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Extended-spectrum beta-lactam-resistant *Klebsiella pneumoniae* in sub-Saharan Africa: a systematic review and meta-analysis from a One Health perspective

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Abstract

Background Extended-spectrum beta-lactamase (ESBL)-producing *Klebsiella pneumoniae* is a critical priority pathogen for which there is a need for new antimicrobials and poses a great public health threat to many parts of the world including sub-Saharan Africa (SSA). This study aims to determine the prevalence of ESBL-producing *K. pneumoniae* in SSA using a one health perspective, and the predominant ESBL genes in the region.

Methods Databases such as PubMed, Scopus, Web of Science, Africa Journal Online, and Google Scholar were searched for eligible articles based on pre-set eligibility criteria. After screening of titles, abstracts, and full texts, a meta-analysis using a random-effect model was conducted on the eligible studies to determine the overall and subgroup prevalence of ESBL-producing *K. pneumoniae* in SSA.

Results This meta-analysis included 119 eligible studies from 25 SSA countries in all SSA subregions. The overall prevalence of ESBL-producing *K. pneumoniae* in SSA is estimated to be 8.6% [95% CI: 6.4–11]. South Africa (18.5%) and Central Africa (4.6%) subregions have the highest and lowest prevalence of ESBL-producing *K. pneumoniae* in the region, respectively. Additionally, South Africa (23.3%), Kenya (23%), and Nigeria (11.1%) are the top three countries with ESBL-*K. pneumoniae*. Animal samples were also seen to have the highest prevalence compared to clinical and environmental samples in this study. Lastly, $bla_{CTX-M-15}$ was the most reported ESBL gene in SSA.

Conclusion The widespread presence of resistant strains in certain regions poses a significant risk of inter-country transmission, highlighting the need for collaborative regional surveillance and control efforts.

Keywords Antibiotic resistance, *Klebsiella pneumoniae*, Sub-Saharan Africa, ESBL epidemiology, One Health, Public Health

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Introduction

Increased treatment failure of infectious diseases caused by microbes globally is attributed to antimicrobial resistance (AMR), which occurs due to widespread or indiscriminate use of antibiotics. AMR significantly impacts mortality and morbidity, bringing substantial economic burdens to people and countries [1]. An estimation revealed five million AMR-linked deaths in 2019, which portend that the projected ten million deaths in 2050 and 24 million people below the poverty lines in 2030 as a result of AMR may be attained sooner than initially anticipated [2, 3]. Most of the deaths were believed to occur in sub-Saharan Africa and were attributed to infections caused by a cohort of both gram-positive and negative bacteria called ESKAPE pathogens. The ESKAPE pathogens include *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterococci faecium* [4].

K. pneumoniae is a ubiquitous bacterium found in water, soil, and the gut of healthy humans and animals [5]. Classified under the family *Enterobacteriaceae*, they are known to be non-motile and lactose fermenting. *K. pneumoniae* is notorious for its role as an opportunistic pathogen, capable of causing both community and healthcare-associated infections [6]. In fact, 10% of nosocomial bacterial infections are attributed to *K. pneumoniae* [7]. These strains of *K. pneumoniae* have been further classified into classical, hypervirulent, and multidrug resistant strains based on phenotypic and genotypic differences [8].

K. pneumoniae is responsible for a range of difficult-to-treat infections, including pneumonia, sepsis, bloodstream infections, meningitis, pyogenic liver abscesses, urinary tract infections (UTIs), and wounds [8]. They are particularly associated with ventilator-associated pneumoniae (VAP), and are the leading cause of bacteraemia among the Gram-negative members of the ESKAPE pathogens, with a relatively high mortality rate [9–12].

A significant concern for *K. pneumoniae* has been the rate at which they develop antibiotic resistance, as they harbour a lot of AMR plasmids [10, 13]. Thus, *K. pneumoniae* is listed as a critical pathogen in need of urgent drug development by the World Health Organisation (WHO) [14]. Several studies have revealed the vast array of mechanisms adopted by this pathogen to evade both host immune defence and antibiotics, including the production of antibiotic-modifying enzymes such as Extended Spectrum Beta-Lactamase (ESBL) [15, 16]. ESBL confers resistance to a group of antibiotics with a beta-lactam ring, including penicillin, monobactams (aztreonam), and the first, second, and third-generation cephalosporin by hydrolysing the ring [6]. *K. pneumoniae* has been reported to harbour several plasmid-encoded ESBL enzyme families and their variants, such as Sulfhydryl variable (bla_{SHV}), Temoniera (bla_{TEM}), and Oxacillinases (bla_{OXA}) [17]. In recent years, cefotaximase ($bla_{CTX\text{-}M}$) has emerged, which is increasingly reported on a global scale and is currently the most predominant ESBL enzyme in numerous continents and countries worldwide [18–20].

Despite growing concerns about ESBL-producing *K. pneumoniae*, to the best of our knowledge, there are no available study on systematic review and meta-analyses of the pooled prevalence status in sub-Saharan Africa. Understanding the prevalence of these resistant strains is essential for guiding clinical decision-making, informing public health interventions, and ultimately improving patient outcomes in the face of growing antibiotic resistance. This systematic review and meta-analysis aim to comprehensively determine the prevalence of ESBL-producing *K. pneumoniae* in sub-Saharan Africa using a one health perspective, describe the epidemiology within the region, and investigate the predominant ESBL genes in the region.

Methods

Study design, search strategy and screening

This study is a systematic review and meta-analysis and was conducted in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2020 guideline for systematic reviews and meta-analysis [21]. A comprehensive literature search was done on databases such as PubMed, Scopus, Web of Science, and African Journal Online were searched using combinations of the following keywords "ESBL", "Extended-spectrum beta-lactamase", "resistance", "*Klebsiella pneumoniae*", "*K. pneumoniae*", "sub-Saharan Africa", "SSA". The last search was done in December 2023. A supplementary search to identify grey literature was done on Google Scholar by only considering the first 5 search result pages. The articles' titles, abstracts, and full texts were screened to check if they comply with the preset eligibility criteria.

Eligibility criteria

Articles included in the final meta-analysis include articles published in English, between 2013 and 2023, articles that reported the presence of at least one ESBL-producing *K. pneumoniae* from human, animal and/or environmental samples. In studies where the total *K. pneumoniae* isolate count was not reported, inclusion was based on the explicit identification of ESBL-producing *K. pneumoniae* by the study authors. We did not include general ESBL prevalence unless the organism was clearly specified as *K. pneumoniae*. Only articles published in at least one country in SSA were included. Studies that reported *K. pneumoniae* prevalence but no ESBL-producing strains were excluded. Only primary

studies were included, while any type of review articles and meta-analyses were excluded.

Data extraction and quality assessment

A data extraction table was created in Microsoft Excel to include important details from the articles such as first author, year of publication, study design, sample source, country of study, sub-region, sample size, number of *K. pneumoniae* isolates, number of ESBL strains, and ESBL gene. All human samples were grouped as clinical sources in this study while samples from either food or water sources were put under environmental sources. RBS, AAO, GMO, RAY, and KIY extracted the data independently, MOO and OQO did the final verification of the extracted data and resolved discrepancies. The qualities of the studies were assessed based on the method used to characterise ESBL strains. Studies that used only phenotypic methods like disc diffusion, broth microdilution, and automated antimicrobial susceptibility testing methods like VITEK were grouped as low, studies that used only genotypic/molecular characterisation methods were classified as medium, while studies that used both phenotypic and molecular methods were classified as high quality (Supplementary Figure 1).

Meta-analyses

To estimate pooled prevalence, the sample size and number of ESBL-producing *K. pneumoniae* strains were extracted and pooled together using a random effect model with the meta package in R (version 4.3.3). Subgroup analysis based on subregion, sample source, and country was done but only subgroups with more than two eligible articles are reported in this study. The sub-Saharan Africa map was created in R using the *rnaturalearth* package. A random effects model was used in this study to account for expected variations between studies, including differences in sample size and study settings. Both funnel plot and Egger's test of the overall effect size were used to estimate publication bias, while I^2, based on Cochran's Q test statistic, was used as a measure of heterogeneity.

Results

Search outcome

A total of 4746 search results were retrieved from five databases namely Google Scholar (4230), PubMed (162), Scopus (270), Web of Science (28), and African Journal Online (56). One hundred and nineteen (119) eligible studies were finally included in the meta-analysis after the screening of titles, abstracts, full texts, and the exclusion of duplicates and ineligible studies (Fig. 1).

Study characteristics

This study analysed a total of 119 eligible articles from 25 sub-Saharan African countries. East Africa (53) had the highest number of studies reporting ESBL resistance in *K. pneumoniae*, followed by West Africa (43), South Africa (12), and Central Africa (10) (Fig. 2A). One of the articles reported ESBL resistance in *K. pneumoniae* from multiple sub-regions in SSA. Most of the eligible articles reported ESBL resistance in *K. pneumoniae* from clinical samples (104), followed by environmental (10), and animal (5) samples (Fig. 2B). Additionally, Ethiopia (20) had the highest number of eligible studies, followed by Tanzania (16), Nigeria (14), Ghana (12), South Africa (10), Uganda (6), Gabon (4), Cameroon (4), Kenya (4), Malawi (3), Madagascar (3), Benin (3), DRC (3), Sierra Leone (2), Chad (2), and Burkina Faso (2) (Fig. 2C). Others (Mali, Zimbabwe, Gambia, Sudan, Togo, Guinea Bissau, Mozambique, Côte d'Ivoire, and Central Africa Republic) had just one eligible study each (Fig. 2C) while two studies were carried out in multiple countries. The characteristics of the 119 eligible studies are presented in the Supplementary Table 1.

Prevalence of ESBL-resistance in *K. pneumoniae*

The overall pooled prevalence of ESBL-resistance in *K. pneumoniae* in sub-Saharan Africa is estimated to be approximately 8.6% [95% CI: 6.4–11.0] (Fig. 3). The South African subregion was estimated to have the highest prevalence (18.5% [95% CI: 5.07–37.1]) of ESBL-producing *K. pneumoniae*, followed by West Africa (9.3% [95% CI: 5.8–13.4]) (Fig. 4). On the other hand, the subregion with the lowest prevalence was Central Africa (4.6% [95% CI 1.9–8.3]) (Fig. 4). The highest ESBL prevalence in *K. pneumoniae* in SSA was seen in animals (12.1% [95% CI: 0.8–33.1]) compared to 8.6% [95% CI: 6.4–11.2]) from clinical specimens and 6.2% [95% CI: 0.97–14.4] from the environment (Fig. 5). Among the countries included in this analysis (countries with at least three eligible studies), South Africa (23.3% [95% CI: 6.5–45.8]) has the highest burden of ESBL-producing *K. pneumoniae*, followed by Kenya (23% [95% CI: 0–68]), Nigeria (11.1% [95% CI: 5.1–18.9]), and Tanzania (8.1.% [95% CI: 3.8–13.8]) (Fig. 6). Madagascar had the lowest prevalence of ESBL-producing *K. pneumoniae* (Fig. 6). The forest plot of subgroup analysis of ESBL-producing *K. pneumoniae* based on countries in sub-Saharan Africa is presented in the Supplementary Fig. 2. A high I^2 value was seen in this result which is an indication of high heterogeneity in this study. Both funnel plot (asymmetrical) and Egger's test (p-value < 0.0001) indicate publication bias (Supplementary Figure 3).

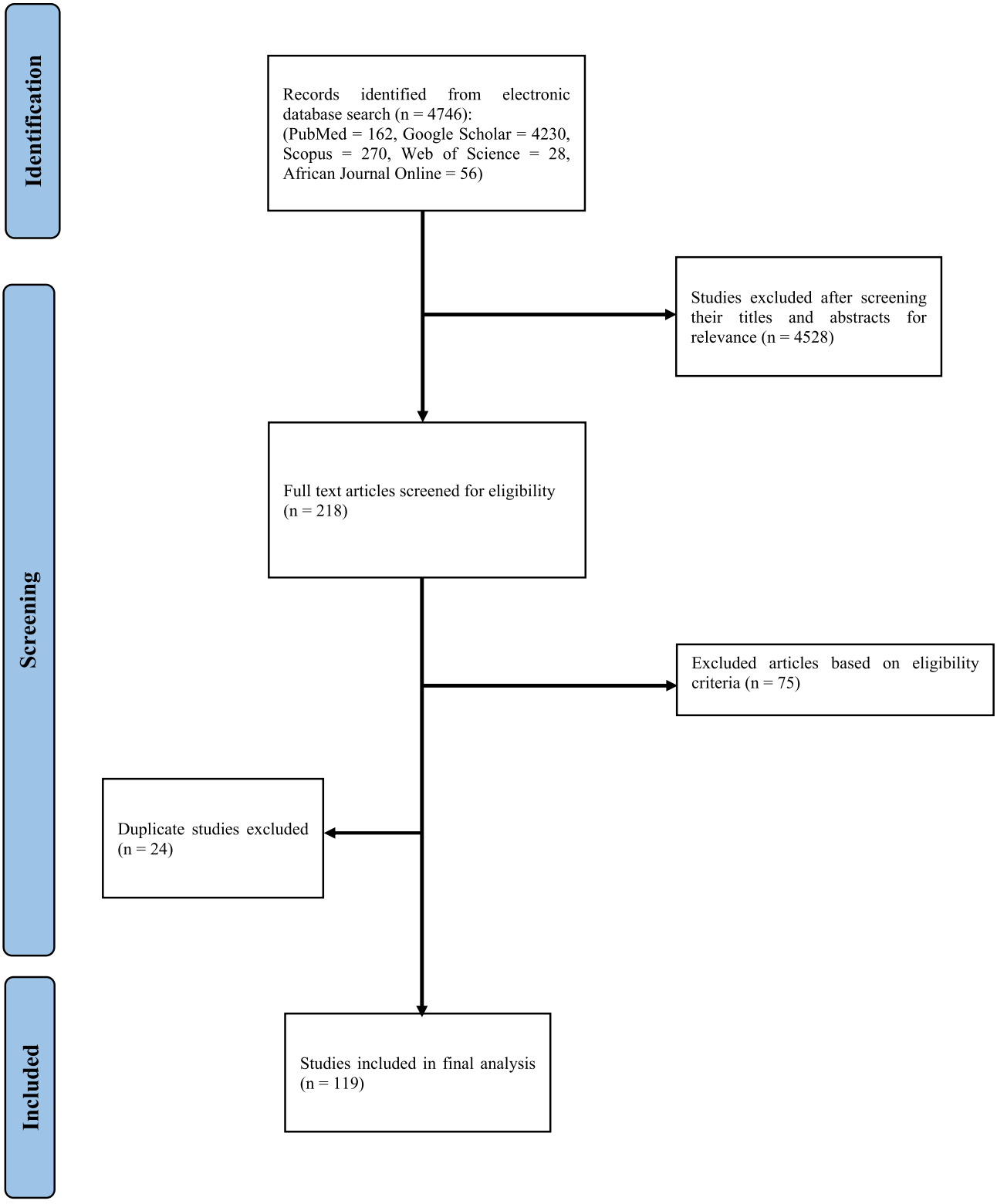

Fig. 1 PRISMA Flow diagram of search and screening strategy

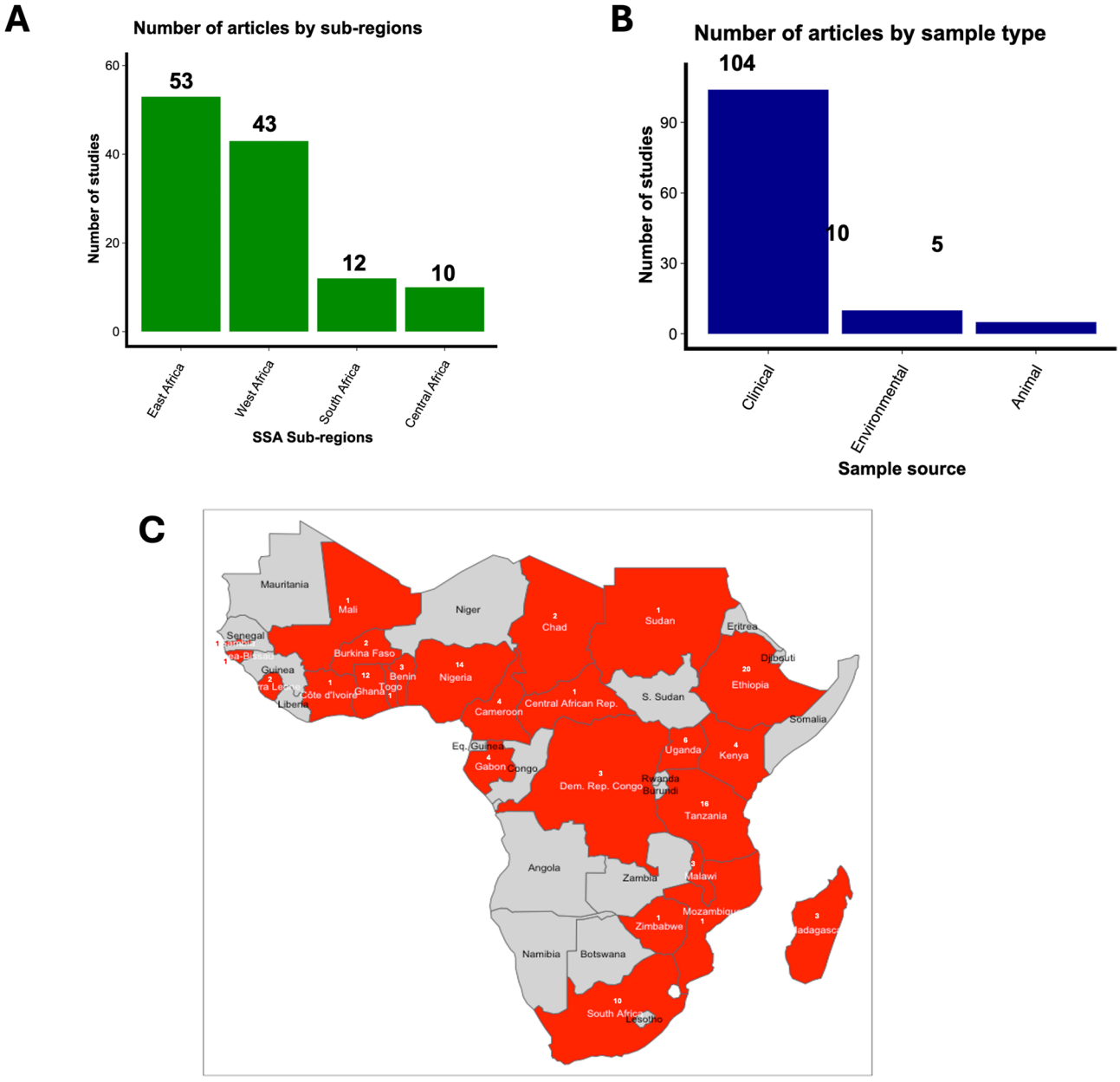

Fig. 2 Classification of included studies based on sub-region (**A**), sample type (**B**), and country (**C**)

Genomic epidemiology of ESBL genes in SSA

Fifty-three (53) out of the 119 eligible studies included in this analysis used genotypic assays to characterise ESBL genes in *K. pneumoniae* (Supplementary Fig. 1). The ESBL genes reported in the studies include $bla_{\text{CTX-M}}$ (including $bla_{\text{CTX-M-1}}$, $bla_{\text{CTX-M-2}}$, $bla_{\text{CTX-M-8}}$, $bla_{\text{CTX-M-9}}$, $bla_{\text{CTX-M-11}}$, $bla_{\text{CTX-M-14}}$, and $bla_{\text{CTX-M-15}}$), bla_{SHV} ($bla_{\text{SHV-11}}$, $bla_{\text{SHV-12}}$, $bla_{\text{SHV-28}}$), bla_{TEM}, and bla_{OXA}. Among these genes, $bla_{\text{CTX-M-15}}$ was the most reported in most articles analysed. Additionally, all three major ESBL genes ($bla_{\text{CTX-M}}$, bla_{SHV}, and bla_{TEM}) were reported in all the sample types (clinical, animal, and environment).

Discussion

Klebsiella pneumoniae remains an important human and animal pathogen due to its position as a member of the ESKAPE pathogens and a WHO's critical priority pathogen due to the growing threat of multidrug resistance globally [22]. Additionally, the presence of ESBL genes in *K. pneumoniae* confers resistance to many antibiotics, hence, making it difficult to treat infections resulting from these resistant strains. Understanding the prevalence of ESBL-resistant *K. pneumoniae* strains in sub-Saharan Africa is an important step to curbing the spread of this pathogen within the region as well as to other parts of the world.

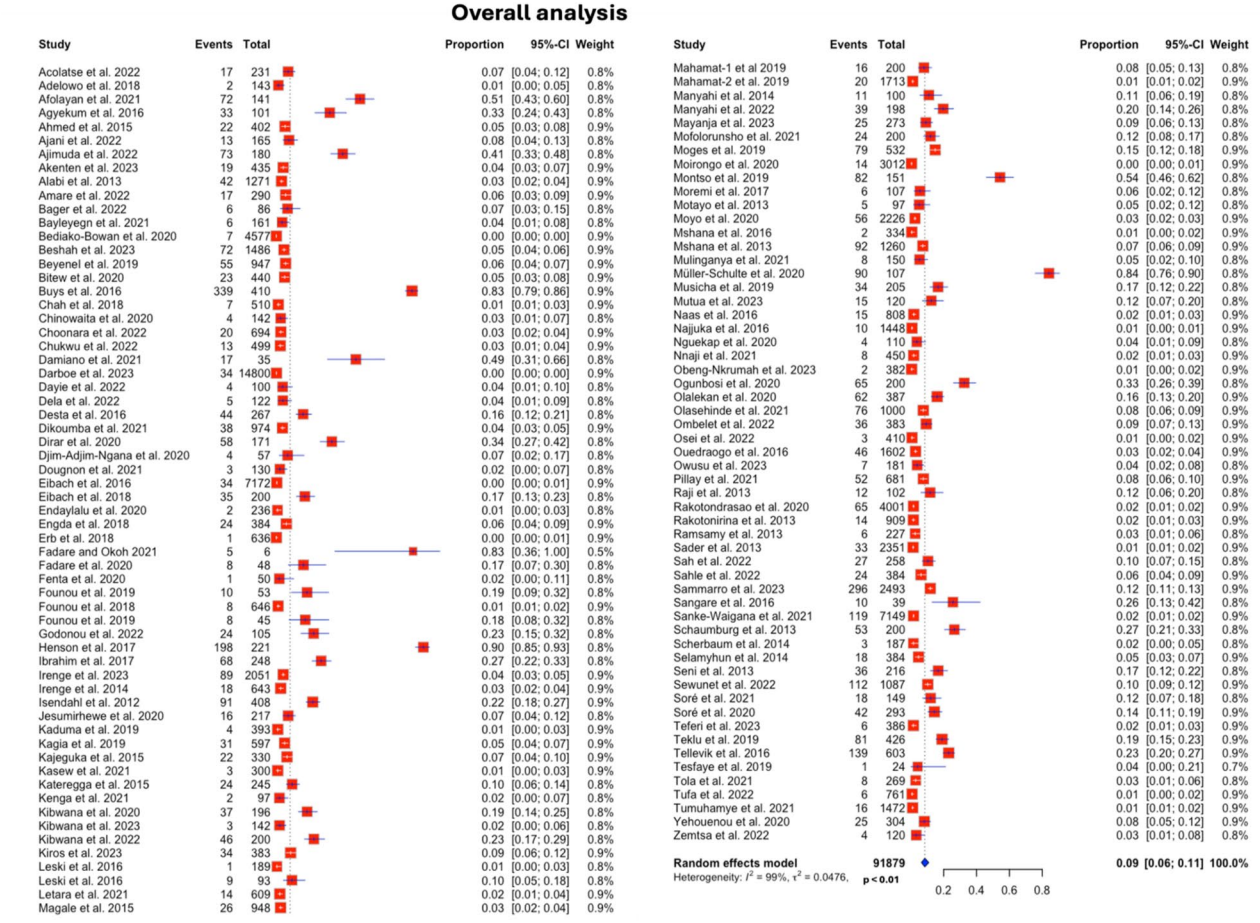

Fig. 3 Forest plot of overall prevalence of ESBL-producing *K. pneumoniae* from sub-Saharan Africa

This study analysed articles that reported ESBL-resistance in *K. pneumoniae* from clinical, environmental, and animal sources across 25 countries in sub-Saharan Africa (SSA). The overall prevalence of ESBL-producing *K. pneumoniae* in sub-Saharan Africa is 8.6%. Similarly, the highest prevalence of ESBL-producing *K. pneumoniae* in SSA subregion was estimated at 18.5% in Southern Africa, followed by 9.3% in West Africa, and the lowest at 4.6% in Central Africa. These are lower than what has previously been reported in South East Asia (27%), Middle East (35.4%) [23], and elsewhere [24]. Paradoxically, the recent global burden of AMR report estimated sub-Saharan Africa as one of the highest burdens of AMR [2]. However, this low prevalence might have cropped up from the point that many laboratories and healthcare facilities in the region lack familiarity with the significance of detecting ESBL-producing Gram-negative organisms. This might have contributed to the low prevalence. Notwithstanding, Mohd et al. [24] reported a 28.7% prevalence of MDR *K. pneumoniae* in Africa which is a much higher value than we reported in this study. The disparity might be due to the fact that the authors considered all countries in Africa while ours only focused on SSA. Moreover, the authors considered all multidrug-resistant strains of *K. pneumoniae*, including carbapenem-resistant strains, whilst ESBL-producing strains are our focal point.

Animal studies in our review showed the highest prevalence of ESBL-producing *K. pneumoniae* (12.1%), compared to clinical (8.6%) and environmental studies (6.2%). This disparity may be explained by the intensity and purpose of antibiotic use across these sectors, with animal production settings often applying antibiotics more frequently and with less regulatory oversight. This finding underscores the critical role of animals as reservoirs for resistant bacteria. The widespread use of antimicrobials in animal husbandry - for disease prevention, treatment, and growth promotion - has significantly contributed to this trend [25]. Such practices, including in aquaculture, have resulted in drug residues being detected in edible fish species like carp and chub, often exceeding permissible limits [26]. Prolonged and subtherapeutic antibiotic use in livestock fosters resistance development, and these resistant strains can be transmitted to humans through contaminated food, water, manure, or direct animal contact [27–29]. Furthermore, horizontal gene transfer

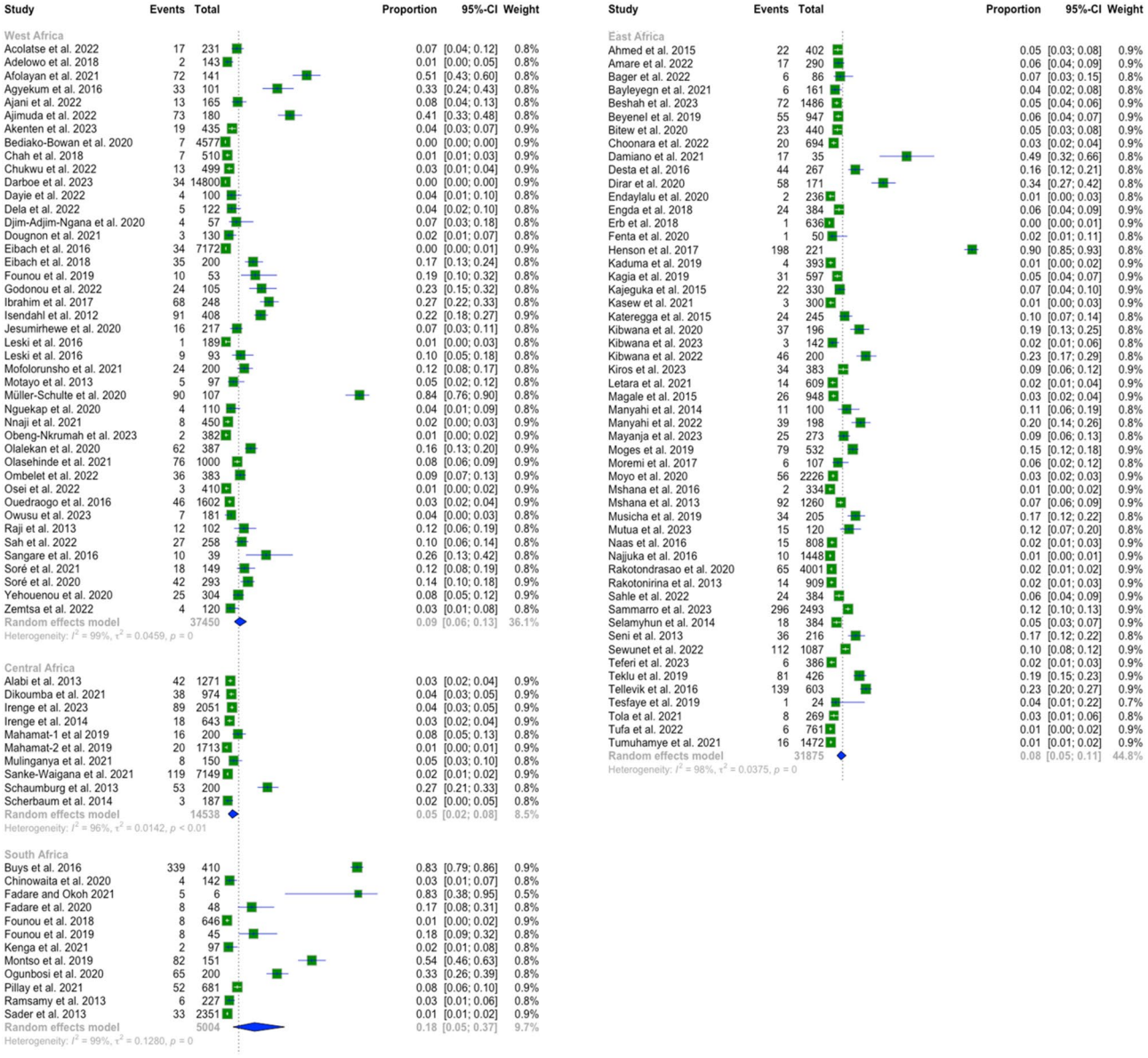

Fig. 4 Forest plot showing subgroup analysis of ESBL-producing *K. pneumoniae* based on subregions in sub-Saharan Africa

via plasmids and other mobile elements facilitates the rapid spread of resistance between bacterial species [30], increasing occupational risks for farm workers and veterinarians.

Many of the resistant pathogens found in animals, particularly within the *Enterobacteriaceae* family, such as *Klebsiella pneumoniae*, are capable of causing severe infections in humans. ESBL-producing strains are not only resistant to beta-lactams but also to multiple drug classes including tetracyclines, fluoroquinolones, and aminoglycosides [31]. The misuse of antimicrobials in both clinical and agricultural settings - often without prescription - exacerbates resistance levels [32]. Moreover, the structural similarity between antibiotics used in animals and humans intensifies cross-resistance concerns. Environmental sources such as hospital wastewater and contaminated animal feces further contribute to resistance gene dissemination [33, 34]. These findings support the urgent need for integrated AMR surveillance under a One Health framework that captures human, animal, and environmental interactions.

Among countries with at least three eligible studies, South Africa had the highest burden of ESBL-producing *K. pneumoniae* at 23.3%, followed by Kenya at 23%, Nigeria at 11.1%, and Tanzania at 8.1%. Madagascar reported the lowest prevalence (1.63%). The prevalence of ESBL-producing *K. pneumoniae* in some sub-Saharan African countries in this study is similar to previous reports in

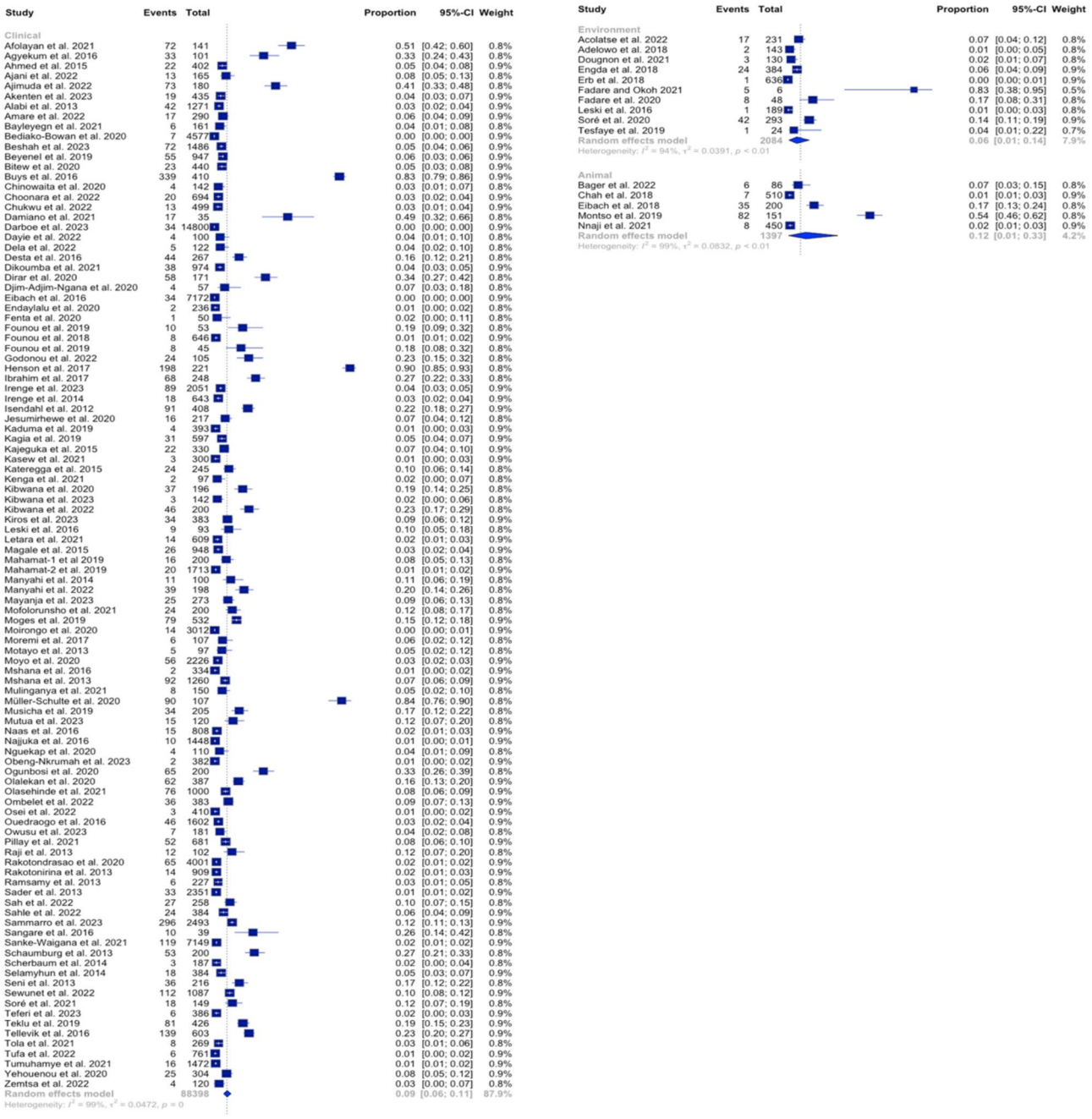

Fig. 5 Forest plot showing subgroup analysis of ESBL-producing *K. pneumoniae* based on sample source in sub-Saharan Africa

Egypt [35]. They reported prevalence rates of 17% and 38.8%, suggesting an increasing spread of ESBLs, possibly due to the widespread use of third-generation cephalosporins. Prevalence varies by species, region, infection control practices, and antibiotic use patterns. Selective pressure from excessive cephalosporin use in certain countries contributes to rising ESBL rates [36].

Our analysis highlights gaps in the existing literature, suggesting that some countries in sub-Saharan Africa may have limited or no available data on ESBL-producing *K. pneumoniae*. These grey areas pose a great challenge in curbing the spread of AMR pathogens and genes. The ease of migration and porous borders between these countries and other countries within the region – especially those that share the same boundaries – would make it easy to spread multidrug-resistant pathogens like *K. pneumoniae* [37]. To avoid this, both country and regional governments in SSA should deploy resources to grey areas to help understand the epidemiology of multidrug-resistant pathogens and control their spread.

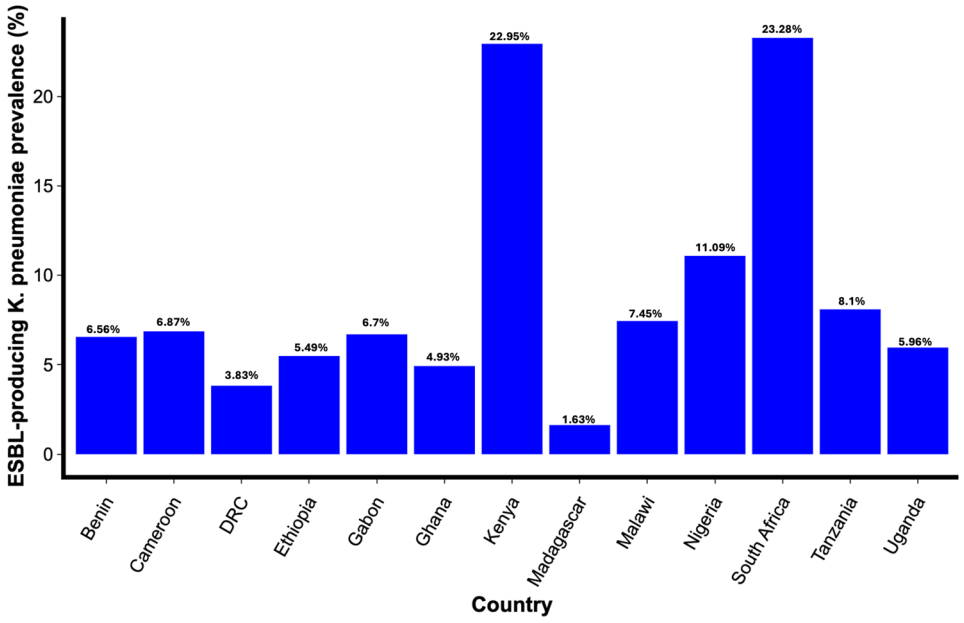

Fig. 6 ESBL-producing *Klebsiella pneumoniae* prevalence in 13 sub-Saharan African countries

Additionally, some of the countries in this study (Côte d'Ivoire, Central Africa Republic, Zimbabwe, Mozambique, Togo, Gambia, Guinea Bissau, Mali, Burkina Faso, Chad, Sudan and Sierra Leone) have less than 3 eligible articles, making it difficult to estimate the prevalence of ESBL-producing *K. pneumoniae* in these countries.

Globally, there is growing concern about how ESBL-producing bacteria affect the effectiveness of treatments for bacterial infections. This study identifies the major ESBL genes present in *K. pneumoniae* isolates in sub-Saharan Africa. Our study revealed bla_{TEM}, bla_{SHV}, and $bla_{\text{CTX-M}}$ as the three main ESBL genes in *K. pneumoniae* in SSA. The detection of these resistance genes in *K. pneumoniae* suggests the spread of bacteria producing ESBL enzymes, specifically bla-beta-lactamases. Additionally, other beta-lactamase genes identified include carbapenem-hydrolyzing beta-lactamases such as $bla_{\text{OXA-1}}$, $bla_{\text{OXA-10}}$, $bla_{\text{OXA-48}}$, $bla_{\text{OXA-1}}$-like, metallo-beta-lactamase gene IMP, class C beta-lactamases *AmpC* (which inactivates first- and second-generation cephalosporins, including cephamycins like cefoxitin and cefotetan, and third-generation cephalosporins like ceftazidime), *LEN* (which confers resistance to ampicillin, amoxicillin, carbenicillin, and ticarcillin but not extended-spectrum beta-lactams), *OKP* (which confers resistance to penicillins and early cephalosporins in *K. pneumoniae*), and *CMY*–2 (which confers broad-spectrum resistance to beta-lactam antimicrobials, including ceftriaxone and ceftiofur, as well as beta-lactamase inhibitors like clavulanic acid). The $bla_{\text{CTX-M}}$ gene emerged as the most common, followed by bla_{SHV} and bla_{TEM}, consistent with findings from other regions [38]. Despite numerous studies, some areas in SSA still underreport ESBL cases, leaving prevalence unclear. It is evident that $bla_{\text{CTX-M}}$, bla_{SHV}, and bla_{TEM} are the most commonly detected genes, highlighting the need for comprehensive monitoring and infection control measures.

Research has shown that bla_{TEM} genes have been reported in vegetables from Finland [39] and southern Thailand [40], while $bla_{\text{CTX-M}}$ is the most commonly detected gene in animals, humans, and the environment. Additionally, *K. pneumoniae* and *E. coli* from dogs and cats have been found to possess $\text{bla}_{\text{CTX-M-9}}$ type genes [41]. $bla_{\text{CTX-M}}$ enzymes are now the most prevalent ESBL types, likely due to their environmental origins [42]. These enzymes are classified into five subgroups based on amino acid composition: $bla_{\text{CTX-M-1}}$, $bla_{\text{CTX-M-2}}$, $bla_{\text{CTX-M-8}}$, $bla_{\text{CTX-M-9}}$, and $bla_{\text{CTX-M-25}}$ [43]. Our results underscore the importance of the "One Health" approach, as ESBL-producing *K. pneumoniae* was found in animals, clinical specimens, and the environment. The presence of $bla_{\text{CTX-M}}$ and bla_{SHV} in ESBL-producing *K. pneumoniae* from these sources further emphasizes the need for a "One Health" perspective. Future research should adopt this approach to better understand the links between human, animal, and environmental health, particularly regarding antibiotic resistance in zoonotic diseases.

Detection of ESBL *K. pneumoniae* in the studies appraised revealed utilization of various methods, including phenotypic assays, genomic assays, Polymerase Chain Reaction (PCR), NMK-203 card on the Phoenix system, Disc Diffusion (Standard and Kirby-Bauer methods), Etest, Double Disc Diffusion, Vitek 2 Compact System, Double Disc Synergy Test (DDST), Whole Genome

Sequencing, Broth Microdilution, and EUCAST Breakpoints. The use of diverse detection methods contributed to significant heterogeneity in our study. Whole genome sequencing remains an important method for identifying antibiotic-resistant genes, however, many laboratories in SSA do not have resources for this. Hence, result to phenotypic detection methods which could give false positive or negative results. As a result, many antibiotic-resistant pathogens are under-reported in the region.

One limitation of this study is the reliance on disc diffusion methods in many included articles, which may increase the risk of false positives or negatives without genomic confirmation. Another limitation is the absence of eligible studies or the presence of less than three eligible studies from some SSA countries, which prevents the true understanding of the burden of this multidrug-resistant pathogen in those regions. Despite these limitations, our review provides the most comprehensive synthesis to date of ESBL-producing *K. pneumoniae* in sub-Saharan Africa, encompassing data from humans, animals, and the environment across 25 countries and various subregions. Using robust statistical methods, we generated pooled estimates that offer valuable insights into the burden of this critical public health threat in SSA.

In conclusion, our study highlights the urgent need for sustained surveillance in sub-Saharan Africa of multiple drug-resistant microorganisms, especially in locations where data is scarce or non-existent. The high prevalence of these resistant strains in countries such as Tanzania, Nigeria, Kenya, and South Africa is particularly alarming given the region's porous borders and the potential for cross-border transmission. The underreporting of AMR in the region further exacerbates the threat, potentially allowing resistant bacteria to spread swiftly from areas with high, yet unreported, prevalence to those with lower documented cases. To effectively identify and mitigate these emerging threats, it is imperative that policymakers in sub-Saharan Africa prioritize the establishment of comprehensive surveillance systems to curb the spread of multidrug-resistant infections in the region.

Abbreviations

ESBL	Extended-Spectrum Beta-Lactamase
SSA	sub-Saharan Africa
AMR	Antimicrobial Resistance
ESKAPE	Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterococci faecium
WHO	World Health Organisation
bla_{CTX-M}	Cefotaximase
bla_{OXA}	Oxacillinases
bla_{TEM}	Temoniera
bla_{SHV}	Sulfhydryl variable

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-025-11276-9.

Supplementary Material 1.

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None.

Authors' contributions
MOO conceptualised and administered the project. MOO and OQO supervised the project, provided resources and software, validated and interpreted the results. MOO, OQO, RBS, AAO, GMO, MTA, AEK, KIY and RAY contributed to methodology. MOO, OQO, RBS, AAO, GMO, KIY and RAY conducted the investigations. OQO performed the formal analysis. MOO, OQO, RBS, AAO and GMO curated the data. MOO, OQO and MTA visualized the results. MOO, OQO, MTA and AEK wrote original draft of the manuscript and MOO and OQO wrote review and editing.

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Data availability
All dataset generated and analysed in this study are included within the article and/or its Supplementary data file.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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