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Molecular epidemiology of extended-spectrum beta-lactamases and carbapenemases-producing *Shigella* in Africa: a systematic review and meta-analysis

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Abstract

Background The treatment of *Shigella* infections has become a major challenge due to the emergence of multidrug-resistant *Shigella*. There is however insufficient knowledge regarding the molecular epidemiology of *Shigella* strains producing beta-lactamases in Africa. This systematic review investigated the scientific literature on the molecular epidemiology of extended-spectrum beta-lactamase (ESBL) and carbapenemases producing *Shigella* in Africa.

Methods Papers published in English and French from African countries on the molecular epidemiology of ESBL and carbapenemase producing *Shigella* from January 1999 to July 5, 2024 were reviewed. An extensive literature search was conducted through electronic databases including PubMed, Scopus, Web of Sciences, African Journals Online (AJOL) and Google scholar using specific keywords. The meta-analysis and forest plots of *Shigella* species, ESBL and carbapenemases genes were done using the comprehensive Meta-Analysis software. All data were analyzed using a binary random-effects model by the DerSimonian-Laird method at a 95% confidence interval.

Results Out of the 583 research articles, only 18 (3.1%) articles representing eleven countries were included in the meta-analysis. The overall pooled prevalence of ESBL and Carbapenem Resistant (CR)-producing *Shigella* was estimated as 41.2% (95% CI: 22.8–62.4; $I^2 = 93.7\%$, $p < 0.05$). The leading ESBL and CR-producing *Shigella* species reported in this review was *Shigella flexneri*, 34.5% (95% CI: 16.6–58.2; $I^2 = 94.9\%$, $p < 0.05$). ESBL and CR-producing *Shigella sonnei* was the least reported with estimated prevalence of 6.7% (95% CI: 3.4–13.2; $I^2 = 80.7\%$, $p < 0.05$). In this review, bla_{TEM}, bla_{OXA-1}, and bla_{CTX-M} were the most prevalent genes in Africa with prevalence of 25.9% (95% CI: 13.9–43.2; $I^2 = 90.9\%$, $p < 0.05$), 25.7% (95% CI: 14.9–43.0; $I^2 = 93.7\%$, $p < 0.05$), and 10.8% (95% CI: 4.5–23.4; $I^2 = 85.6\%$, $p < 0.05$) respectively. The prevalence of Carbapenemases genes on the other hand was low, reported as 0.8% (95% CI: 0.2–10.3; $I^2 = 51.4\%$; $p < 0.05$) for bla_{NDM}, 1.1% for bla_{KPC}, and 0.5% for bla_{IMP}

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Conclusion This study highlighted *Shigella flexneri* as the most prevalent ESBL and CR-producing *Shigella* species found in various African countries. The findings from this review indicate bla_{TEM}, bla_{OXA-1} and bla_{CTX-M} as the most prevalent genes in Africa while carbapenemases are least prevalent. The findings from the study suggest that ESBL and CR-producing *Shigella* pose a significant public health threat in Africa. Effective antimicrobial resistance (AMR) surveillance strategies are needed to improve the management and treatment of *Shigella* infections in Africa.

Keywords Molecular epidemiology, Meta-analysis, ESBL, Carbapenemases, *Shigella*, Antibiotic resistance, Shigellosis, Public health, Africa

Background

Shigella is one of the bacteria in the Enterobacterales family responsible for diarrheal diseases. Among the four serogroups, composed of group A (*Shigella dysenteriae*), group B (*Shigella flexneri*), group C (*Shigella boydii*) and group D (*Shigella sonnei*), *Shigella flexneri* and *Shigella dysenteriae* have been identified as the lead cause of bacterial dysentery in developing countries [1]. *Shigella* is a pathogen which is mostly transmitted to humans through various means especially through contaminated food or water and person-to-person contact. According to The et al., *Shigella* is largely responsible for severe dysentery with bloody stools and mild diarrhea. *Shigella* can also cause fatal dehydration, especially in vulnerable populations, such as children under five years, the elderly and immunocompromised individuals [2]. Shigellosis is a global public health concern. Annually, there are about 165 million reported or confirmed cases of shigellosis and approximately 1 million deaths worldwide [3]. On a global scale, developing countries have a reportedly greater risk than developed countries [4]. *S. flexneri*, *S. dysenteriae*, and *S. boydii* are considered as the most prevalent species found in developing countries [5]. According to Ayele et al., it is difficult to evaluate the burden of *Shigella* infection in developing countries due to the limited scope of studies and lack of coordinated epidemiological surveillance systems [6]. However, in East Africa, the prevalence of *Shigella* was estimated at 6.2% [6]. A recent study conducted in Mali, Gambia and Kenya showed a 7.4% prevalence of *Shigella* among diarrhea samples [7].

Nowadays, the multidrug resistance of *Shigella* spp. is increasingly recognized as of significant concern in developing countries especially in Africa. Reports from different studies have suggested an ever increasing resistance of *Shigella* to β-lactam, quinolones, aminoglycosides, sulfonamides and tetracyclines [5, 6, 8, 9]. Only carbapenem was considered as a last resort alternative to fight against shigellosis [5, 10]. β-lactam, which were once considered antibiotics of last resort, are now ineffective against Enterobacterales, which explains the recent increased use of carbapenem antibiotics [11]. This phenomenon contributes to accelerate the emergence and dissemination of carbapenem-resistant Enterobacterales (CRE). These bacteria have been identified as high priority antimicrobial resistance (AMR) pathogens of public health concern according World Health Organization (WHO) [12]. According to WHO, CRE and third-generation cephalosporin-resistant (ESBL) Enterobacterales are considered critical priority pathogen, while fluoroquinolones-resistant *Shigella* spp. are considered high priority pathogen [13].

Many studies in Africa have focused on the multidrug-resistance of *Shigella* but, more of these studies have emphasized its phenotypic resistance [6, 14]. Therefore, for the establishment of a robust system for monitoring and combating multidrug-resistant (MDR) *Shigella*, molecular data is essential. Data on the molecular epidemiology of ESBL and carbapenem resistance (CR) producing *Shigella* in Africa are scarce and are not well documented in the literature. We undertook this systematic review focusing on the molecular characterization of ESBL and CR producing *Shigella* in the literature to provide supplementary information to the scientific community and policymakers to support the effective implementation of a surveillance system against multidrug-resistant *Shigella*. To our knowledge, this is the first study that has reported an assessment concerning the molecular epidemiology of ESBL and CR producing *Shigella* in Africa. This review aimed to generate a database concerning molecular epidemiology of ESBL and CR producing *Shigella* in Africa. The main objectives were to (i) highlight the prevalence of ESBL and carbapenemases-producing *Shigella* isolates in Africa, (ii) identify the most prevalent ESBL and CR-producing *Shigella* species associated with this resistance and (iii) determine the most common ESBL and carbapenemase resistance genes found in *Shigella* in Africa.

Methods

Study design

This study was conducted from May 5, 2024 to July 5, 2024. Its objective was to review publications from African countries published between January 1999 to July 5, 2024, including those found in scientific databases such as PubMed, Scopus, Web of Science, African Journals Online (AJOL) and Google Scholar, following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines. The authors selected these databases for their comprehensive coverage,

authority and rigorous indexing and quality control. These databases also have a strong reputation in systematic literature reviews. Additionally, a Google scholar search was conducted to capture any grey literature or articles not found in the four selected databases. The search was carried out using specific keywords "*Shigella*, *Shigella* species, *Shigella flexneri*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella sonnei*, shigellosis, *Shigella* infections, Extended-Spectrum Beta-Lactamase, beta-lactamase as penicillinase (such as TEM-1), oxacillinase (OXA-1), AmpC (CMY), carbapenemase (NDM, KPC, IMP, VIM, OXA-48), ESBL (CTX-M, TEM-3, SHV-2), Multidrug-resistant, MDR, antibiotic resistance, antimicrobial resistance genes, carbapenem resistance, carbapenemase-producing, Metallo-β-lactamase, molecular epidemiology, molecular characterization, Africa, and the country name" (Supplementary Table S1). Only articles published in English and French were considered for inclusion in the study.

Study eligibility criteria

All articles downloaded on the different databases were reviewed, the results exported to Excel software and then compiled. Rayyan AI was utilized to eliminate any remaining duplicates and to categorize and consolidate the results (available at https://new.rayyan.ai/reviews/ https://doi.org/10.60801/screening) while Endnote soft ware was used to manage the collected publications and citations.

Inclusion criteria

The inclusion criteria for the various articles were full-text available research articles reporting the prevalence of ESBL and carbapenemase-producing *Shigella* isolated in African countries, as well as studies detailing the study population and the phenotypic and molecular methods used to detect ESBL and carbapenem-resistance. The literature search spanned all publications from the last 25 years (January 1999 to July 5, 2024). The screening of articles for inclusion were done by three reviewers SNS, RN, and AT.

Exclusion criteria

Any article that contained incomplete information or only used phenotypic methods for antimicrobial detection as well as review articles, conference proceedings, duplicate articles, abstracts, posters, and studies from non-African countries were removed.

Data extraction

Full texts of the screened publications were obtained from the appropriate sources and the data was collected and organized in an MS Excel spreadsheet by the three reviewers SNS, RN, and AT. The data extraction was done by two independent reviewers (SNS and RN) to ensure accuracy. Data were categorized under multiple headings such as study period, publication year, country, samples source, number of isolates, number of ESBL and CR producing *Shigella* spp., ESBL and CR Producing, *Shigella* species, methods for gene detection, prevalence of ESBL and CR genes (Fig. 1).

Study quality

The Joanna Briggs Institute (JBI) checklist for prevalence studies was used to assesses the quality of the studies [15]. It was done by two independent reviewers (NSS and RN). The JBI checklist contains nine questions that were weighted as follows: 1 for a YES response or 0 for a NO response.

Data analysis

The extracted data were used for descriptive statistics analysis. Excel 2013 was used for data entry while the meta-analysis, forest plots, funnel plots of *Shigella* species and different resistance genes, as well as estimation of the country effect, were done using the comprehensive meta-analysis by SNS and RN. All data generated were analyzed using a random-effects model based on the DerSimonian-Laird method for estimating the between-study variance with a 95% confidence interval. The random-effects model was also used in calculating the pooled prevalence of each ESBL and CR-producing *Shigella* species, and also ESBL and CR genetic determinants. We used the inverse variance index (I^2) to quantify the heterogeneity across the studies included in the random-effects model. An I^2 value > 50% indicated considerable heterogeneity. Statistical significance was denoted as p value < 0.05 [16]. Egger's test was used to validate the asymmetry of the funnel plot. The Heatmap plot was generated using the R programming language (version 4.4.1) in R Studio for Windows Version: 2024.04.2 + 764 with the ggplot2 package used to generate the heatmap.

Results

Characteristics of the included studies

The search generated 583 research articles (Fig. 1). A total of 18 (3.1%) full text articles were accessible and utilized for the meta-analysis. The study characteristics are detailed in Table 1. The included studies were found in only 11 countries, namely Egypt (4/18), Nigeria (3/18), Ghana (2/18), Senegal (2/18), Gabon, Libya, Malawi, Mozambique, Niger, Tanzania and Zimbabwe (1/18 in each country) (Table 1). The reviewed studies included clinical, animal and food products samples. Out of the 18 included studies, 11 studies pertained to clinical samples, 4 focused on food products, 1 addressed animal samples, and 2 targeted mixed samples (comprising clinical, environment, animal and food products) (Table 1).

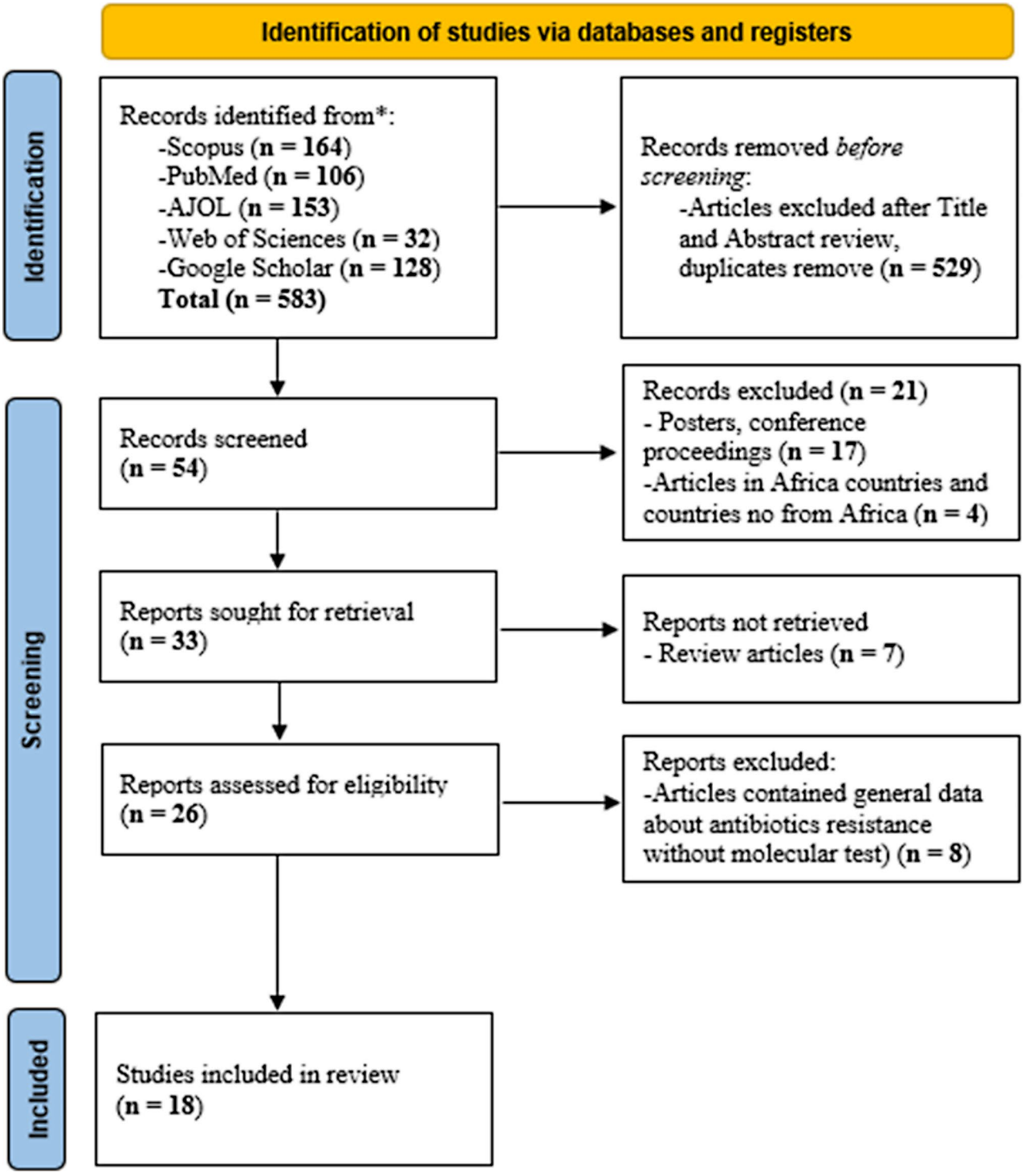

Fig. 1 Flow chart of systematic literature search, identification, screening, and article selection

Meta-analysis

Pooled prevalence of ESBL and CR producing Shigella in Africa

The included studies revealed a total of 403 ESBL and carbapenem-resistant isolates, with an average pooled prevalence of 41.2% (95% CI: 22.8–62.4, $I^2 = 93.7\%$, $p < 0.05$) (Fig. 2). Figure 3 displays a funnel plot showing publication bias in effect estimates among studies examining the prevalence of ESBL and CR producers in Africa. This publication bias was statistically confirmed

Table 1 Review of Africa based extended spectrum beta-lactamase and carbapenem-resistance studies in Africa

Countries	Authors	Period	Samples (Numb)	No. of isolates	*Shigella* species (Numb)	Prev %	Methods	ESBL and CR isolates (Numb)	ESBL and CR prevalence %	EBSBL and CR genes	ESBL/CR Numb	Prev of ESBL and CR genes %
Egypt	[45]	1990–1994 and 2000–2004	Stool (46)	46	*Shigella flexneri1c* (46)	100.0	PCR, PFGE, Sequencing	46 *[Shigella flexneri1c]*	100.0	bla_{TEM}, bla_{SHV}, bla_{OXA-1}	32; 0; 8	70.0; 0.0; 30.0
Egypt	[46]		meat products (800) and dairy products (800)	27	*Shigella flexneri* (18), *Shigella sonnei* (6), *and Shigella dysenteriae* (3)	1.69	PCR, Sequencing	21 [*S. flexneri* (15), *S. sonnei* (5), and *S. dysenteriae* (1)]	77.8 (*S. flexneri* 55.6, *S. sonnei* 18.5, and *S. dysenteriae* 3.7)	bla_{OXA-1}; $bla_{CTX-M-15}$, $bla_{CTX-M-3}$;$bla_{CTX-M-14}$; bla_{TEM-1}, bla_{CMY-2}; bla_{SHV-2}	9; 3; 1; 1; 4; 2; 1	33.3; 11.11; 3.70; 3.70; 14.8; 7.4; 3.70
Egypt	[47]	2018	raw cow milk and milk products (600)	42	*Shigella flexneri* (12), *Shigella sonnei* (6), *and Shigella dysenteriae* (24)	7.0	PCR	42 *[Shigella flexneri* (12), *Shigella sonnei* (6), *and Shigella dysenteriae* (24)]	100	bla_{TEM}, bla_{CTX-M}	42; 12	100.0; 28.6
Egypt	[48]		beef, chicken meat, cow's milk, and diarrheic child stool (260 (65 each product)	13	*Shigella flexneri* (12), *Shigella sonnei* (1)	5.0	PCR	5 [*S. flexneri* (4), *S. sonnei* (1)]	38.46	bla_{TEM}	5	38.46
Gabon	[49]		Stool (37)	37	*S. flexneri* (29); *S. boydii* (5); *S. Sonnei* (3)	12.5	PCR, MLST	8 [*S. boydii* (4), *S. flexnri* (3), *S. sonnei* (1)]	22.0	bla_{TEM}	8	22.0
Ghana	[50]	2012 to 2014	Clinical (111)	1	*Shigella sonnei* (1)	0.9	PCR	1 [*Shigella sonnei* (1)]	0.9	bla_{NDM-1}	1	0.9
Ghana	[51]	2012 to 2014	Clinical (131)	2	*Shigella sonnei* (2)	1.53	ERIC-PCR	2[*Shigella sonnei* (2)]	1.53	bla_{NDM-1}; bla_{TEM}	1; 1	0.76; 0.76
Libya	[20]	2009 and 2017	Clinical (NA)	54	*Sonnei sonnei* (25); *Shigella flexneri* (15); *Shigella boydii* (10); *Shigella dysenteriae* (4)	NA	WGS (Nanopore MinION); MLST	21 [(8 *S. sonnei* 6 *S. flexneri*; 3 *S. boydii*; 4 *S. dysenteriae*]	38.89	$bla_{CTX-M-15}$; $bla_{CTX-M-3;}bla_{TEM}$, bla_{OXA-1}	10; 5; 9; 9	18.52; 9.27; 16.67; 16.67
Malawi	[52]	2012 and 2015	Stool (10)	6	*Shigella flexneri* (5); *Shigella boydii* (1)	60.0	PCR	3 [*S. flexneri* (2); *S. boydii* (2)]	30.0	bla_{TEM}, bla_{OXA-1}	2; 1	20.0; 10.0
Mozambique	[53]	2007 to 2012	Stool (3757)	67	*Shigella flexneri* (52); *Shigella sonnei* (15)	1.78	PCR; PFGE	32 [*S. flexneri* (29); *S. sonnei* (3)]	47.76	bla_{OXA-1}; bla_{CTX-M}	32; 1	47.76; 1.49
Niger	[54]	03 to 12 2016	Stool (316)	16	*Shigella boydii* (2); *Shigella flexneri* (7); *Shigella sonnei* (2); *Shigella spp.* (5)	5.06	PCR	16[*Shigella boydii* (2); *Shigella flexneri* (7); *Shigella sonnei* (2); *Shigella spp.* (5)]	100.0	bla_{TEM}; bla_{OXA-1}	13; 10	81.25; 62.5

Table 1 (continued)

Countries	Authors	Period	Samples (Numb)	No. of isolates	*Shigella* species (Numb)	Prev %	Methods	ESBL and CR isolates (Numb)	ESBL and CR prevalence %	EBSBL and CR genes	ESBL/CR Numb	Prev of ESBL and CR genes %
Nigeria	[55]		536 (Urine (148), stool (70), wound swabs (64), ear discharge (38), and blood (94); Tap water (122))	38	*Shigella sonnei* (38)	8.8	PCR	*5* [*Shigella sonnei* (5)]	13.16	bla_{TEM}; bla_{CTX-M}	3; 2	7.89; 5.26
Nigeria	[56]		Door swabs (70)	2	*Shigella spp.* (2)	2.86	PCR	1[*Shigella spp.* (1)]	50.0	bla_{TEM}	1	50.0
Nigeria	[57]		yoghurt samples (30)	4	*Shigella spp.* (4)	13.33	PCR	1[*Shigella spp.* (1)]	25.0	bla_{SHV}	1	25.0
Senegal	[58]		Stool (1)	1	*Shigella spp.* (1)	100	PCR	1[*Shigella spp.* (1)]	100.0	$bla_{CTX-M-1}$	1	100.0
Senegal	[59]	2001 to 2010	Mixed (NA)	190	*Shigella flexneri* (190)	NA	PCR, sequencing	163[*Shigella spp.* (163)]	86.0	bla_{OXA-30}; bla_{TEM}; bla_{SHV}; bla_{CTX-M1}; bla_{KPC}; bla_{IMP}	155; 85; 13; 9; 2; 1	81.58; 44.74; 6.84; 4.74; 1.05; 0.53
Tanzania	[60]	07 to 09 1997	Stool (NA)	86	*Shigella flexneri* (78), *Shigella dysenteriae* (4), *and Shigella sonnei* (4)	NA	PFGE, REP-PCR	14 [*S. flexneri* (10), *S. sonnei* (1); *S. dysenteriae* (3)]	16.28	bla_{TEM}, bla_{OXA}	3; 11	3.49; 12.79
Zimbabwe	[61]	08 2016 and 05 2017	feaces, urine and blood (NA)	123	*Shigella flexneri* (87); *Shigella sonnei* (18), *Shigella boydii* (11), *Shigella dysenteriae* (7)	NA	PCR	14 [*S. flexneri* (11), *S. sonnei* (2), *S. boydii* (1)]	11.38	bla_{TEM}, bla_{SHV}, bla_{CTXM}	12; 9; 3	9.76; 7.32; 2.44

NA = not available; Numb. = Number, % = Percent; Prev. = Prevalence; CR = Carbapenem Resistance, ESBL = Extended-spectrum beta-lactamases.

Mixed samples = composed of several elementary samples

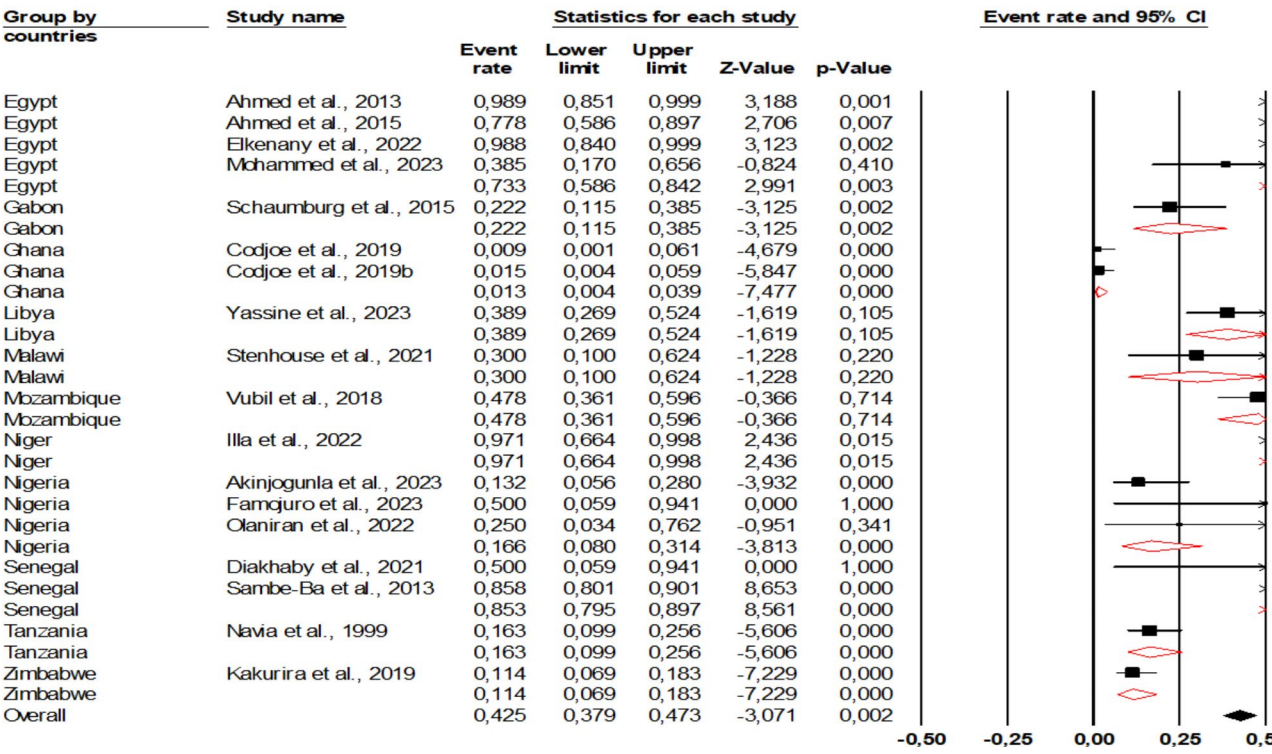

Fig. 2 Forest plot with adjusted average prevalence of ESBLs and carbapenem-resistance of *Shigella* in Africa. **Legend**: Random Effects Mode (95% CI: 22.8–62.4, $I^2 = 93.71\%$, $p < 0.05$). X-axis is the proportion of the countries reported in individual studies as listed along the Y-axis, with the range of proportion in 95% confidence interval (CI). I^2 = heterogenicity, $p = p$-value. The estimate of prevalence was calculated by pooling 18 studies using the random-effects model

with Egger's test ($p < 0.0001$). The majority of the isolates were from Senegal ($n = 164$, 40.7%), with a low incidence reported from Ghana and Malawi ($n = 3$, 0.7% each country). Following the meta-analysis, ESBL and CR-producing *Shigella* spp. (species not individually identified) were reported in Africa, with a pooled prevalence of 35.1% (95% CI: 18.4–56.3, $I^2 = 97.7\%$, $p < 0.05$; Fig. 4. The highest prevalence was observed for *Shigella flexneri* at 34.5% (95% CI: 16.6–58.2, $I^2 = 94.9\%$, $p < 0.05$; Fig. 4), followed by *Shigella dysenteriae* at 10.6% (95% CI: 1.5–48.5, $I^2 = 93.5\%$, $p < 0.05$; Fig. 4), *Shigella boydii* at 8.3% (95% CI: 3.7–17.4, $I^2 = 50.4\%$, $p = 0.09$; Fig. 4), and *Shigella sonnei* at 6.7% (95% CI: 3.4–13.2, $I^2 = 80.7\%$, $p < 0.05$; Fig. 4). The analysis indicated a heterogenous distribution of effect estimates across the studies as confirmed by the funnel plot and statistically significant results from Egger's test ($p < 0.0001$) (Fig. 5).

Majority of ESBL and CR producing *Shigella flexneri* were reported in Senegal (163/308, 52.9%), and Egypt (77/308, 25.0%). Conversely, lower reports were observed in Mozambique (29/308, 9.4%), Malawi (2/308, 0.6%) and Gabon (3/308, 1.0%). Furthermore, ESBL and CR producing *Shigella* spp. were only reported in Niger (5/23, 21.7%), Nigeria (2/23, 8.7%) and the least of *Shigella* spp. reported in Senegal (1/23, 4.3%). *Shigella dysenteriae* were predominantly reported in Egypt (25/32, 78.1%) followed by Libya (4/32, 12.5%) and Tanzania (3/32, 9.4%). Likewise, *Shigella boydii* were largely reported in Gabon (4/13, 30.8%), followed by Libya (3/13, 23.1%), Malawi and Niger (2/13, 15.4%, each) and Zimbabwe (1/13, 7.69%). As for ESBL and CR producing *Shigella sonnei*, the majority were reported in Egypt (12/42, 28.6%) with lower reports in Gabon and Tanzania (1/42, 2.4%).

Pooled prevalence of ESBL and CR genetic determinants in Africa

Figure 6 shows the distribution of ESBL and CR in African countries, with a pooled prevalence of 36.4% (95% CI: 16.1–63.2, $I^2 = 96.7\%$, $p < 0.05$). The funnel plot in Fig. 7 shows a heterogenous distribution (bias) of effect estimates of ESBL and CR genetic determinants in Africa statistically confirmed with Egger's test ($p < 0.0001$). The prevalence of ESBL and carbapenemases genes in Africa considerably varied among countries and depends also on the genes detected. From the analysis, the most widespread gene in Africa is bla_{TEM} ($n = 220$) with an average pooled prevalence of 25.9% (95% CI: 13.9–43.2, $I^2 = 90.9\%$, $p < 0.05$), followed by bla_{OXA-1} ($n = 80$) 25.7% (95% CI: 14.9–43.0, $I^2 = 83.7\%$, $p < 0.05$), bla_{CTX-M} ($n = 48$) at 10.8% (95% CI: 4.5–23.4, $I^2 = 85.6\%$, $p < 0.05$) and bla_{SHV}

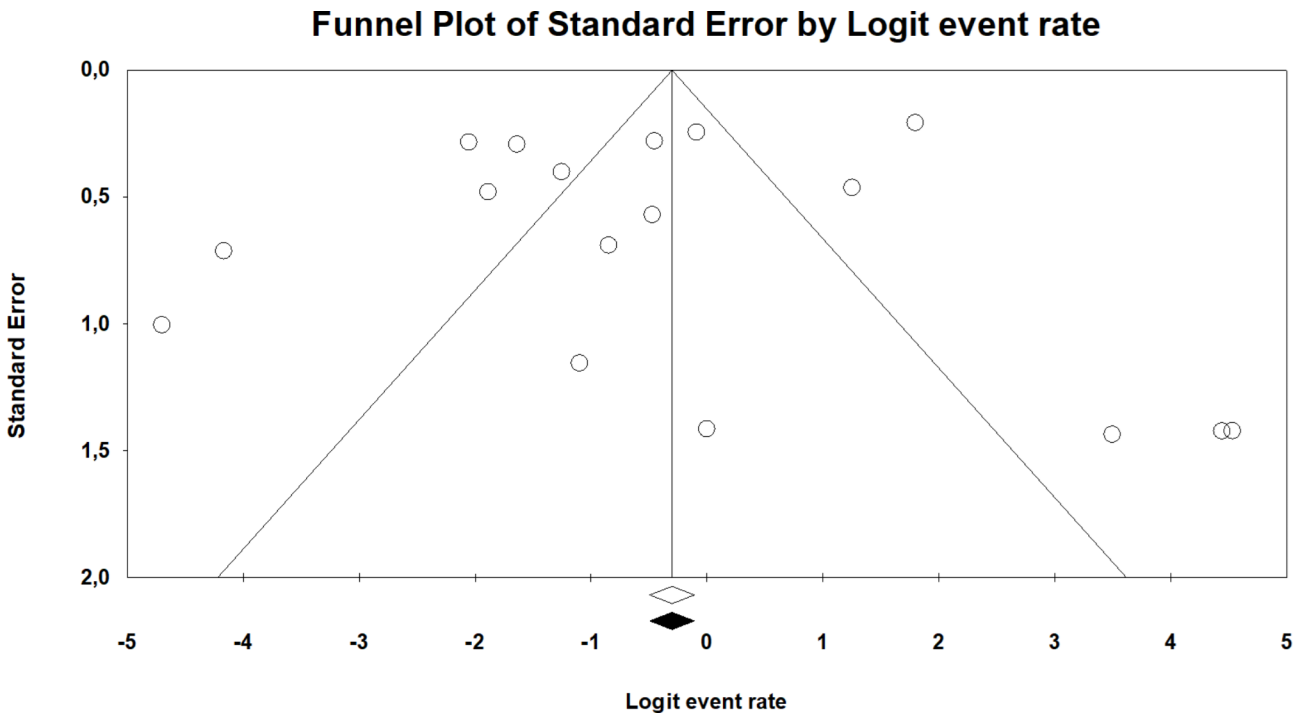

Fig. 3 Funnel plot with adjusted average prevalence of ESBLs and carbapenem-resistance of *Shigella* in Africa. **Legend**: The distribution of effect estimates is shown by a funnel plot of publication bias. The graph displays the standard error of the estimate (prevalence) on the Y-axis, while the X-axis represents the transformed proportions (prevalence) with individual studies represented by small circles. The 95% confidence interval is indicated by solid lines on the graph

($n = 24$) 7.2% (95% CI: 4.8–10.5, $I^2 = 0\%$, $p = 0.55$) as shown in Fig. 6. Furthermore, bla_{OXA-30} ($n = 155$) was reported at 81.58% in one included study from Senegal, while the prevalence of the bla_{CMY-2} gene at 7.4% was low. The bla_{TEM} genes were predominantly reported in Senegal (85/220, 38.6%) and Egypt (83/220, 37.7%). Of the 220 isolates with bla_{TEM}, fewer were from Ghana (1/220; 0.5%), Malawi (2/220, 0.9%), Tanzania (3/220, 1.4%) and Nigeria (4/220, 1.8%). Additionally, the bla_{SHV} genes were only reported from Senegal (13/24, 54.2%), from Zimbabwe (9/24, 37.5%) and from Nigeria and Egypt (1/24, 4.2%). The study findings show that the majority of bla_{CTX-M} genes were reported from Egypt (17/48, 35.4%) followed by Libya (15/48, 31.3%) and Senegal (10/48, 20.8%) with low occurrence reported from Zimbabwe (3/48, 6.3%), from Nigeria (2/48, 4.2%) and from Mozambique (1/48, 2.1). The prevalence of carbapenem genes was low with occurrences of bla_{NDM} ($n = 2$) 0.8% (95% CI: 0.2–10.3, $I^2 = 51.4\%$, $p < 0.05$) from Ghana and bla_{KPC} ($n = 2$) 1.1% (one included study), and bla_{IMP} ($n = 1$) 0.5% (one included study) from Senegal.

Pooled prevalence of ESBL and carbapenemases genes patterns of Shigella species

The only study conducted in Niger, as noted in this review, did not provide specific details about ESBL and carbapenemase-producing *Shigella* species. Figure 8 shows the distribution of ESBL and CR gene patterns of *Shigella* species.

Shigella flexneri Analysis of 18 eligible studies in our meta-analysis reveal that generally, the prevalence of *S. flexneri* and bla_{TEM} genes were most reported (Fig. 8). The pooled prevalence of bla_{TEM}-producing *Shigella* was 12.0% (95% CI: 5.0-26.1, $I^2 = 92.5\%$, $p < 0.05$). Our review showed that the highest prevalence of bla_{TEM} in *Shigella flexneri* was recorded in Senegal ($n = 85$, 44.5%) followed by Egypt ($n = 51$, 39.8%) and the lowest prevalence recorded in Libya ($n = 1$, 1.9%). Also, bla_{SHV} gene-producing *S. flexneri* was reported in only three countries, with the highest prevalence in Senegal ($n = 12$, 6.3%) followed by Zimbabwe ($n = 7$, 5.7%), and the lowest in Egypt ($n = 1$, 0.8%). The overall pooled prevalence of bla_{CTX-M}-producing *Shigella flexneri* was 5.3% (95% CI: 3.3–8.3, $I^2 = 28.8\%$, $p = 0.234$). A similar observation of low prevalence was seen in Egypt ($n = 10$, 7.8%), Libya ($n = 4$, 7.4%), Senegal ($n = 10$, 5.2%), Zimbabwe ($n = 3$, 2.4%), and in Mozambique ($n = 1$, 1.5%). Additionally, the pooled prevalence of bla_{OXA-1}-producing *Shigella flexneri* was found to be 13.4% (95% CI: 5.0-31.5, $I^2 = 89.7\%$, $p < 0.05$) with the highest prevalence reported in Mozambique ($n = 29$, 43.3%) and the lowest in Libya ($n = 3$, 5.6%). Further, bla_{CMY-2}-producing *Shigella flexneri* was only recorded in Egypt ($n = 1$, 0.8%). On the other hand, bla_{KPC} ($n = 2$, 1.1%), and bla_{IMP} ($n = 1$,

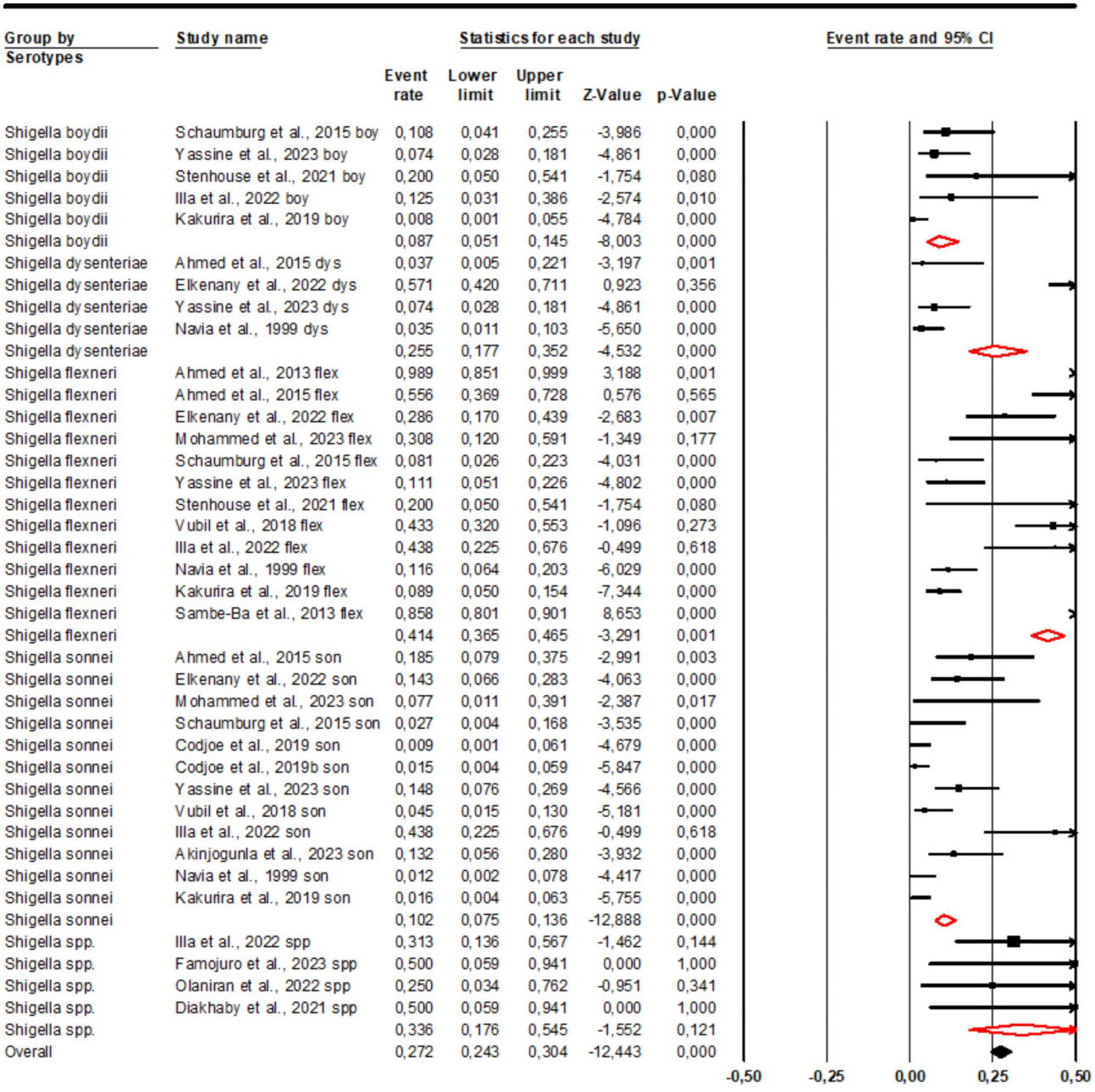

Fig. 4 Forest plot with adjusted average prevalence of *Shigella* species in Africa. **Legend**: Random Effects Mode (95% CI: 18.4–56.3, $I^2 = 0\%$, $p = 0.666$). X-axis is the proportion of the *Shigella* species reported in individual studies as listed along the Y-axis, with the range of proportion in 95% confidence interval (CI). I^2 = heterogenicity, p = p-value. The estimate of prevalence was calculated by pooling all studies reported different *Shigella* species using the random-effects model

0.5%) were reported in Senegal while bla_{OXA-30}, bla_{NDM}, were not reported in *Shigella flexneri*.

Shigella sonnei The prevalence of bla_{TEM}-producing *S. sonnei* was found to be low at 3% (95% CI: 1.5–5.9, $I^2 = 46.5\%$, $p = 0.08$). Notably, bla_{CTX-M}-producing *S. sonnei* was recorded in Egypt ($n = 7$, 5.5%), Libya ($n = 3$, 5.6%), and in Nigeria ($n = 2$, 4.5%) while bla_{OXA-1} was only reported in Egypt ($n = 2$, 1.6%) and Mozambique ($n = 3$, 4.5%). Additionally, bla_{NDM} and bla_{CMY-2} were reported respectively in Ghana ($n = 2$, 0.8%), and in Egypt ($n = 1$, 0.8%).

Shigella dysenteriae The prevalence of bla_{TEM} and bla_{OXA-1} in Egypt were reported as ($n = 24$, 18.8%), and ($n = 1$, 0.8%) respectively while in Libya it was ($n = 1$, 1.9%) and ($n = 2$, 3.7%). In addition, bla_{SHV} producing *S. dysenteriae* was only found in Zimbabwe ($n = 1$, 0.8%). However,

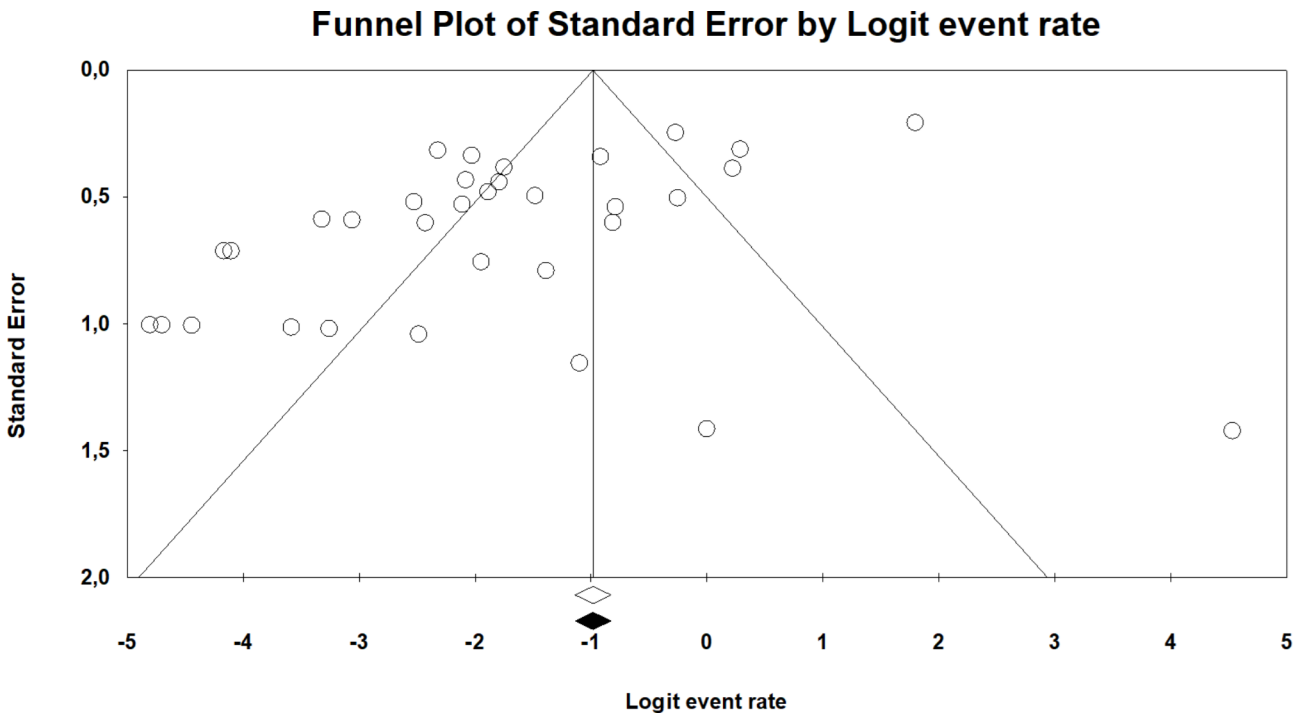

Fig. 5 Funnel plot with adjusted average prevalence of *Shigella* species in Africa. **Legend**: The distribution of effect estimates is shown by a funnel plot of publication bias. The graph displays the standard error of the estimate (prevalence) on the Y-axis, while the X-axis represents the transformed proportions (prevalence) with individual studies represented by small circles. The 95% confidence interval is indicated by solid lines on the graph

bla_{CTX-M}, bla_{OX-30}, bla_{NDM}, bla_{KPC}, bla_{IMP} and bla_{CMY-2} producing *S. dysenteriae* were not recorded in this review.

Shigella boydii The prevalence of bla_{TEM}-producing *S. boydii* was reported in four countries with a pooled prevalence of 4.9% (95% CI: 1.6–14.0, $I^2 = 54.2\%$, $p = 0.09$) and was found in Gabon ($n = 4$, 11.1%), Malawi ($n = 1$, 10.0%), Libya ($n = 2$, 3.7%), and Zimbabwe ($n = 1$, 0.8%) (Fig. 8). However, bla_{SHV} and bla_{CTX-M} were only reported in Zimbabwe ($n = 1$, 0.8%), and Libya ($n = 3$, 5.6%) respectively.

Risk of Bias

In this review, the included studies reported high heterogeneity indicated by the $I^2 = 93.7\%$ and Cochrane Q test ($Q = 269.470$, $p < 0.0001$). Visual inspection of the funnel plot shows a slight asymmetrical distribution. The intercept of the Eggers regression model was 1.76026 (95% CI: -4.54937 — 2.9378) with a t statistic of 0.46 and a p-value of 0.6485. This finding suggests that potential publication bias in the included studies is unlikely (Fig. 3).

Discussion

This systematic review sought to describe the prevalence of ESBL and CR-producing *Shigella* in Africa, specifically by examining the distribution of species, ESBL and carbapenemase genes. Only 18 publications included in the review. This reveals a dearth of information on the molecular epidemiology of ESBL and carbapenemase-producing *Shigella* in Africa. The limited data on ESBL and carbapenemase producing *Shigella* from certain African countries may not necessarily indicate a lack data of those genes but rather reflects limited capabilities for technical resources, absence of real national or regional surveillance system, and data not registered. According to Kedišaletše et al., in many African countries research budgets are referred for other healthcare issues, like infectious diseases such as malaria and HIV/AIDS, Covid 19 and many other healthcare issues. This in turn could contribute to a failure in monitoring AMR [17]. Additionally, the lack of data might be due to inadequate technical laboratory resources. In most developing countries and in Africa, the non-application of quality systems in laboratories and a lack of suitable technical laboratory resources, are factors that justify that bacteria are traditionally diagnosed on the basis of biochemical methods in most cases [18]. This review revealed that *Shigella flexneri* was the most species reported in Africa while *S. dysenteriae* was the least reported. These results are similar to those of a study conducted in Asia [10]. Our results are consistent with another study which established that *S. flexneri* is commonly found in developing countries, while *S. sonnei* is traditionally isolated in developed countries which aligns with our findings [19]. However, reports in the last decade have revealed that *S. sonnei* is the most frequently isolated species of *Shigella* in developing countries [10,

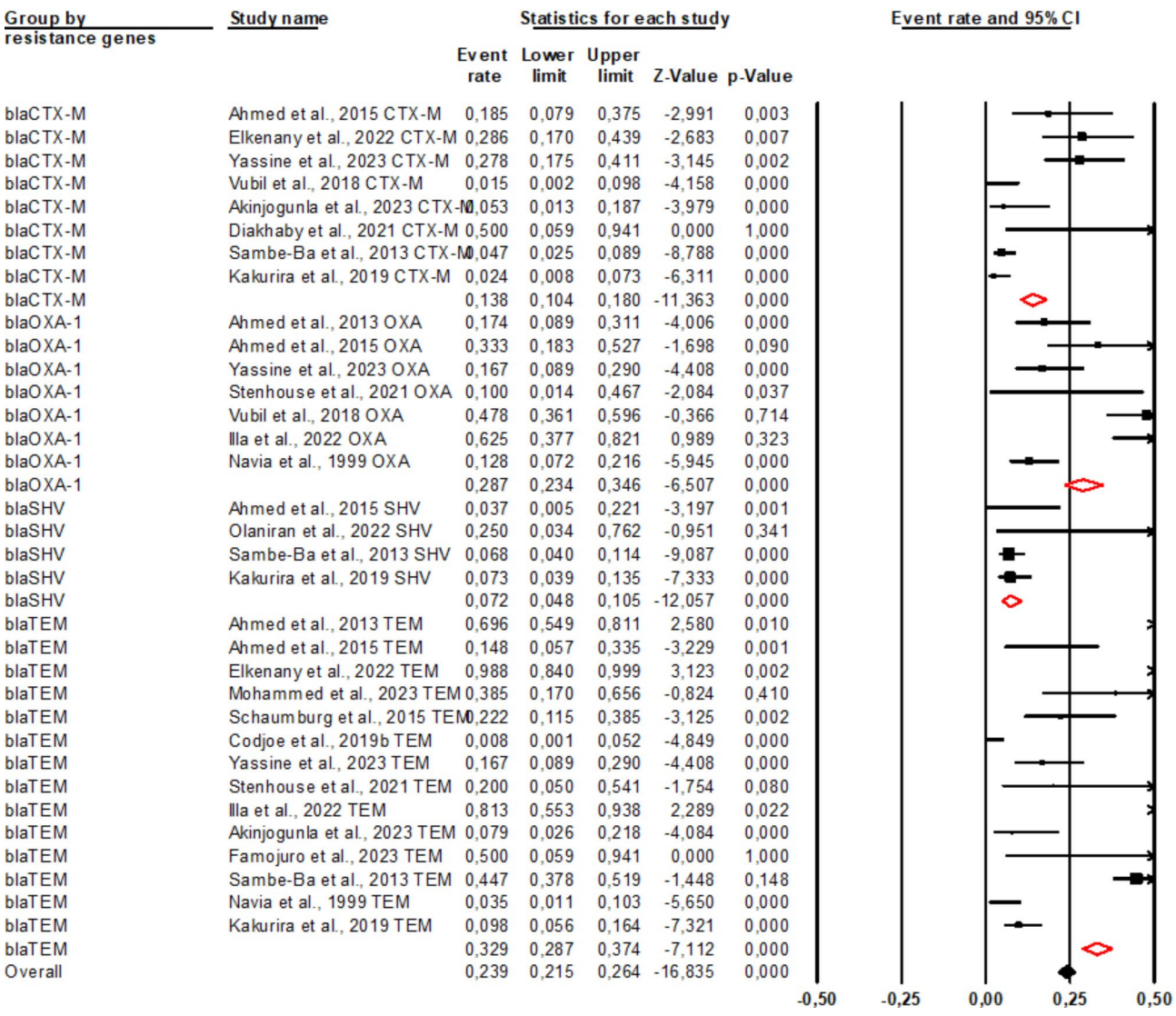

Fig. 6 Forest plot with adjusted average prevalence of ESBLs and CR gene in Africa. **Legend**: Random Effects Mode (95% CI: 16.1–63.2, $I^2 = 96.72\%$, $p < 0.05$). X-axis is the proportion of the ESBLs and carbapenem resistance genes reported in individual studies as listed along the Y-axis, with the range of proportion in 95% confidence interval (CI). I^2 = heterogenicity, p = p-value. The estimate of prevalence was calculated by pooling all studies reported ESBL and CR producing *Shigella* species using the random-effects model

20, 21]. One recent study reported that *Shigella flexneri* and *Shigella sonnei* are responsible for over 90% of shigellosis cases worldwide [22].

Research globally indicates a rise in antimicrobial resistance (AMR) within *Shigella* [5, 6, 10, 17]. According to this review, antimicrobial resistance patterns was varied across different regions. So, to treat shigellosis, the choice of antibiotic should be based on the specific AMR profiles observed in each region. Our systematic review identified a high prevalence of bla_{TEM}, bla_{OXA-1}, and bla_{CTX-M} genes which is consistent with findings from other studies. Dey et al. in their study reported the presence of bla_{CTX-M1}, bla_{TEM} and bla_{CTX-M3} in cow milk samples from India [23]. Similarly, other studies have observed a high prevalence of bla_{CTX-M}, bla_{SHV}, and bla_{TEM} families in *Shigella* species [24–26]. Today, many antibiotic classes have become ineffective against Enterobacterales including *Shigella*. Several studies have shown that *Shigella* strains have developed resistance to ceftriaxone, cefoperazone, azithromycin and fluoroquinolones. This resistance is generally linked to mutations and horizontal transfer of plasmid-mediated resistance mechanisms [27]. However, it has been demonstrated that strains resistant to cephalosporins are likely to produce extended-spectrum beta-lactamases (ESBLs), particularly those of the *CTX-M*, *TEM* and *SHV* groups [28]. Notably, the widespread use of third-generation cephalosporins antibiotics, which are readily available,

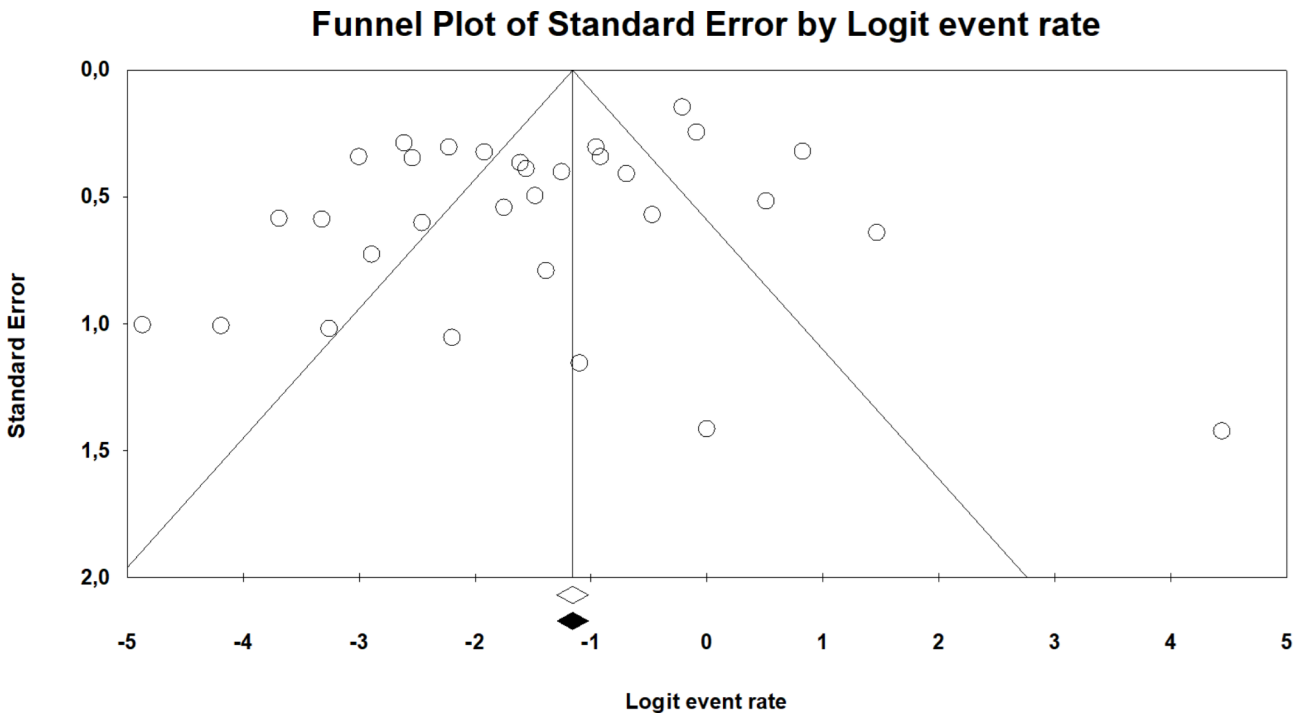

Fig. 7 Forest plot with adjusted average prevalence of the ESBLs and CR gene in Africa. **Legend**: The distribution of effect estimates is shown by a funnel plot of publication bias. The graph displays the standard error of the estimate (prevalence) on the Y-axis, while the X-axis represents the transformed proportions (prevalence) with individual studies represented by small circles. The 95% confidence interval is indicated by solid lines on the graph

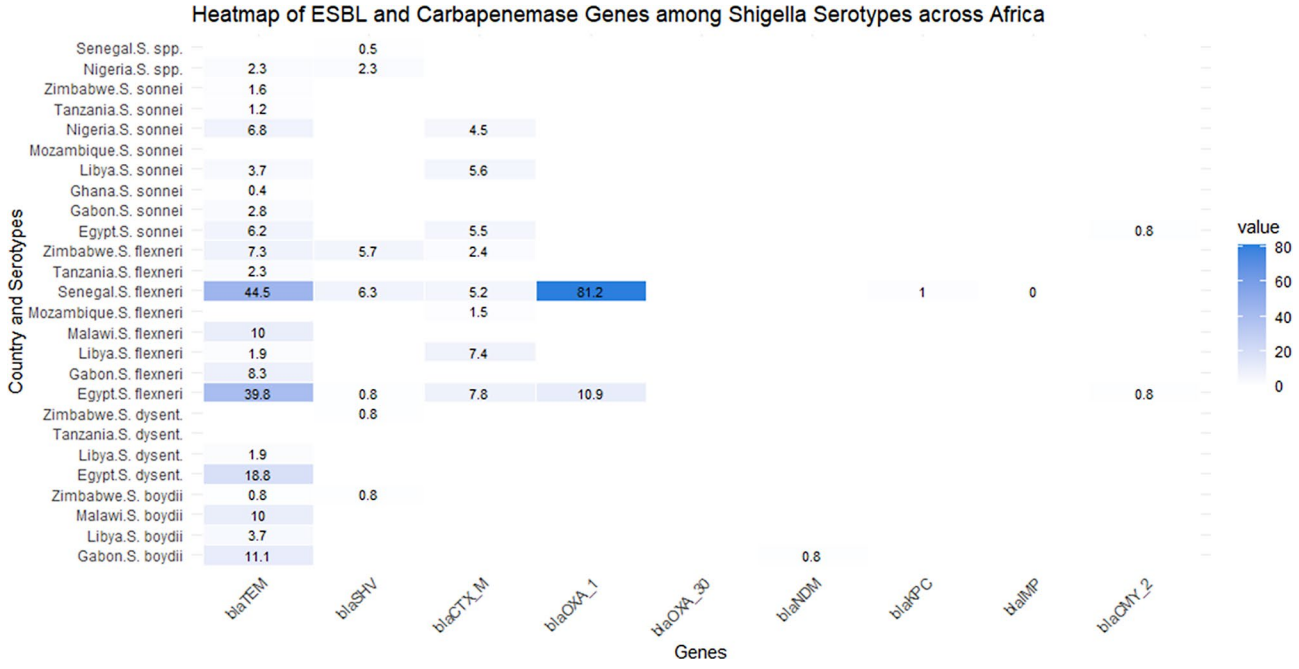

Fig. 8 Distribution of ESBL and carpenemases genes patterns of *Shigella* species in Africa. **Legend**: S. dysent. = *Shigella dysenteriae*, Y-axis represented different *Shigella* species by country and X-axis the different ESBL and Carbapenems resistance genes. The intensity of the color (white to blue) represents the increase in number of ESBL and CR producing *Shigella* species by country

affordable, and commonly used in humans without prescription, may contribute to this trend [29]. Third-generation cephalosporins antibiotics are generally prescribed in severe cases of bacterial infections because they are considered more recently, the last resort. These antibiotics are also used frequently in agriculture and veterinary medicine [30]. In developing countries, antibiotics are easily and readily available in informal markets and even on the streets, and are sold cheaply. These drugs are known as 'street drugs' [31]. As such, these antibiotics are commonly used in without prescription. In this review, carbapenemases such as bla_{NDM}, bla_{KPC} and bla_{IMP} have been identified. These findings were similar to those found in a systematic review and meta-analysis on the prevalence of *Shigella* species and its drug resistance pattern in Ethiopia, although this study is based on phenotypic data [32]. The findings from our study suggests, carbapenemases-producing *Shigella* are less prevalent in Africa. This fact could mean that carbapenemases-producing *Shigella* are under-researched in Africa. This phenomenon could possibly be due to the predominant use of first-line antibiotics such as the third-generation cephalosporin, quinolones and fluoroquinolones to treat shigellosis [33]. On the other hand, the limited availability and the expensive nature of these antibiotics could contribute to the lower prevalences of these genes [31]. The WHO recommends that fluoroquinolone be the first choice for treating adults and children with dysentery. Some antibiotics, such as, azithromycin, cefixime, sulfamethoxazole + trimethoprim and ceftriaxone are recommended as second choices, with ceftriaxone advised for children over 41 weeks of corrected gestational age [13]. All these factors could explain the low prevalence of CR-producing Shigella reported in our review.

In recent years, some studies conducted in France and China have reported CR-producing Enterobacterales from dogs, pork, poultry and cat [34–37]. The presence of carbapenemase-producing strains in animals could lead to dissemination when these animals are treated with beta-lactams or other antibiotics to which the bacteria is resistant.

Our findings give an insight into the pooled prevalence of ESBL and CR-producing *Shigella*, over the past 25 years in Africa. Although the pooled prevalence of ESBL and CR-producing *Shigella* was low in this study it still constitutes a public health risk in Africa. Many studies suggest that *Shigella* spp. can be transmitted to susceptible individuals from an infected person via the faecal–oral route, through contaminated water, food, fomites, or through direct contact [38–40]. Furthermore, some studies reported that *Shigella* could also be transmitted to human by sexual relation, especially among men who have sex with men [41, 42]. Other reports suggest that persons travelling to *Shigella* endemic areas may be at increased risk of being infected with *Shigella* spp [38, 42]. Poor hygiene and sanitation, unsafe water and malnutrition also increases the risk of *Shigella* infection in developing countries. Indeed, transmission of resistance clones to other non-*Shigella* spp. is also possible. Many studies report that bla_{CTX-Ms} are usually carried by plasmids, allowing resistance clones to be exchanged horizontally between different enterobacterial species (e.g., from *E. coli* to *S. sonnei* in the human gut) [43, 44].

Refined prevalence estimates for ESBL and CR-producing *Shigella* spp. in Africa, along with long-term impact data, are essential to guide funders, public health officials, and policy makers in allocating resources, promoting vaccine development and implementing effective strategies to reduce the diarrhoeal infections and antimicrobial resistance in Africa.

Our systematic review has some limitations that should be considered. For instance, our study protocol was not registered on the standard PROSPERO platform like other studies. In addition, the available data is not representative and varies from one country to another (Table 1). Some of the included studies did not report sample numbers, making it difficult to calculate the prevalence of *Shigella* strains isolated. Furthermore, many of the reviewed articles had small sample sizes, potentially biased our statistical analyses.

Conclusion

Our systematic review and meta-analysis findings affirmed that *Shigella flexneri* is the most prevalent species of ESBL and carbapenemases producing *Shigella* within Africa based on the publications included in the study. The review identified bla_{TEM}, bla_{OXA-1} and bla_{CTX-M} as the most commonly reported genes. Additionally, ESBLs were most frequently reported in Egypt while carbapenemases were only found in Ghana, Egypt, and Gabon at low prevalences. Emergence of multidrug resistant *Shigella* strains, including those expressing ESBLs and carbapenemases, could pose a significant threat to public health in Africa.

Abbreviations

AJOL	African Journals Online
AMR	Antimicrobial Resistance
CRE	carbapenem-resistant Enterobacteriaceae
CR	Carbapenem resistance
ESBL	Extended-spectrum beta-lactamases

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-024-10266-7.

Supplementary Material 1

Supplementary Material 2

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Author contributions
Conception and design: SNS and ESD; development of data screening form: SNS; data screening: SNS, RN and AT; data analysis and interpretation: SNS, RN, PBT-Q, AT, and OJIB ; draft preparation and revisions: SNS, RN, PBT-Q, AT, OJIB and ESD; funding acquisition: ESD. All the authors approved of the final version of the manuscript.

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Data availability
All data generated or analyzed are included in this review.

Declarations

Ethical approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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