies, the resistance rate to colistin was reported to be high with an alarming trend. Jamil et al. indicated that the amount of resistance to colistin in *Morganella morganii* was 100% (24). Salimizand et al. also reported that resistance to colistin in *Acinetobacter baumannii* was about 95% (25). In another study, colistin resistance in *Klebsiella pneumonia* was found to be about 88.9% (26). Nahaei et al. reported a resistance rate of 74% (27) in *Pseudomonas* Spp., and Bathoorn et al. indicated a resistance rate of about 61% in *K. pneumoniae* (28). Fortunately, in most studies, the prevalence of colistin resistance was 0% (Tables 1-3). Some factors affect the reported resistance of organisms to colistin, for example different testing methods such as disc susceptibility and dilution methods that are considered more reliable for susceptibility testing of colistin (16, 29-31). Another factor is the geographical variance of where the samples were isolated, also affecting the pattern of antibiotic-resistant isolates. Depending on the treatment strategy, the resistance pattern changes (32). Colistin is a lipopeptide antibiotic also effective for infections of the urinary tract, wounds, and bloodstream (33). The variation observed for colistin resistance in different studies may be associated with several factors such as the public health condition, availability of antibiotics, type and severity of the disease, sample size, and the resistance mechanism of the organisms (34).

Colistin however causes nephrotoxic problems. Although the use of this antibiotic class has limitations because of its toxicity, it is frequently used for life-threatening infections (35, 36). Colistin is prescribed as the last line of treatment for gram-negative bacilli; the increase in the prevalence rate of resistance to this antibiotic can therefore be alarming for the health care systems (37). According to existing data, the rate of resistance to colistin among Iranians (except a few cities) is much lower compared to neighboring countries such as Pakistan and India (38, 39). One of the possible reasons for this lower colistin resistance in Iran can be the sanctions that have made this antibiotic less accessible in Iran.

Combination therapy could be a suitable solution to reduce antibiotic resistance, and it will also increase the efficiency of antibiotic therapy in infectious diseases. Previous meta-analyses reported that the combination of

different antibiotics could enhance the bactericidal activity and act synergistically against GNB such as *A. baumannii* (40, 41). For example, colistin-glycopeptide and polymyxin–carbapenem combinations have a considerable synergistic effect, enhancing the bactericidal activity, and relatively low toxicity in comparison with monotherapy. The antibiotic that is commonly used in combination with colistin is rifampin. The synergic mechanism of these two will increase the colistin's effect on the outer membrane of gram-negative bacilli that enhances the rifampin penetration into the bacterial cell (41-43).

Utilization of accurate methods for the identification of colistin resistance in diagnostic laboratories, improved monitoring along with the report of resistance cases, and raised awareness of clinical microbiologists and infection control specialists can all help controlling resistance to colistin among gram-negative bacilli.

Conclusion

This study, which is a systematic review and meta-analysis of the existing data, revealed that the rate of resistance to colistin is low in many studies. It is therefore suggested that the best class of antibiotics to be used for MDR, XDR, or PDR gram-negative bacilli is polymyxins (colistin & polymyxin B), and it is considered a viable agent to manage MDR gram-negative bacilli outbreaks, especially in developing countries.

On the other hand, since a dramatic rise of colistin resistance in gram-negative bacilli has been reported in some studies, our findings demonstrated the urgent need for effective and comprehensive monitoring of antimicrobial resistance in GNB. It is also essential to use antibiotics cautiously to prevent the emergence of colistin-resistant strains. This is a growing public health concern, particularly in the clinical management of the patients with life-threatening gram-negative bacilli, especially *A. baumannii*, infections.

In summary, the growing resistance rate against colistin among gram-negative bacilli underlines the urgency to comprehensively monitor antimicrobial drug resistance. To prevent and manage resistance to colistin, antibiotic susceptibility testing, the establishment of diagnostic laboratories with advanced equipment, and continuous monitoring of the resistance reports and patterns are the recommended steps and approaches.

Conflict of Interest: None

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