Review Article

Colistin Resistance among Multi-Drug Resistant Gram-Negative Bacteria in Iran: A Systematic Review and Meta-Analysis

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Abstract

Background: Colistin, a last-resort antibiotic, faces a growing threat from antibiotic resistance. This study aims to comprehensively assess colistin resistance in clinical isolates of Escherichia coli, Pseudomonas aeruginosa, Acinetobacter baumannii, and Klebsiella pneumoniae in Iran.

Materials and Methods: Relevant studies on the prevalence of colistin resistance among multidrug-resistant Gram-negative bacteria in Iran, published up to December 15, 2023, were identified through searches of databases such as PubMed/Medline, EMBASE, and Scopus. The overall frequency of colistin resistance for each bacterial species was determined using CMA version 3.

Results: The comprehensive analysis of clinical isolates revealed varying frequencies of colistin resistance among the studied Gram-negative bacteria. *E. coli* displayed a resistance rate of 3.6%, while *P. aeruginosa* exhibited a rate of 6.5%. *A. baumannii* demonstrated a resistance rate of 4.7%, and *K. pneumoniae* displayed the highest resistance rate at 7.2%. Importantly, the analysis found no significant evidence of publication bias, enhancing the reliability of these resistance rate estimates.

Conclusion: Colistin resistance among these clinically significant Gram-negative bacteria in Iran is rising, limiting treatment options and posing serious challenges to healthcare providers. These findings underscore the urgency of enhanced surveillance, the development of alternative treatments, and the implementation of strict infection control measures. Addressing colistin resistance is crucial to effectively managing infections caused by these pathogens in Iran and globally.

Keywords: Colistin resistance, *Klebsiella* pneumonia, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Escherichia coli*, Iran

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Introduction

Multidrug-resistant Gram-negative bacteria (MDR-GNB) strains pose significant challenges, leading to severe infections and unfavorable clinical outcomes[1, 2]. Recognizing the urgency of the situation, the World

Health Organization (WHO) emphasized in 2017 the critical need for research, discovery, and development of new antimicrobials targeting *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and Enterobacteriaceae[3]. Over the past decades, there has been an increase in the spectrum of resistance of GNB to various antibiotics, including cephalosporins, ciprofloxacin, and carbapenems, significantly narrowing down treatment options to agents like polymyxins. Polymyxin E, commonly known as colistin, represents a last-line treatment option for MDR-GNB infections[4-7].

Although colistin's clinical use has been impacted by its high nephrotoxicity and neurotoxicity, its reintroduction into clinical practice has been necessitated by the growing reports of resistance among GNB worldwide[8-10]. However, the heavy use of colistin has contributed to the emergence of colistin resistance in several bacterial species.

Iran, one of the largest countries in Asia, has reported elevated levels of antibiotic resistance in major GNBs. However, most available surveys provide localized information, lacking a comprehensive analysis. As a result, this study has been designed to perform a systematic review and meta-analysis to ascertain the prevalence of colistin-resistant *A. baumannii*, *P. aeruginosa*, *Escherichia coli*, and *Klebsiella pneumoniae* in Iran.

Methods

The current investigation adhered to the PRISMA guidelines, and the preliminary protocol was registered with PROSPERO (registration ID: pending, ID: 459938)[11].

Search strategy: A systematic search was conducted in medical databases, including PubMed/Medline, EMBASE, and Scopus, to identify pertinent studies reporting the prevalence of colistin resistance among MDR-GNB in Iran, with a publication date up to Dec 15, 2023. Only observational studies published in the English language were considered. The search strategy encompassed combinations of MeSH terms and keywords related explicitly to colistin, *A. baumannii*, *P. aeruginosa*, *E. coli*, *K. pneumoniae*, and Iran. Additionally, we performed backward and forward citation searches within selected studies to identify any additional relevant publications.

Study Selection: After retrieving records, two independent reviewers (FKH and MJN) individually assessed each record for eligibility criteria, excluding irrelevant studies based on title, abstract, and full texts. In cases of disagreement, a third investigator resolved the discrepancy. Eligible studies had to fulfill the following criteria: clinical isolates were diagnosed using standard drug susceptibility testing adhering to CLSI Guidelines, and they reported the number of isolates exhibiting drug resistance patterns.

Data extraction: Two reviewers (FKH and MJN) designed a data extraction form. Data were extracted from all included studies, with two reviewers independently extracting data from each record and resolving discrepancies through consensus. The extracted data included study design, population characteristics, demographics, the method employed for detecting colistin resistance, drug resistance patterns, and the total number of clinical isolates.

Quality assessment: Two reviewers (FKH and MJN) independently assessed the study quality, with a third reviewer intervening to resolve any discrepancies. The evaluation included the sampling methods, study population, statistical analysis, condition identification, and measurement using the JBI's critical appraisal tool for prevalence studies.

Statistical analysis: Pooled frequencies and their 95% confidence intervals (CIs) were estimated using random-effect models. Study heterogeneity was evaluated using Cochran's Q and the I^2 statistic, with I^2 values of 50% or greater indicating substantial heterogeneity. Publication bias was assessed through Begg's tests, where a p-value below 0.05 indicated significant bias. All statistical analyses were conducted with Comprehensive Meta-Analysis software, Version 3.0.

Results

Figure 1 details the step-by-step process used to select relevant studies. Initially, 758 potentially relevant studies were identified from various databases. After thorough screening, 55 studies were deemed eligible based on the inclusion criteria. Table 1 succinctly presents the characteristics of these studies, which collectively involved 8282 clinical isolates. The predominant methods employed in these studies were microbroth dilution and the E test. All included studies

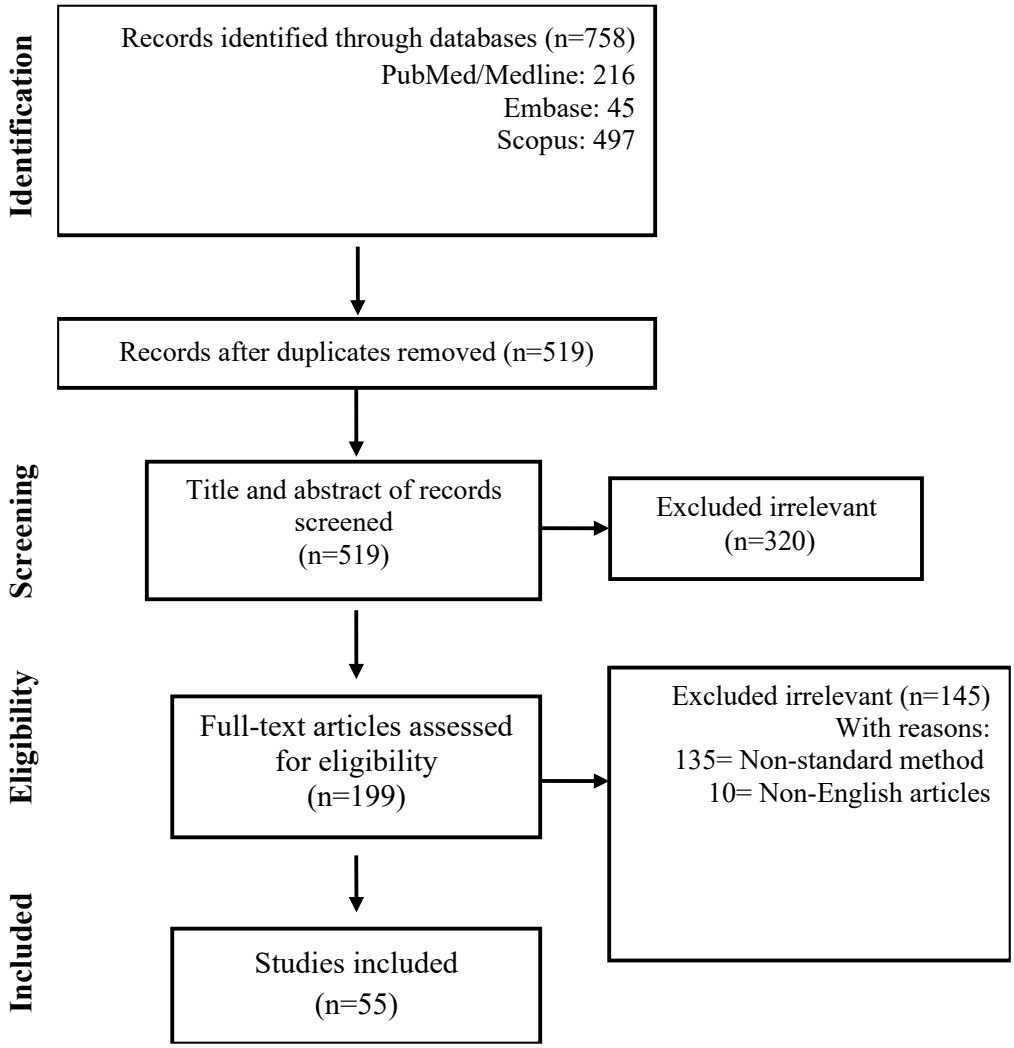

Figure 1. Flow chart of study selection.

followed a cross-sectional design and were predominantly conducted in Iran's central and capital regions. Evaluation using the JBI checklist for prevalence studies indicated a low risk of bias across the included studies, with detailed assessments outlined in Table 2.

Frequency of colistin resistance:

E. coli: The pooled frequency of colistin resistance was 3.6% (95%CI: 1.8-6.9; I^2 = 52%) (Figure 2). Begg's test indicated no evidence of publication bias (p = 0.15) (Table 3).

P. aeruginosa: The pooled frequency of colistin resistance was 6.5% (95%CI: 3.0-13.0; I^2 = 90%) (Figure 3). Begg's test also showed no evidence of publication bias (p = 0.53).

A. baumannii: Colistin resistance had a pooled frequency of 4.7% (95%CI: 3.0–7.4; I^2 = 83%) (Figure 4). Begg's test indicated no significant publication bias (p = 0.26).

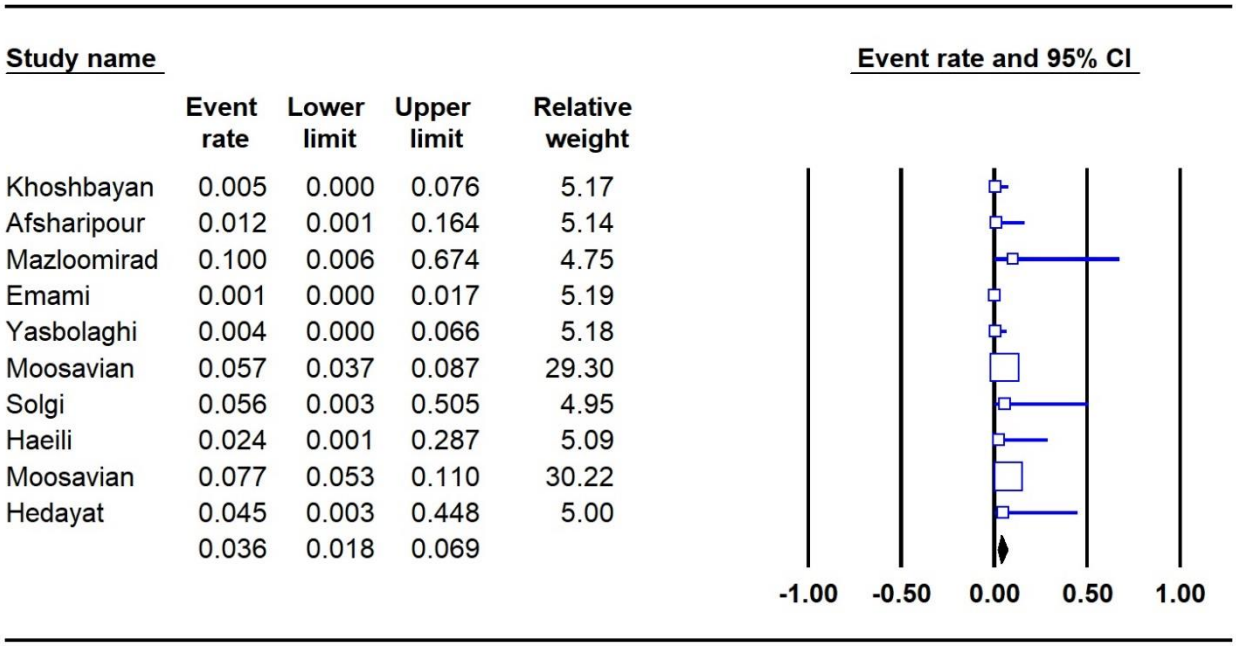

Figure 2. Pooled frequency of colistin resistance in clinical isolates of *E. coli*.

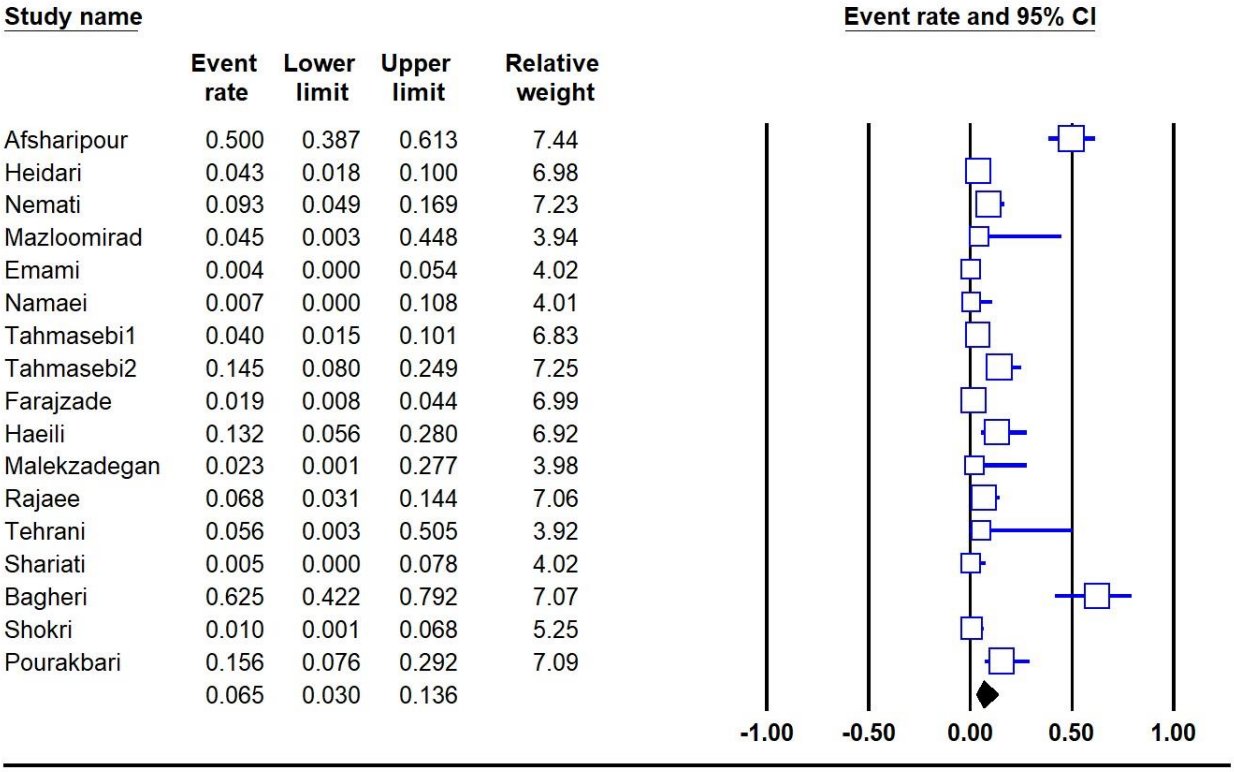

Figure 3. Pooled frequency of colistin resistance in clinical isolates of *P. aeruginosa*.

K. pneumoniae: The pooled frequency of colistin resistance was 7.2% (95%CI: 4.1–12.0; I^2 = 88%) (Figure 5). Similarly, Begg's test showed no evidence of publication bias (p = 0.23).

Discussion

The study discovered concerning levels of colistin resistance among four important Gram-negative

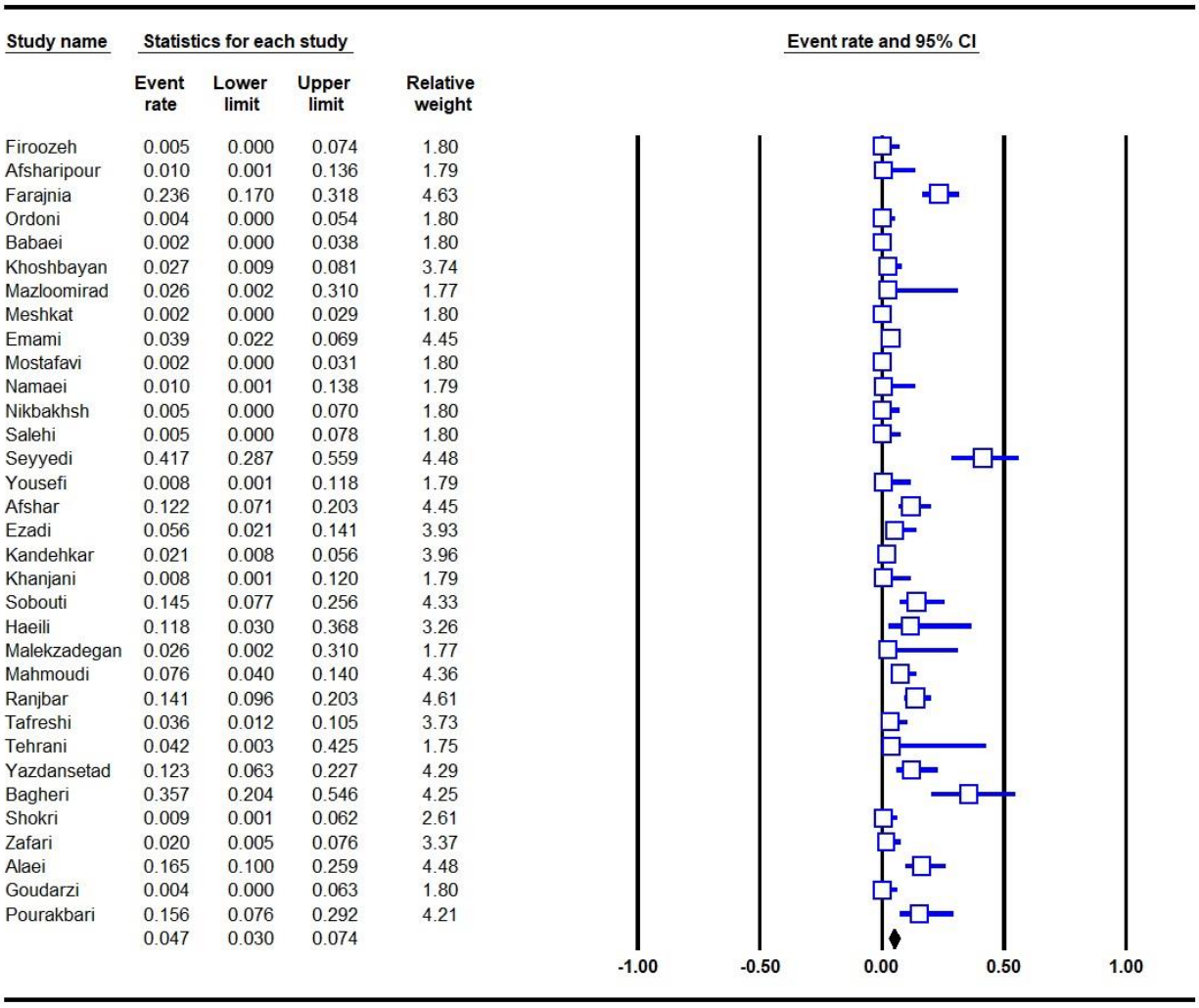

Figure 4. Pooled frequency of colistin resistance in clinical isolates of *A. baumannii*.

bacteria. *E. coli* exhibited a 3.6% resistance rate, which is concerning as it limits treatment options for infections caused by this bacterium. *P. aeruginosa*, known for causing hospital-acquired infections, displayed an even higher resistance rate at 6.5%, suggesting a potential loss of effectiveness of colistin against this pathogen. *A. baumannii*, with a resistance rate of 4.7%, warrants substantial attention due to its capacity to cause multidrug-resistant infections in healthcare settings. *K. pneumoniae* had the highest resistance rate at 7.2%, posing a significant threat, especially in healthcare-associated infections. These findings emphasize the pressing need for effective strategies to address colistin resistance, although comparing them with results from Iran or other regions necessitates region-specific data.

Clinical Implications and Future Directions: The high prevalence of colistin resistance across these clinically significant bacterial species carries profound clinical implications[12, 13]. Colistin is often used as a last-line defense against multidrug-resistant infections. The emergence of resistance severely limits the therapeutic options available to clinicians, potentially leading to treatment failures, prolonged hospital stays, and increased mortality rates.

Furthermore, the interconnected nature of modern healthcare systems and global travel facilitates the rapid spread of colistin-resistant strains among healthcare facilities and across borders. In light of these findings, robust infection control measures, stringent antibiotic stewardship programs, and enhanced surveillance are imperative to curb the dissemination of colistin resistance. Research efforts must also intensify better to understand the mechanisms behind colistin resistance

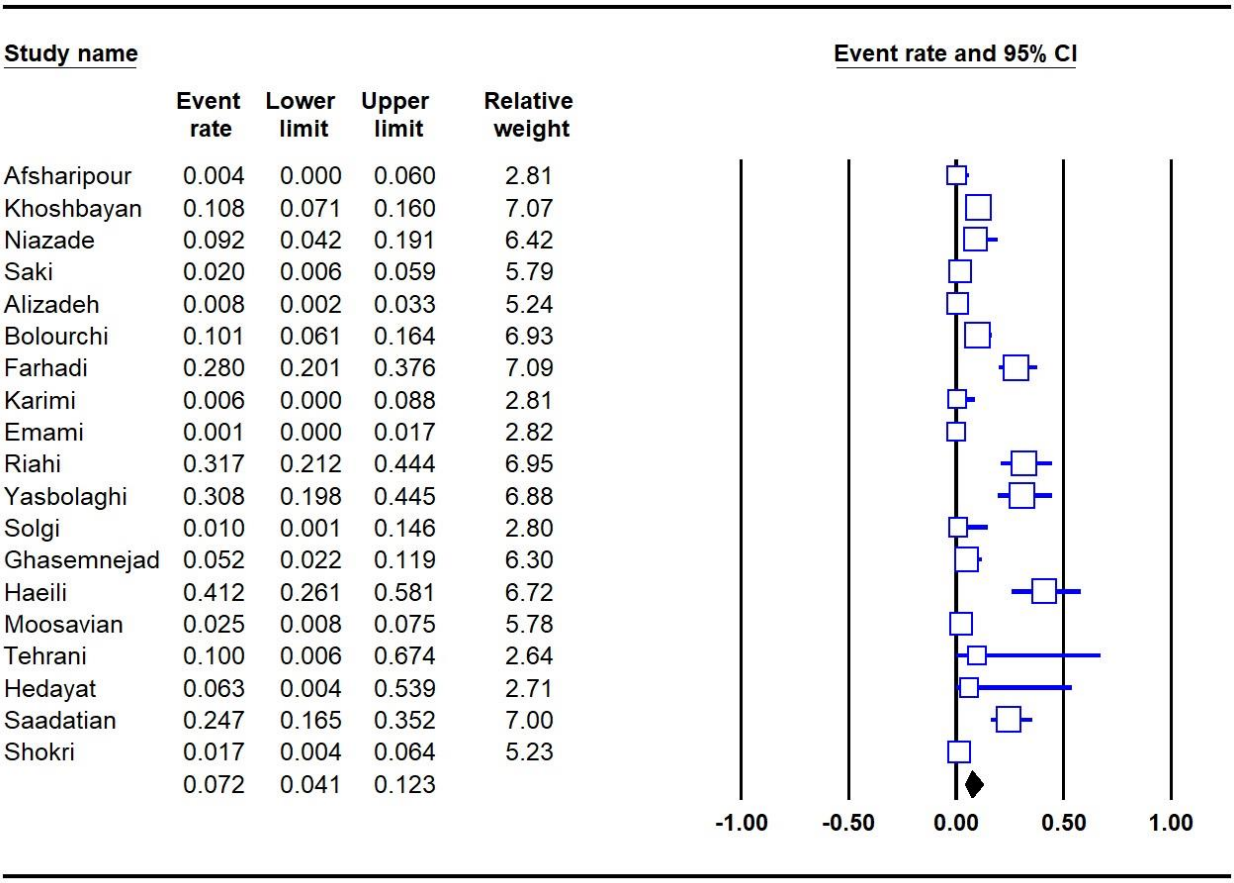

Figure 5. Pooled frequency of colistin resistance in clinical isolates of *K. pneumoniae*.

in these bacteria. This understanding can pave the way for developing alternative treatment strategies and preserving colistin as a viable therapeutic option.

Limitation: Heterogeneity, as indicated by the I2 statistic, ranged from 60 to 90%. This variation is attributed to diverse factors, such as geographical locations, patient demographics, and methodological disparities among the included studies. Such heterogeneity necessitates a cautious interpretation of the pooled resistance rates, as they may not fully represent the complexity of colistin resistance in these bacteria. Furthermore, it cannot fully represent the prevalence of colistin resistance in GNB in Iran because the magnitude of drug resistance has not yet been investigated in many areas of the country.

Conclusion

In conclusion, the concerning frequencies of colistin resistance identified in clinical isolates of *E. coli, P. aeruginosa, A. baumannii, and K. pneumoniae* highlight an urgent need for immediate attention and coordinated efforts. The study's findings serve as a clarion call for the national healthcare community to intensify efforts to combat antibiotic resistance, preserve the efficacy of colistin, and explore innovative approaches to infection prevention and treatment. The stakes are high, and addressing colistin resistance is essential to effectively managing severe infections caused by these notorious GNBs.

Acknowledgment

The authors thank Behestandarou for their contribution.

Conflict of interest

The authors further declare that they have no conflict of interest.

Table 1. Characteristics of Included Studies**.**

Authors	Published year	Study population	Source of Sample	Number of isolates	Number of colistin resistant isolates	Diagnostic test
Firoozeh[14]	2023	Hospitalized burn patients & healthcare workers	Nasal samples	*A. baumannii=100*	0	Broth microdilution method
Afsharipour [15]	2022	Hospitalized patients	Blood , Sterile fluid, wound	*K. pneumonia=125/ P. aeruginosa=72/ A. baumannii=51/ E. coli=41*	*K. pneumonia=0/ P. aeruginosa=36/ A. baumannii=0/ E. coli=0*	E-test
Farajnia[16]	2022	Intensive Care Unit hospitalized patients	Various clinical specimens	*A. baumannii=127*	30	E-test
Heidari [17]	2022	Hospitalized patients	Various clinical specimens	*P. aeruginosa*=115	5	Broth microdilution method
Khoshbayan [18]	2022	Individual patients	BAL, tracheal aspirate, wound, urine, abdominal fluid, blood	*E. coli*=98 and *K. pneumoniae*=195	*E. coli*=0, *. k. pneumoniae=21*	Broth microdilution method
Niazade [19]	2022	Urinary tract infections hospitalized in ICU	Urine samples	*K. pneumoniae*=65	6	Broth microdilution method
Ordoni [20]	2022	Hospitalized patient	Urine, blood, wound, and BAL	*A. baumannii*=141	0	Broth microdilution method
Saki [21]	2022	Patients referred to hospital	Various clinical specimens	*K. pneumoniae=153*	3	Broth microdilution method
Nemati[22]	2022	Hospitalized patients	Various clinical specimens	*P. aeruginosa*=97	9	Broth microdilution method
Alizadeh [23]	2021	Hospitalized patients	Various clinical specimens	*K. pneumoniae*=240	2	Broth microdilution method Broth microdilution method
Babaei[24]	2021	Hospitalized patients with VAP in ICU	BAL & tracheal aspirate	*A. baumannii=200*	0	Broth microdilution
Bolourchi [25]	2021	Hospitalized patient	Various clinical specimens	*K. pneumoniae*=138	14	Broth microdilution
Farhadi [26]	2021	Hospitalized patients	Blood, sputum, BAL, wound exudates, urine, CSF and synovial fluid	*K. pneumoniae*=100	28	Broth microdilution
Karimi[27]	2021	Hospitalized patient	Various clinical specimens	*K. pneumoniae*=83	0	Broth microdilution
Khoshbayan [28]	2021	Hospitalized patient	Various clinical specimens	*A. baumannii=110*	3	Broth microdilution
Mazloomirad[29]	2021	Hospitalized patients	Sputum and	*A. baumannii=18 / P.*	A.*baumannii=0 /*	Broth

		with Hospital-acquired pneumonia (HAP)	endotracheal aspirate	*aeruginosa=10/ E. coli=4*	*P. aeruginosa=0/ E.coli=0*	microdilution
Meshkat [30]	2021	Hospitalized patient	Tracheal aspirates, wounds, urine and blood, CSF	*A. baumannii=270*	0	Broth microdilution
Emami [31]	2021	Hospitalized patient	Various clinical specimens	*E. coli* =469 *K. pneumoniae* = 457/ *P. aeruginosa* =139/ A. *baumannii*= 282	*E. coli* =0/ *K. pneumoniae=0/P. aeruginosa=0/* A. *baumannii=11*	E-test
Mostafavi[32]	2021	Patients with healthcare associated infection & ICU patients	Various clinical specimens	*A. baumannii*=0	0	E-test
Namaei[33]	2021	Inpatient and out-patients	Urine, wound swab, blood, and lung secretions	*P. aeruginosa*=66// A. *baumannii* =50	0	Broth microdilution
Nikibakhsh[34]	2021	Hospitalized burn patients	Burn wounds	106 *A. baumannii*	0	Broth microdilution
Riahi [35]	2021	Hospitalized patient	Various clinical specimens	*K. pneumoniae=60*	19	Broth microdilution
Salehi [36]	2021	Inpatients	Respiratory secretions, blood, wound, urine, CSF, Catheter	95 *A. baumannii*	0	Broth microdilution
Seyyedi [37]	2021	Hospitalized patient in ICU	Respiratory, wound drainage, urine, blood	*A. baumannii*=48	20	Broth microdilution
Yasbolaghi [38]	2021	Hospitalized patients	Wound, urine, blood, tracheal aspirates	*E. coli*=113/ *K. pneumoniae*=52	*E. coli*=0/ *K. pneumoniae* =16	Broth microdilution
Yousefi[39]	2021	Hospitalized pediatric patients	Various clinical specimens	*A. baumannii*=60	0	Broth microdilution
Afshar[40]	2020	Burn patient	Clinical samples	*A. baumannii*=98	12	Broth microdilution
Ezadi[41]	2020	Hospitalized patient	Various clinical specimens	*A. baumannii*=71	4	Broth microdilution
Kandehkar[42]	2020	Hospitalized patients in ICU	BAL, blood, urine, wound, CSF	*A. baumannii=187*	4	Broth microdilution
Khanjani [43]	2020	Hospitalized patients with VAP, burned wounds and bloodstream infections in ICU	Various clinical specimens	*A. baumannii*=59	0	Broth microdilution
Moosavian [44]	2020	Hospitalized patients	Blood, urine, and wounds	*E. coli*=351	20	E-test
Sobouti [45]	2020	Children burn inpatient	Burn wound infections	*A. boumannii*=62	9	Broth microdilution
Solgi [46]	2020	Hospitalized patient in ICU	Various clinical specimens	*K. pneumoniae*=47/ *E. coli*=8	0	Broth microdilution

Tahmasebi [47]	2020	Hospitalized patients	Various clinical specimens	*P. aeruginosa*=101	4	Broth microdilution
Tahmasebi[48]	2020	Hospitalized patients with bloodstream infections	blood	*P. aeruginosa=69*	10	E-test
Farajzade[49]	2019	Hospitalized patients	Various clinical specimens	*P. aeruginosa*=269	5	E-test
Ghasemnejad[50]	2019	Hospitalized patients	Various clinical specimens	*K. pneumoniae*=96	5	Broth microdilution
Haeili[51]	2019	Hospitalized patient	Various clinical specimens	*K. pneumoniae*=34/, *E. coli* =20/ *A. boumannii*= 17/ *P. aeruginosa=38*	*K. pneumoniae* =14/ *E. coli*=0/ *A. boumannii* =2 / *P. aeruginosa* =5	Broth microdilution
Malekzadegan [52]	2019	Hospitalized patients	Blood, endotracheal tube, sputum	*A. baumannii* =18/ *P. aeruginosa=21*	*A. baumannii=0/ P. aeruginosa=0*	E-test
Mahmoudi [53]	2019	Hospitalized patients	Various clinical specimens	*A. baumannii*=118	9	Broth microdilution
Moosavian[54]	2019	Hospitalized patients	Various clinical specimens	*E. coli*=351/ *K. pneumoniae*=119	*E. coli*=38/ *K. pneumoniae*=26	E-test
Rajaee [55]	2019	Burn hospitalized patients	Wound, tissue biopsy, urine	*P. aeruginosa*=88	6	Broth microdilution
Ranjbar [56]	2019	Hospitalized patients	Burn wounds	*A. baumannii*=163	23	Broth microdilution
Tafreshi [57]	2019	Patients with burn wounds	Burn wounds	*A. baumannii*=84	3	Broth microdilution
Tehrani[58]	2019	Hospitalized VAP patients	Tracheal samples	*A. baumannii= 11/ P. aeruginosa= 8/K. pneumoniae=4*	*A. bumannii*=0/ *P. aeruginosa*=0/ *K. pneumoniae*=0	E-test
Hedayat[59]	2019	Hospitalized patients	Various clinical specimens	*E. coli*=10/ *K. pneumoniae* =7	*E. coli*==0/ *K. pneumoniae* =0	E-test
Yazdansetad [60]	2019	Patients with burn wound infections	Burn wounds	*A. baumannii*=65	8	Broth microdilution
Saadatian[61]	2018	Inpatients and outpatients	Various clinical specimens	*K. pneumoniae*=81	20	Broth microdilution
shariati [62]	2018	Hospitalized patient	Wound swabs	*P. aeruginosa*=95	0	Broth microdilution
Bagheri [63]	2017	Hospitalized patient with VAP in ICU	Tracheal sample	*P. aeruginosa*=24/ *A. baumannii*=28	*P. aeruginosa*=15, *A. baumannii* =10	Broth microdilution
Shokri [64]	2017	Hospitalized patient	Various clinical specimens	*P. aeruginosa*=100, *K. pneumoniae*=120, *A. baumannii*=110	*P. aeruginosa*=1/ *K. pneumoniae*=2/ *A. baumannii*=1	E-test
Zafari [65]	2017	Hospitalized patient	Blood, wound, urine, sputum, respiratory trac	*A. baumannii*=100	2	Broth microdilution
Alaei [66]	2016	Hospitalized patients in ICU	Various clinical specimens	*A. baumannii* =85	14	Broth microdilution
Goudarzi [67]	2016	Hospitalized patient in ICU	Various clinical specimens	*A. baumannii* =120	0	Broth microdilution
Pourakbari [68]	2016	Hospitalized patients	Urine,	*P. aeruginosa*=45	7	Broth

				exudates, eye, ear, CSF, blood, trachea, lung secretions					microdilution

Table 2. Quality Assessment**.**

First author	Was the sample representative of the target population?	Were study participants recruited in an appropriate way?	Was the sample size adequate?	Were the study subjects and the setting described in detail?	Was the data analysis conducted with sufficient coverage of the identified sample?	Were objective, standard criteria used for the measurement of the condition?	Was the condition measured reliably?	Was there appropriate statistical analysis?	Was the response rate adequate, and if not, was the low response rate managed appropriately?
Firoozeh	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Afsharipour	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Farajnia	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Heidari	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Khoshbayan	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Niazade	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Ordoni	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Saki	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Nemati	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Alizadeh	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Babaei	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Bolourchi	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Farhadi	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Karimi	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Khoshbayan	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Mazloomirad	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes
Meshkat	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Emami	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Mostafavi	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Namaei	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Nikbakhsh	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Riahi	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Salehi	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Seyyedi	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Yasbolaghi	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Yousefi	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Afshar	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ezadi	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Kandehkar	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Khanjani	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Moosavian	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Sobouti	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

solgi	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes
Tahmasebi	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Tahmasebi	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Farajzade	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ghasemnejad	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Haeili	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Malekzadegan	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Mahmoudi	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Moosavian	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Rajaee	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ranjbar	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Tafreshi	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Tehrani	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Hedayat	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Yazdansetad	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Saadatian	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Shariatic	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Bagheri	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Shokri	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Zafari	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Alaei	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Goudarzi	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Pourakbari	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Table 3. Pooled frequency of colistin resistance**.**

Bacterial name	No. of study	No. of isolates	Pooled frequency (CI 95%)	I2 %	Begg *p* value
E. coli	10	1465	3.6 % (1.8-6.9)	52	0.15
P. aeroginosa	17	1288	6.5 % (3.0-13.0)	90	0.53
A. baumannii	33	3353	4.7 % (3.0-7.4)	83	0.26
K. pneumoniae	19	2176	7.2 % (4.1-12.0)	88	0.23

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