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Prevalence of colistin resistance in multidrug-resistant *Klebsiella pneumoniae* recovered from clinical samples in Africa: a systematic review and meta-analysis

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Background: Colistin resistance in multidrug-resistant (MDR) *Klebsiella pneumoniae* is a growing concern in Africa, complicating treatment and public health management. Colistin is a last-resort antibiotic for Gram-negative infections, but its resistance in clinical settings presents significant challenges. This study aims to determine the pooled prevalence of colistin resistance in MDR *K. pneumoniae* isolates from clinical specimens in Africa.

Methods: Articles were sourced from PubMed, Scopus, ScienceDirect and Google Scholar. Studies included were those reporting colistin resistance in MDR *K. pneumoniae* from clinical specimens in Africa, using EUCAST and CLSI-standard drug susceptibility testing. Data were extracted into Excel and analysed using STATA 17 with a random-effects model to determine the pooled prevalence. Heterogeneity was assessed using the I^2 statistic, and publication bias was checked with Egger's test. Subgroup analyses were performed to explore heterogeneity.

Results: The study analysed data from 30 articles on colistin resistance in MDR *K. pneumoniae*. The pooled prevalence was 21.59% (95% CI: 12.12–31.06), with high heterogeneity ($I^2 = 99.71\%$). Sub-regional variation was significant ($P < 0.001$), with prevalence rates differing across regions: 42.34% in East Africa, 37.1% in West Africa, 17.1% in Southern Africa and 13.0% in North Africa. Country-specific rates were highest in Nigeria (39.12%), followed by Kenya (22.52%), South Africa (17.12%) and Egypt (14.0%) ($P < 0.001$).

Conclusions: Colistin resistance in MDR *K. pneumoniae* is high in Africa, with notable regional differences. The study calls for strict colistin regulations, robust antimicrobial stewardship and rapid diagnostic tools for resistance detection.

Introduction

A global rise of multidrug-resistant (MDR) Gram-negative bacteria represents an increasing threat to humans.[1] *K. pneumoniae* is a Gram-negative bacterium and one of the top three pathogens identified by the WHO as being of international concern emphasizing the urgency of addressing the issue.[2,3] This bacterium causes various infections such as urinary tract infections, respiratory infections, bacteraemia and pneumonia.[4–6] Studies have reported that *K. pneumoniae* is responsible for one-third of all Gram-negative bacterial infections in hospital settings.[3,7] MDR isolates were identified as isolates showing resistance to at least one antimicrobial agent in three or more antimicrobial classes.[8] MDR bacteria like *K. pneumoniae* not only cause a wide variety of infections but also complicate treatment options, leaving fewer effective antibiotics available for clinicians to use.[3,9] *K. pneumoniae* has a global drug resistance rate of up to 70%, with mortality rates due to this infection also ranging from 40% to 70%.[10]

Colistin resistance in *K. pneumoniae*, especially in MDR strains, is a growing concern in Africa. *K. pneumoniae* swiftly acquires

MDR, posing a major threat to treatment, resulting in high mortality rates and limited effective therapies.[3,11,12] In recent years, MDR *K. pneumoniae* and carbapenem-resistant *K. pneumoniae* have emerged as a major global public health problem.[3,13]

Treating infections caused by antibiotic-resistant *K. pneumoniae* is challenging due to its inherent and acquired resistance to multiple medications, including β-lactam antibiotics. *K. pneumoniae* produces extended-spectrum β-lactamases and carbapenemases enzymes that confer resistance to a broad range of β-lactam antibiotics, including penicillins, cephalosporins and carbapenems.[3,14] This is a major concern, as colistin is one of the few last-resort antibiotics available for treating infections caused by carbapenem-resistant and MDR *K. pneumoniae*, particularly in critically ill patients.[12,15]

Thus, colistin resistance among MDR *K. pneumoniae* pathogens is an escalating concern in modern medicine.[3] This further limits treatment options and exacerbates the challenge of managing infections caused by MDR pathogens,[16] particularly in settings with limited access to advanced diagnostic tools, antimicrobial stewardship programmes and infection control measures.[3] Several African countries have reported high levels of colistin resistance in *K. pneumoniae*.[12,17] Factors driving the rise of colistin-resistant *K. pneumoniae* in Africa include the high burden of healthcare-associated infections, inappropriate use of colistin, weak infection control measures and limited diagnostic capacity.[18]

Studies suggest that colistin resistance rates among MDR *K. pneumoniae* strains in parts of Africa vary from low to moderate. Some reports indicate resistance rates ranging from 10% to 50%, with certain hotspots exhibiting even higher levels.[11] Comprehensive data on colistin resistance in MDR *K. pneumoniae* clinical isolates across Africa, however, remain limited.[19] To address this gap, we conducted a systematic review and meta-analysis to determine the pooled prevalence of colistin resistance in MDR *K. pneumoniae* strains isolated from clinical samples across Africa.

Methods

Study protocol and registration

In conducting this systematic review and meta-analysis, we adhered strictly to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[20] The protocol for this systematic review and meta-analysis was carefully developed and registered with the International Prospective Register of Systematic Reviews (PROSPERO) (CRD: 648198).

Literature search

A systematic literature search was conducted to retrieve articles reporting colistin resistance in the time interval of 1 January 2010 to 30 April 2024. Publicly available electronic databases, including PubMed, Scopus, ScienceDirect and Google Scholar search engines, were used to access potential papers. Two reviewers, Y.G. and M.A.R., independently conducted the literature search using predefined search terms and phrases across selected electronic databases. The medical subject headings and other relevant searching words/phrases were used in combination using the operator Boolean, 'AND' or 'OR', such as ('prevalence' OR 'epidemiology' AND 'colistin' OR 'polymyxin' OR 'Antimicrobial resistance' OR 'Drug resistance' OR 'Multi-drug resistance' AND '*Klebsiella pneumoniae*' OR '*Klebsiella*' AND 'clinical isolates' OR 'clinical samples' AND 'Africa'). Each African country was searched individually or in combination with relevant keywords to improve the retrieval of studies from each specific country. The search strategy used for one of the electronic databases, PubMed/MEDLINE, is provided in Table S1 (available as Supplementary data at *JAC-AMR* Online).

Eligibility

Inclusion and exclusion criteria

Three reviewers, Y.G., Z.A. and A.S., independently assessed the titles and abstracts of the papers to select the full-text articles. Any disagreements among the three authors were resolved with the assistance of another reviewer (M.A.R.). To identify and select eligible articles, we established clear, predetermined inclusion and exclusion criteria.

Articles meeting the inclusion criteria were reviewed and included, while those that did not meet the criteria were excluded. The inclusion criteria were as follows: (i) all original articles published in English between 1 January 2010 and 30 April 2024 that reported colistin resistance in MDR *K. pneumoniae* isolates recovered from clinical samples; (ii) studies that used antibiotic susceptibility testing based on criteria established by CLSI[21] and EUCAST[22] for colistin resistance testing; and (iii) studies conducted exclusively in the African region. The method used for colistin susceptibility testing was microdilution, which is the only recommended technique for antibiotic susceptibility testing of colistin.[22] The exclusion criteria wereas follows: (i) studies that reported systematic reviews or meta-analysis results; (ii) studies that only reported antibiotic resistance without specifically addressing colistin resistance, or studies that used colistin susceptibility testing methods other than microdilution; and (iii) studies with inaccessible full-text articles after two emailing, case reports, conference papers, letters of communication and studies with only abstracts. A manual search and the bibliographies of each study were reviewed to identify additional potential papers.

Quality assessments

The quality of the included studies was evaluated using the Joanna Briggs Institute critical appraisal tool for prevalence data.[23] Two reviewers, Y.G. and M.A.R., independently conducted a critical appraisal of each study. All studies included in the analysis had a quality assessment score of 50% or higher on the checklist, indicating high quality and eligibility for inclusion in the study (Table S2).

Data extraction

Three reviewers, Y.G., Z.A. and A.S., independently extracted relevant data from the included articles using a standardized data extraction form in Microsoft Excel 2013. The extracted data included the country, first author's surname, year of publication, methods, diagnostic techniques, sample size, types of clinical samples (e.g. urine, blood, sputum, endotracheal aspirate and swabs), bacterial species isolated, MDR isolates and colistin susceptibility profiles of *K. pneumoniae*. Any disagreements during data extraction were resolved through discussion and consensus. If consensus could not be reached, the other reviewer, M.A.R., was consulted.

Data management and statistical analysis

The data extracted from the included studies using Microsoft Excel 2013 were exported to STATA 17.0 software (StataCorp, TX, USA) for the final analysis. A random-effects model was used to calculate the pooled prevalence due to the presence of heterogeneity across the included studies. The inverse variance (I^2) test was conducted to assess heterogeneity across studies, with I^2 values interpreted as follows: 0% (no heterogeneity), 0%–25% (low heterogeneity), 25%–50% (moderate heterogeneity) and >75% (high heterogeneity).[24] In some studies, a continuity correction was applied to those reporting 0% or 100% colistin resistance values to calculate the pooled prevalence, preventing a zero standard error during the meta-analysis.[25] Subgroup analysis was performed for specific categories to explore sources of high heterogeneity

among the studies. Egger's test was used to detect potential publication bias, with a significance level set at $P<0.05$. Additionally, a trim-and-fill analysis was conducted to adjust for any potential bias.

Results

Searching results

All retrieved articles from searched databases were imported into EndNote version 20 reference management software (Thomson Reuters, New York, NY, USA). In this systematic review and meta-analysis, a total of 10 380 studies were identified through searches in electronic databases and the Google Scholar search engine. Out of the total studies, 6780 non-duplicate articles were selected for further evaluation. After reviewing titles, abstracts and other reasons, such as duplicate studies, reviews, studies not reporting colistin resistance and non-English papers, 6630 articles were excluded. As a result, 150 papers were retained for full-text assessment. After a full-text review, 30 eligible articles[26–55] were included in the final meta-analysis, reporting the prevalence of colistin resistance in MDR *K. pneumoniae* clinical isolates across Africa (Figure 1).

A descriptive summary of the included studies

This systematic review and meta-analysis included 30 studies[26–55] from 11 countries, documenting the colistin resistance profile in MDR *K. pneumoniae* clinical isolates. The majority of the data (50%) were sourced from North Africa, while fewer studies were available from Central and South-Eastern Africa (Tables 1 and 2). The number of studies included from each country is as follows: Egypt ($n=13$), Nigeria ($n=4$), South Africa ($n=3$), Uganda ($n=2$) and Kenya ($n=2$). The remaining studies were from the Democratic Republic of the Congo, Algeria, Ethiopia, Mali, Ghana and Mozambique, with one study from each country ($n=1$) (Table 1). All studies included in the final quantitative review (meta-analysis) utilized the minimum inhibitory concentration dilution technique for colistin susceptibility testing and followed a cross-sectional study design. Of the 30 articles that met the inclusion criteria based on their use of the broth microdilution method for colistin susceptibility testing, 12 (40%) of the articles reported the use of quality control strains. Among these, six (20%) and seven (23.33%) reported the use of positive and negative quality control strains, respectively. The majority of the included studies were conducted in hospitals. These 30 included studies reported a total of

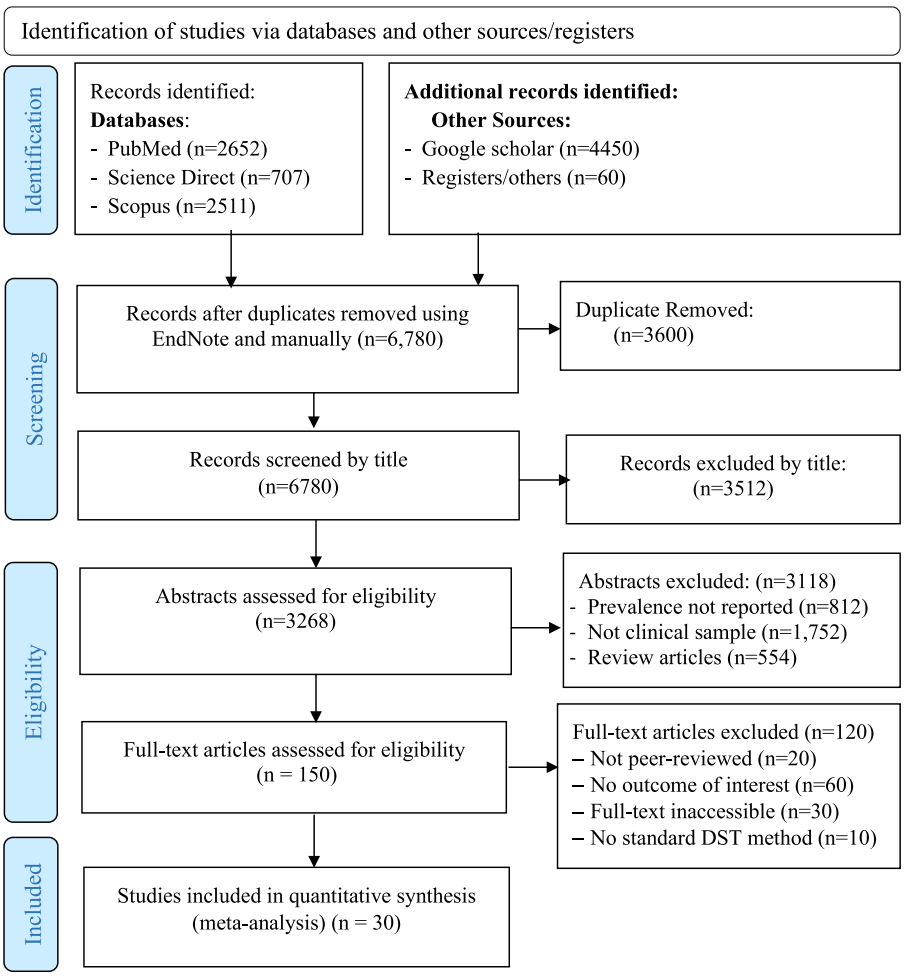

Figure 1. PRISMA flow diagram showing the results of the search and reasons for exclusion.[20]

Table 1. Characteristics of the included studies to estimate colistin resistance in MDR *K. pneumoniae* isolates recovered from clinical samples in Africa

Authors	Year of publication	Country	No. of MDR isolates	No. of MDR CST-R isolates *n*(%)	No. of MDR CST-S isolates *n*(%)	Quality score
Adeosun *et al.*[26]	2019	Nigeria	52	18 (34.6)	34 (65.4)	8
Irenge *et al.*[27]	2023	DR.Congo	37	0 (0)	37 (100)	9
Maina *et al.*[28]	2023	Kenya	25	0 (0)	25 (100)	7
Ramadan *et al.*[29]	2022	Egypt	66	8 (12.12)	58 (87.88)	9
Gizachew *et al.*[30]	2019	Ethiopia	18	18 (100)	0 (0)	8
El-Mahallawy *et al.*[31]	2022	Egypt	100	39 (39)	61 (61)	9
Mahmoud *et al.*[50]	2023	Egypt	72	30 (41.67)	42 (58.33)	7
Magulye *et al.*[32]	2023	Uganda	31	7 (22.58)	24 (77.42)	8
Mmatli *et al.*[33]	2022	South Africa	306	81(26.47)	225 (73.33)	8
Mbelle *et al.*[34]	2020	South Africa	42	11(26.20)	31 (73.80)	7
Zafer *et al.*[35]	2019	Egypt	234	22 (9.4)	212 (90.6)	9
Ayandele *et al.*[36]	2020	Nigeria	48	44 (91.67)	4 (8.33)	7
Olowo-Okere *et al.*[37]	2020	Nigeria	58	16 (27.60)	42 (72.40)	8
Agyepong *et al.*[38]	2018	Ghana	37	0 (0)	37 (100)	9
Norsigian *et al.*[39]	2019	Egypt	22	2 (9.1)	20 (90.9)	8
Kaapu[40]	2022	South Africa	184	0 (0)	184 (100)	7
Wasfi *et al.*[51]	2016	Egypt	36	0 (0)	36 (100)	8
El-Kholy *et al.*[41]	2020	Egypt	261	19 (7.28)	242 (92.72)	9
Ejaz *et al.*[52]	2021	Egypt	185	9 (4.86)	176 (95.14)	9
Tohamy *et al.*[42]	2018	Egypt	70	4 (5.71)	66 (94.29)	8
Olowo-Okere *et al.*[37]	2020	Nigeria	38	1 (2.63)	37 (97.37)	7
Abdel Salam and Hager[43]	2020	Egypt	24	5 (20.83)	19 (79.17)	8
Shaaban *et al.*[54]	2024	Egypt	26	0 (0)	26 (100)	8
Magulye *et al.*[32]	2023	Uganda	27	5 (18.52)	22 (81.48)	9
Maina *et al.*[28]	2023	Kenya	28	13 (46.43)	15 (53.57)	7
Sumbana *et al.*[44]	2022	Mozambique	29	0 (0)	29 (100)	9
Shebl and Mosaad[45]	2019	Egypt	116	19 (16.38)	97 (83.62)	7
Hecini-Hannachi *et al.*[46]	2016	Algeria	661	0 (0)	661 (100)	8
Attia *et al.*[47]	2023	Egypt	13	5 (38.46)	8 (61.54)	9
Aminata *et al.*[48]	2023	Mali	10	7 (70)	3 (30)	7
Total			2856	383 (13.41)	2473 (86.59)	

CST-R, colistin-resistant; CST-S, colistin-susceptible; DR.Congo, Democratic Republic of the Congo; MDR, multidrug-resistant.

2856 MDR *K. pneumoniae* clinical isolates, of which 383 were colistin-resistant, obtained from various clinical specimens (Table 1).

The pooled prevalence of colistin resistance in MDR K. pneumoniae *isolates*

This meta-analysis investigates the pooled prevalence of colistin resistance among MDR *K. pneumoniae* clinical isolates. The initial pooled prevalence estimate was 21.59%, with significant heterogeneity observed between studies ($I^2 = 99.71\%$, $P < 0.001$) (Figure 2). Publication bias was identified through an asymmetric funnel plot (Figure 3), which was further confirmed by Egger's test, revealing a significant bias ($P = 0.0083$). To address the publication bias, a trim-and-fill analysis was conducted, resulting in the imputation of seven missing studies. After adjusting for publication bias, the final recalculated pooled prevalence of colistin resistance was 28.38% (95% CI: 19.50%–37.26%), with significant heterogeneity ($I^2 = 99.71\%$, $P < 0.001$) (Table S3).

Subgroup meta-analysis

Due to the presence of high heterogeneity across studies, subgroup analysis was employed to investigate the pooled prevalence of colistin resistance in MDR *K. pneumoniae* by country, region and publication time interval. Based on year-based analysis (publication time), a decline in resistance over time was observed. The prevalence of colistin resistance among MDR *K. pneumoniae* isolates was 26.22% (95% CI: 2.56%–50.0%) during the 2010–19 period and 18.02% (95% CI: 10.56%–25.50%) during the 2020–30 April 2024 period. Within each of these time frames, there was a statistically significant decline in colistin resistance ($P = 0.03$ for 2010–19 and $P = 0.00$ for 2020–24). However, when comparing the two periods (2010–19 versus 2020–24), no

Table 2. Subgroup analysis for the pooled prevalence of colistin resistance among MDR *K. pneumoniae* clinical isolates from clinical samples across Africa, 2010–30 April 2024

Subgroup	Characteristics	No. of studies	Pooled prevalence (95% CI)	I^2 (%)	*P* value
Years	2010–19	10	26.22% (2.56%–50.0%)	99.88	0.03
	2020–30 April 2024	20	18.02% (10.56%–25.50%)	98.52	0.001
	Test of group difference: Q (1) = 0.42				0.52
Country	Egypt	14	14.02% (7.13%–20.91%)	96.43	0.001
	Nigeria	4	39.12% (1.96%–76.28%)	98.69	0.039
	South Africa	3	17.12% (−0.36%–34.61%)	97.45	0.055
	Kenya	2	22.52% (22.45%–67.49%)	95.69	0.326
	Test of group difference: Q (10) = 3509.93				0.001
Sub-regional	South Africa	3	17.12% (−0.36%–34.61%)	97.45	0.05
	North Africa	15	12.99% (6.38%–19.60%)	98.16	0.001
	West Africa	6	37.05% (7.56%–66.55%)	99.14	0.001
	East Africa	4	42.34% (−0.02%–84.71%)	99.65	0.05
	Test of group difference				0.001
	Overall		21.59% (12.12%–31.06%)	99.71	0.001

statistically significant difference was observed ($P = 0.52$). Despite the observed decline in resistance, high heterogeneity persisted in both periods, with an I^2 value exceeding 99.5% (Table 2).

The country-based analysis revealed significant differences in resistance ($P < 0.001$). The pooled prevalence of colistin resistance varied substantially across nations: 39.12% (95% CI: 1.96%–76.28%) in Nigeria, 17.12% (95% CI: −0.36%–34.61%) in South Africa, 14.02% (95% CI: 7.13%–20.91%) in Egypt and 22.52% (95% CI: 22.45%–67.49%) in Kenya. High heterogeneity was also observed across the included studies, as indicated by an I^2 statistic ($I^2 > 95.0\%$) (Table 2).

Sub-regional subgroup analysis also revealed significant differences across regions ($P < 0.01$), with pooled prevalence rates of 37.1% (95% CI: 7.56%–66.55%) in West Africa, 17.1% (95% CI: −0.36%–34.61%) in South Africa and 13.0% (95% CI: 6.38%–19.60%) in North Africa, accompanied by high heterogeneity and a statistically significant association ($P < 0.001$). East Africa had a high pooled prevalence of colistin resistance at 42.3% (95% CI: −0.02%–84.71%) with high heterogeneity (Table 2). The study highlights significant variability in colistin resistance among MDR *K. pneumoniae* isolates across different countries and regions, with notable differences in resistance rates.

Discussion

Colistin is one of the effective antibiotics for treating severe infections caused by MDR Gram-negative pathogenic bacteria, particularly those resistant to many other antibiotics.[56] However, the development of plasmid-mediated colistin resistance in Enterobacteriaceae significantly limits its use.[3,57] Chromosomal mutations in *K. pneumoniae* also contribute significantly to colistin resistance. Mutations in the mgrB gene, which regulates the phoPQ two-component system, lead to upregulation of phoPQ and subsequent modification of lipopolysaccharides (LPS), reducing colistin binding. Similarly, mutations in the phoP gene, a key regulator of the phoPQ system, also result in LPS modifications and colistin resistance.[58]

Colistin-resistant MDR *K. pneumoniae* is a growing public health concern.[59] The emergence of *K. pneumoniae* strains resistant to colistin and multiple other classes of antibiotics has been reported throughout the world, particularly in hospital settings where the prevalence of MDR *K. pneumoniae* pathogen is highest.[60] Colistin resistance in *K. pneumoniae* is often associated with high morbidity and mortality, especially in critically ill patients, and its spread poses a serious challenge to treatment options across the African continent.[3,61] The detection of colistin resistance in clinical samples has become more essential as the use of colistin has increased for the treatment of MDR *K. pneumoniae* and other carbapenem-resistant organisms.[62] Hence, the rationale of the present study was to estimate the pooled prevalence of colistin resistance in MDR *K. pneumoniae* isolates from clinical specimens in Africa.

In our study, data were collected from 11 African countries: Egypt, Nigeria, South Africa, Uganda, Kenya, the Democratic Republic of the Congo, Algeria, Ethiopia, Mali, Ghana and Mozambique, with the majority of the data accessed from Egypt. In this meta-analysis, the pooled prevalence of colistin resistance in MDR *K. pneumoniae* isolates was 21.6%, higher than the 11.6% reported in a global systematic review,[63] the 3.1% in a meta-analysis of bloodstream infections[59] and the 4.4% in the SENTRY Antimicrobial Surveillance Program between 2014 and 2015.[64] It was also higher than the 6.9% reported in Iran,[65] 9.2% in India,[66] 8.2% in China and 5.4% across 18 European countries (2015–17).[67] However, our findings are consistent with a study on colistin resistance among patients with carbapenem-resistant *K. pneumoniae* in Italy from 2010 to 2011, which reported a resistance rate of 36.1%,[68] as well as reports from Australia (28.6%)[69] and Oman (24.2%)[70] on colistin resistance.

The prevalence of colistin resistance among MDR *K. pneumoniae* isolates within periods (2010–19 and 2020–30 April 2024) was 26.22% (95% CI: 2.56%–50.0%) and 18.02% (95% CI: 10.56%–25.50%), respectively. There were statistically significant declines in colistin resistance, one for each period ($P = 0.03$ and

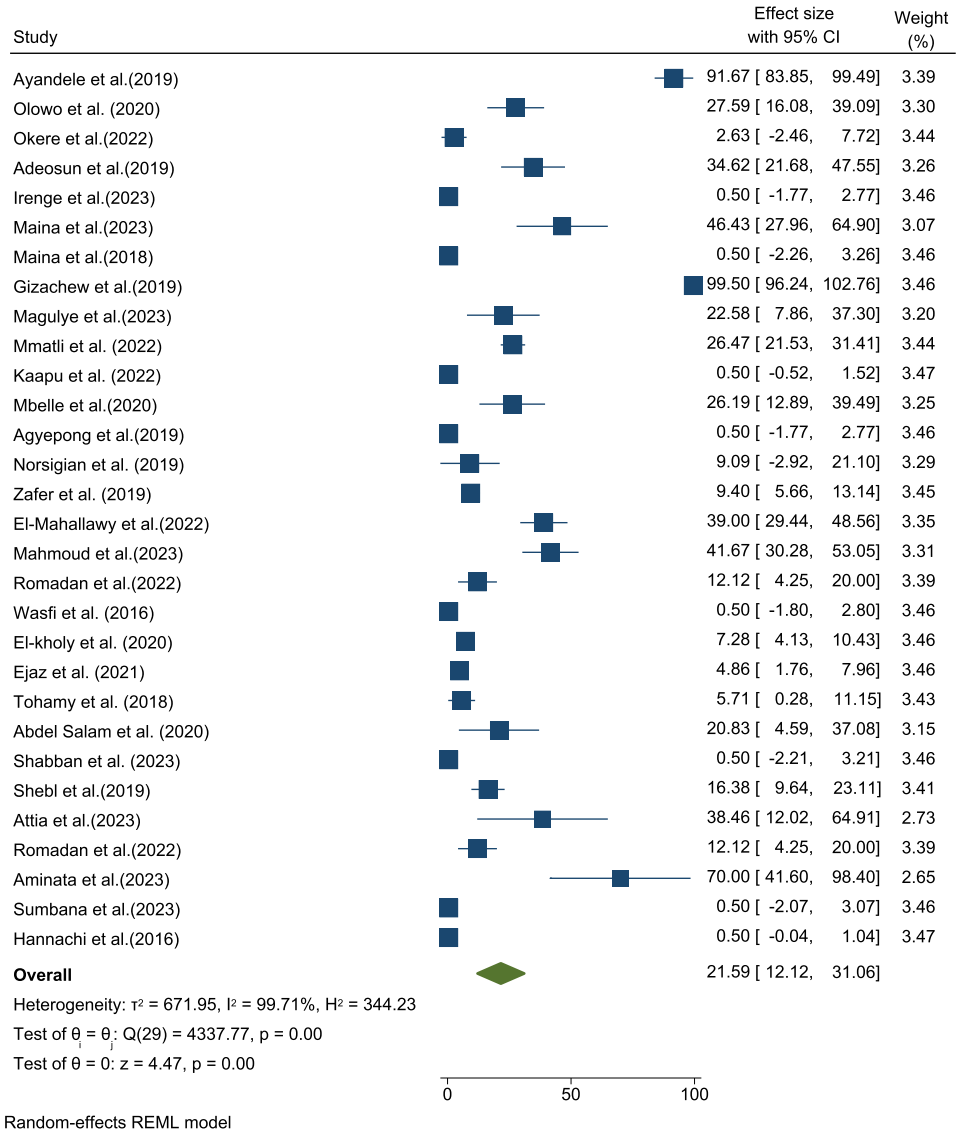

Figure 2. Forest plot illustrating the pooled prevalence of colistin resistance among MDR *K. pneumoniae* isolated from clinical samples across Africa.

P=0.00). However, between the two periods (2010–19 versus 2020–30 April 2024), no statistically significant difference was found (*P*=0.52), indicating that the overall reduction between the two time frames was not significant. This suggests that these changes may be episodic, localized or influenced by short-term interventions, rather than reflecting a sustained or uniform downward trend. Additionally, the country-based subgroup analysis showed statistically significant differences (*P*<0.001). Our meta-analysis revealed varying pooled prevalence of colistin resistance across nations: Nigeria (39.1%), Kenya (22.5%), South Africa (17.1%) and Egypt (14.0%). The limited number of studies included in the meta-analysis may lead to either an overestimation or underestimation of the pooled prevalence. As shown in the subgroup analysis, the pooled prevalence of colistin resistance in Egypt was 14.0%, which aligns with a 2019 study conducted in Egypt on MDR *K. pneumoniae* clinical isolates.[35]

Limitations of the study

This study offers valuable insights into colistin resistance in MDR *K. pneumoniae* in Africa, highlighting long-term trends and the growing resistance issue. However, this meta-analysis had a few limitations, including geographical and socio-economic variations, inconsistent reporting across countries and potential biases arising from the inclusion of only English-language publications sourced from a limited number of databases. In addition, there might be sample bias, since the majority of the included studies were conducted in Hospitals.

Conclusions

To the best of our knowledge, this study is the first systematic review and meta-analysis to examine colistin resistance in MDR

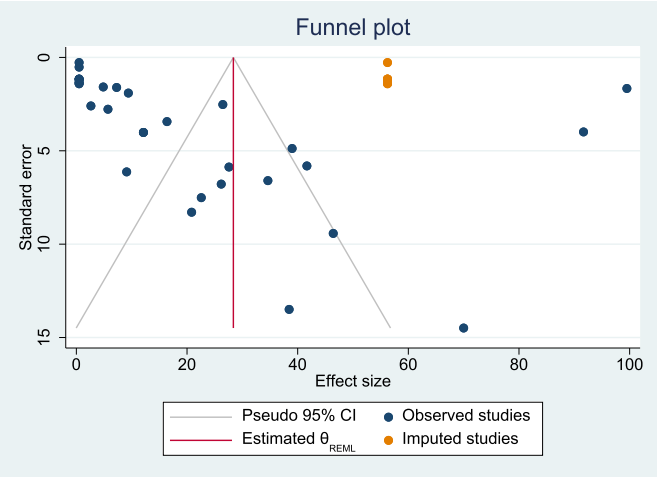

Figure 3. Funnel plot depicting publication bias in the pooled prevalence of colistin resistance among *K. pneumoniae* isolates recovered from clinical samples across Africa.

K. pneumoniae isolates recovered from clinical samples across Africa. Given the recent use of colistin as a life-saving treatment for carbapenem-resistant and MDR *K. pneumoniae*, it is crucial to assess the prevalence of resistance to this antibiotic. This meta-analysis revealed a 21.6% prevalence of colistin resistance among clinical isolates of MDR *K. pneumoniae* in Africa, indicating a high resistance rate. Despite the considerable heterogeneity across the included studies and the limited or absent data from some countries, the estimated pooled prevalence provides a valuable indicator of colistin resistance in Africa. The findings of this meta-analysis support the need for regulatory measures on colistin use. Further research is essential, particularly studies focusing on colistin stewardship and improving access to rapid diagnostic tools for detecting colistin resistance across the continent.

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Transparency declarations

The authors declare that they have no conflicts of interest.

Authors' contributions

Y.G. led the systematic review and meta-analysis, overseeing the study's conceptualization, article selection, data extraction, statistical analysis and manuscript preparation. Y.G., M.A.R., Z.A., E.G. and A.S. were involved in searching for relevant articles, conducting data extraction, performing statistical analysis and contributing to manuscript drafting. M.T., S.G., A.A. and G.B. were involved in reviewing the manuscript. All authors actively participated in reviewing the study, analysing the data and writing the manuscript. They also approved the final version for submission, confirming their endorsement of its content and findings.

Supplementary data

Tables S1–S3 are available as Supplementary data at *JAC-AMR* Online.

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