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Systematic Review

Colistin Susceptibility Patterns Among Gram-Negative Respiratory Isolates from Adult ICU Patients: A Systematic Review

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ABSTRACT

Background: Colistin or polymyxin class of antibiotics are reserve drugs for difficult to treat infections occurring due to multidrug-resistant Gram-negative organisms in intensive care units/ critical care units (ICU), but the raising resistance trends raises concern.
Objective: Review of isolates with MIC ≤2 µg/mL for colistin among Gram-negative bacteria (GNB) isolated from respiratory sources of adult ICU patients in the published literature.
Methods: Literature search was done on major databases from 03.01.2026 to 9.01.2026 and included observational studies reporting a proportion of isolates with MIC ≤2 µg/mL among Gram-negative isolates from adult ICU respiratory specimens. We obtained a total of 159 records, of which 10 we included in our study. Rob was done using the (JBI) Critical Appraisal Checklist for Prevalence Studies. As we encountered methodological heterogeneity, a narrative synthesis was performed.
Results: Studies from different geographic regions had met our inclusion criteria, among them the proportion of isolates with MIC ≤2 µg/mL to colistin was high for Acinetobacter baumannii (87.5–100%) and Pseudomonas aeruginosa (80–100%). Escherichia coli isolates with MIC ≤2 µg/mL to colistin was generally above 85%. significant variability was observed for Klebsiella pneumoniae (13–98.4%), with an emerging report of MIC ≥2 µg/mL were seen in certain regions. ROB was assessed, with five studies being low risk, four moderate and one high risk due to sampling issues.
Conclusion: Colistin has shown to have an in-vitro activity against major ICU respiratory Gram-negative pathogens, but the differences seen between various regions mainly among Klebsiella pneumoniae has stressed the need of local surveillance.

Keywords: *Colistin, Gram-negative bacteria, Intensive care unit, Ventilator-associated pneumonia, antimicrobial resistance, Respiratory infections, Susceptibility patterns.*

INTRODUCTION

1.1 Background

Ventilator-associated pneumonia (VAP) and hospital-acquired pneumonia (HAP) are important causes of mortality and morbidity in intensive care units (ICU)[1] with gram-negative bacteria often being implicated [2]. The global increase in multidrug-resistant (MDR) organisms is seen, which propels the usage of colistin regularly as a last-line resort[3].

1.2 Rationale
Colistin resistance is being increasingly reported[4], which makes the ICU-specific respiratory surveillance data very important in guiding therapy[5] and the reported proportion of isolates with MIC ≤2 µg/mL to colistin vary among the various geographic areas and methodologically[6].

1.3 Objective
Review the available reports of MIC ≤2 µg/mL to colistin among the Gram-negative bacteria of adult ICU patients from respiratory samples.

METHODS
2.1 Protocol
PRISMA 2020 guidelines was used for this review[7],we registered the study in open science framework (DOI:**10.17605/OSF.IO/W3AUH**).

2.2 Eligibility evaluation
Inclusion:
- Observational studies.
- Adult ICU patients.
- Respiratory samples.
- Isolates with MIC ≤2 µg/mL to colistin.
- Gram-negative bacilli.

Exclusion:
- Studies with children.
- Case reports.
- Studies having no organism-specific data.
- Other than respiratory infections
- Disc diffusion methods of colistin sensitivity

2.3 Information Sources and Search Strategy
Search Strategy
Databases
- PubMed
- Ovid Embase
- Google Scholar

Core Search Concepts
- ICU / critical care
- Respiratory sources
- Gram-negative bacteria
- Colistin susceptibility or resistance

Analysis
All the retrieved records were then imported into Rayyan and analysis was done. The flow of Rayyan which is duplicates screening, Title and abstract screening and full text articles were followed. All the records were independently screened by four reviewers. Discrepancies were resolved by consensus.

2.4 Study Selection
Titles and abstracts were reviewed independently. Full texts were reviewed for eligibility.

2.5 Data Extraction
Data extracted included:
- Study characteristics
- Sample size
- Organisms isolated
- Colistin susceptibility (numerator/denominator)
- Testing method
- Breakpoint criteria

2.6 Risk of Bias Assessment
Risk of bias was done using the JBI Critical Appraisal Checklist for Prevalence Studies[8].

2.7 Data Synthesis
Because of heterogeneity in study populations and testing methodologies, pooled prevalence estimates and confidence intervals were not done. There was heterogeneity in breakpoint criteria (CLSI vs EUCAST)[9,10], inclusion of MDR-only populations in some studies, variation in susceptibility testing methods (automated systems vs broth microdilution), and differences in organism distribution and sample size across studies, hence a structured narrative synthesis was conducted.

RESULTS
Study Selection
The database search and study selection process are summarized in Figure 1.

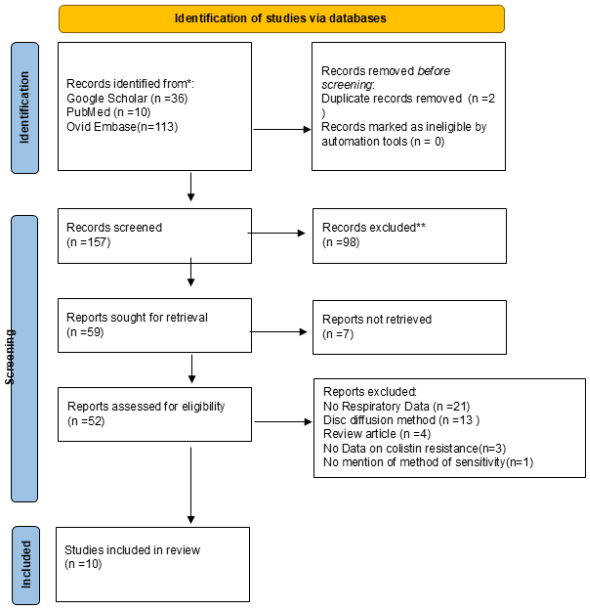

Figure:1 PRISMA 2020 flow diagram

Study Characteristics
The 10 studies that were included were reported between 2013 and 2025 and they from Vietnam (n=2), India (n=2), Turkey (n=3), Saudi Arabia (n=1), Egypt (n=1), and Cuba (n=1).

Sl. No	Author	Year	Location	Sample Size (Total GNB Isolated)	Inclusion/Exclusion Criteria Highlights
1	**Medell et al.**	**2013**	**Cuba**	170	**Inclusion:**ICU patients on ventilators with VAP. **Exclusion:** NR.
2	**Koneru et al.**	**2018**	**India**	84	**Inclusion:** Patients with Pneumonia 48h after ICU admission; new chest infiltrates. **Exclusion:** Active TB, CKD, cardiac issues.
3	**Sağmak Tartar et al.**	**2018**	**Turkey**	584	**Inclusion:** Mechanically ventilated ICU patients, ETA 10^5 CFU/ml. **Exclusion:** Duplicate isolates.
4	**Agarwal et al.**	**2018**	**India**	186	**Inclusion:** Ventilated 48h with new LRTI signs; CPIS. **Exclusion:** NR.
5	**Arici et al.**	**2020**	**Turkey**	385	**Inclusion:** ICU patients with mechanical ventilation; ETA 10^5 CFU/ml. **Exclusion:** Duplicate isolates.
6	**El-Mokhtar et al.**	**2021**	**Egypt**	140 (*E. coli* only)	**Inclusion:** Nosocomial pneumonia in chest ICU; sputum/aspirates. **Exclusion:** Infections incubating on admission.

7	**Vo et al.**	**2022**	**Vietnam**	66 (MDR GNB only)	**Inclusion:** Adult ICU VAP patients; isolated MDR GNB. **Exclusion:** Relatives' refusal; pneumonia <48h.
8	**Gürbüz et al.**	**2023**	**Turkey**	309	**Inclusion:** Properly obtained lower respiratory specimens (sputum, BAL, TA) in ICU. **Exclusion:** Repeated isolates.
9	**Le et al.**	**2024**	**Vietnam**	1,325	**Inclusion:** Hospitalized LRTI patients; sputum, aspirates, pleural fluid. **Exclusion:** Low frequency samples (<2% GNB).
10	**Almouwlid et al.**	**2025**	**Saudi Arabia**	271	**Inclusion:** ICU patients; clinical/microbiological pneumonia diagnosis. **Exclusion:** Duplicate isolates; non-GNB.

All studies were observational in design, predominantly retrospective laboratory-based surveillance studies conducted in adult ICUs and the total number of Gram-negative bacterial (GNB) isolates analyzed across studies ranged from 66 to 1,325 (duplicate isolates from the same patient were excluded in all the studies) . Most studies used automated systems to determine Colistin susceptibility (e.g., VITEK 2), with interpretation based on CLSI or EUCAST criteria. Evidence of broth microdilution was not reported in most of the studies.

One study which reported only multidrug-resistant (MDR) isolates, and one study focused exclusively on *Escherichia coli* isolates.

Sl. No	**Author**	**EC TT**	**EC CI(n)**	**EC CI (%)**	**KP TT**	**KP CI(n)**	**KP CI (%)**	**PA TT**	**PA CI(n)**	**PA CI (%)**	**AB TT**	**AB CI(n)**	**AB CI (%)**
1	**Medell et al.**	12	12	100.00 %	12	9	75.00%	34	34	100.00 %	53	52	98.10%
2	**Koneru et al.**	3	3	100.00 %	28	28	100.00 %	12	12	100.00 %	36	36	100.00 %
3	**Sağmak Tartar et al.**	15	NR	NR	101	96	95.00%	127	124	97.60%	307	298	97.10%
4	**Agarwal et al.**	16	16	100.00 %	32	24	75.00%	31	26	84.00%	83	81	97.60%
5	**Arici et al.**	53	52	98.10%	89	76	85.40%	62	58	93.50%	130	129	99.20%
6	**El-Mokhtar et al.**	140	119	85.00%	NR	NR	NR	NR	NR	NR	NR	NR	NR
7	**Vo et al.**	NR	NR	NR	15	NR	NR	6	5	80.00%	45	44	97.20%
8	**Gürbüz et al.**	36	36	100.00 %	64	63	98.40%	121	114	94.20%	88	86	97.70%
9	**Le et al.**	4	2	50.00%	14	13	92.90%	275	255	92.70%	288	252	87.50%
10	**Almouwlid et al.**	7	NR	NR	92	12	13.00%	73	14	19.00%	32	NR	NR

Abbreviations	
EC	*Escherichia coli*
KP	*Klebsiella pneumoniae*
PA	*Pseudomonas aeruginosa*
AB	*Acinetobacter baumannii*
TT	**Total Tested**
CI	**MIC** ≤2 µg/mL
CI%	**MIC** ≤2 µg/mL%

Risk of Bias Assessment

Risk of bias was performed by using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Prevalence Studies and it was calculated across 9 JBI checklist items. Overall methodological concern was determined based on domain-level assessment.

Five studies were judged to have low overall risk of bias, appropriate sampling frames, adequate sample sizes, standardized microbiological identification methods, and sufficient statistical reporting, four studies were assessed as having moderate methodological concerns, primarily due to small sample sizes, unclear sampling strategies, or limited statistical reporting, one study was considered high risk for prevalence estimation because it included only MDR isolates, limiting the representativeness of the general ICU population.

Microbiological identification and susceptibility testing methods were generally standardized and appropriate, but reporting of sample size calculations and confidence intervals was uncommon.

Formal assessment of publication bias (e.g., funnel plot or Egger's regression) was not performed because a quantitative meta-analysis was not conducted.

Study	Sampling Bias	Coverage Bias	Measurement Bias	Analytical Adequacy
Medell 2013	Moderate	Low	Low	High
Sagmak 2018	Low	Low	Low	Low
Koneru 2018	Moderate	Low	Low	High
Agarwal 2018	Moderate	Low	Low	High
Arici 2020	Low	Low	Low	Low
ElMokhtar 2021	Moderate	Low	Low	High
Vo 2022	High	Moderate	Low	High
Gurbuz 2023	Low	Low	Low	Low
Le 2024	Low	Low	Low	Low
Almouwlid 2025	Low	Low	Low	Low

Colistin Susceptibility Patterns

Acinetobacter baumannii

Colistin was reported by nine studies for *Acinetobacter baumannii*. Isolates with MIC ≤2 µg/mL to colistin ranged from 100% to 87.5%.[11,12] The lowest proportion of MIC ≤2 µg/mL was reported in a Vietnamese study (87.5%), [11] several Turkish and Middle Eastern studies reported rates exceeding 97%.[13,14]. MIC ≥2 µg/mL was not common but was present in certain regions.

Pseudomonas aeruginosa

Susceptibility for *Pseudomonas aeruginosa* was given by nine studies for colistin. Isolates with MIC ≤2 µg/mL to colistin had ranged from 80% to 100%[12,14,16]. Most studies reported rates above 90%. Lower proportion of isolates with MIC ≤2 µg/mL to colistin was observed in one regional study that included MDR isolates[16]. The MDR only study had low proportion of isolates with colistin MIC ≥2 µg/mL despite resistance to other classes.[16]

Klebsiella pneumoniae

The susceptibility data for *Klebsiella pneumoniae* was reported by nine studies. Variability was observed, isolates with MIC ≤2 µg/mL to colistin ranging from 13% to 98.4%[17,18]. The lowest rates were reported in a study from Saudi Arabia[17], whereas studies from Turkey[13] and India reported rates above 85%[12]. This organism demonstrated the greatest heterogeneity in susceptibility across geographic regions. Indian study also reported variable susceptibility.[19]

Escherichia coli

Escherichia coli susceptibility was provided by eight studies. Isolates with MIC ≤2 µg/mL to colistin was more compared to other organisms and ranged from 85% to 100%[18,20]. One Egypt-based study focusing exclusively on *Escherichia coli* reported an 85% of isolates with MIC ≤2 µg/mL to colistin. Escherichia coli is less frequently isolated compared to other organisms.[12,14]

Geographic Variation

Regional differences in colistin susceptibility were evident. Studies from Turkey consistently reported high proportion of isolates with MIC ≤2 µg/mL to colistin across all major Gram-negative organisms. Vietnamese studies demonstrated moderately lower proportion of isolates with MIC ≤2 µg/mL to colistin, particularly for *Acinetobacter baumannii*. Lower rater was reported by Saudi Arabian study for *Klebsiella pneumoniae*. These differences may reflect different antimicrobial usage or infection control practices, and local resistance epidemiology.

Methodological Heterogeneity
We observed heterogeneity across studies; hence we did not perform meta-analysis. Examples of heterogeneity include,

- Specimen types (ETA vs BAL)
- Inclusion of MDR-only isolates
- Testing standards (CLSI vs EUCAST)
- Sample size
- Reporting of statistical precision

DISCUSSION

This systematic review presents available evidence regarding in vitro activity of colistin among Gram-negative pathogens isolated from adult ICU patients with respiratory complaints from 10 observational studies from different regions, colistin showed good in vitro activity against most major Gram-negative pathogens[14], particularly *Acinetobacter baumannii* and *Pseudomonas aeruginosa*. Notable regional variability was observed, especially for *Klebsiella pneumoniae*.

Principal Findings
The some of the most similar finding across studies include; high activity rates of *Acinetobacter baumannii* to colistin, with reported rates ranging from 87.5% to 100%. Due to the presence of widespread carbapenem resistance in numerous ICUs, colistin continues to be used as a last resort therapeutic option for this pathogen[13].

Pseudomonas aeruginosa also demonstrated high proportion of isolates with MIC ≤2 µg/mL to colistin in most studies, generally exceeding 90%[12],which is consistent with current understanding that colistin remains active against many non-fermenting Gram-negative organisms, although sporadic isolates with MIC ≥2 µg/mL for colistin has been reported globally.

In contrast, proportion of *Klebsiella pneumoniae* isolates that exhibited MIC ≤2 µg/mL for colistin, ranged from as low as 13% [17] in one regional study to greater than 95%[12] in others. This may reflect differences in local antimicrobial usage, the presence of transferable MCR gene colistin resistance mechanisms[4], along with regional antimicrobial stewardship practices.

Escherichia coli isolates with MIC ≤2 µg/mL to colistin remained on the higher side across studies, above 85%[20], data regarding this bacteria were limited in some settings, and one study focused exclusively on this bacteria, hence broader interpretation is limited.

All of the above findings reinforce the fact that continued surveillance and local data is the mainstay for treatment of such infections[16].

Geographic and Epidemiological Variation
Marked geographic variation was evident across the included studies. Turkish ICU settings consistently reported high proportion of isolates with MIC ≤2 µg/mL to colistin across organisms[13], whereas some studies from Vietnam[11] and the Middle East demonstrated emerging proportion of isolates with MIC ≥2 µg/mL, particularly among Enterobacterales. Regional variations in antibiotic usage, institution specific infection control measures, difference in healthcare infrastructures, and multiple molecular resistance epidemiology might be the reason for these differences observed. Lower number of isolates with MIC ≤2 µg/mL were observed in Middle Eastern cohorts compared to Turkish studies particularly among *Klebsiella pneumoniae* [17] .

ICU environments in general are known to create conditions that facilitate emergence and spread of multidrug-resistant pathogens due to prolonged hospitalization, usage of invasive devices and procedures, antibiotic exposure, and severe patient illness[21].

Methodological Considerations
While most included studies used standardized microbiological identification systems and interpreted susceptibility according to recognized criteria (CLSI or EUCAST)[9,10], heterogeneity in testing methodology was observed. Breakpoint interpretation differs between the major standards, while, CLSI defines isolates with MIC ≤2 µg/mL as intermediate and ≥4 µg/mL as resistant, whereas EUCAST classifies MIC ≤2 mg/L as susceptible and >2 mg/L as resistant. For the purpose of this review, isolates categorized as intermediate or susceptible by CLSI and susceptible by EUCAST were considered colistin-susceptible, reflecting comparable MIC thresholds across both standards. For the sake of harmonization, ‘sensitive’ or ‘intermediate’ were not used; interpretation should be considered as per standards used in each study. Despite broth microdilution being a reference standard for colistin susceptibility testing, only a few studies used it explicitly, instead many relied on automated systems for MIC determination such as Vitek 2 compact and Microscan[12,13], these systems; while widely used in routine clinical laboratories, they may occasionally misclassify colistin susceptibility[22].

Sample sizes varied considerably across studies, and formal sample size calculations were rarely reported, one study restricted itself to only multidrug-resistant isolates, which would likely underestimate isolates with MIC ≤2 mg/L compared to general ICU populations and another study was restricted to a single organism, which would limit representativeness. The considerable clinical and methodological heterogeneity lead authors not to perform quantitative pooling.

The higher interpretative breakpoints were higher without mentioning the standard in the MDRO only, which may have lead to underestimation relative to contemporary breakpoints.

Clinical significance

The results of the study confirm the continued utility of colistin as a last-resort therapeutic agent for difficult to treat infections by multidrug-resistant Gram-negative bacteria in ICU, however, there is variability observed in *Klebsiella pneumoniae* susceptibility.

Finding of the review implies, routine testing of colistin is important, especially when increasing reports of plasmid-mediated resistance mechanisms exist. Overreliance on colistin without active monitoring may increase the rate of resistance development, potentially compromising one of the only treatment options for extensively drug-resistant infections[23].

Strengths and Limitations of the Review

This review included studies from many continents and provided a review of organism-specific patterns in adult ICU respiratory infections. This review has methodological transparency due to systematic assessment of risk of bias using the JBI checklist.

Limitations.

Heterogeneity in study design, specimen type, and susceptibility testing methodology, in-frequent reporting of confidence intervals, uniform evaluation of molecular mechanisms of colistin resistance. many studies were single-center and retrospective[15,16,19], which may limit generalizability. Due to non-representation of some geographic regions; generalizability is limited and reflects regional publication patterns more than true epidemiological distribution and due to change in the methodology with the standards many studies were excluded due to disc diffusion methodology.

Potential Publication and Reporting Bias

Even though a quantitative meta-analysis was not conducted, there may be a risk of publication bias. The studies which reported emerging or unusually high colistin resistance may be more likely that they were published due to clinical concern, which in turn overestimates the prevalence. The centers with persistently low isolates with MIC ≤2 mg/L may be underrepresented and many of the included studies were single-center and relatively small. Many of these single center studies tend to have small-study effects more so, if resistance patterns were caused by outbreaks localized to the region or hospital and geographic representation was uneven. Predominance of studies from some regions and lack of large multicenter datasets, it has limited global generalizability, mindfull ness of factors are needed while interpreting the reported patterns.

Future Research should prioritize

- Testing using broth microdilution[10].
- Reporting of confidence intervals.
- Molecular characterization[6].
- Multicenter ICU surveillance.
- Prospective studies.

CONCLUSION

Relatively good activity for colistin in vitro against *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Escherichia coli* is noted across settings for adult ICU respiratory infections [14]. However, marked regional variability, especially among *Klebsiella pneumoniae,* which indicates emerging resistance in certain regions[17]. Susceptibility patterns observed across diverse geographic regions are similar other than few variations [11,14,15,17]. Regular local surveillance and careful stewardship are needed to maintain the clinical effectiveness of this last-line agent[18].

DECLARATIONS

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Conflicts of Interest

The authors declare no conflicts of interest.
manuscript.

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