



## Multidrug resistance from a one health perspective in Ethiopia: A systematic review and meta-analysis of literature (2015–2020)

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### SUMMARY

**Purpose:** The emergence of antimicrobial resistance is a major global health challenge and becoming an urgent priority for policymakers. There is a paucity of scientific studies presenting the multidrug resistance pattern from one health perspective in Ethiopia. Therefore, a systematic review and meta-analysis aimed to determine the pooled prevalence of multidrug resistance in bacteria from human, animal, food, and environmental sources.

**Methods:** In this systematic review and meta-analysis, an electronic search was made in PubMed & Google scholar using different keywords. The studies conducted in all areas of Ethiopia, published from 2015 to 2020 in peer-reviewed journals, English full-length papers were included. The meta-analysis was done on STATA version 14. The pooled prevalence of multidrug resistance for each bacterium was analysed using the random-effects model; Cochran Q statistics and the  $I^2$  statistic was used to analyse heterogeneity and considered significant at  $p < 0.01$ .

**Results:** 81 studies were included in the systematic review and meta-analysis; 53 human studies, eight animal studies, and 16 environments/food studies. The meta-analysis included six species from gram-positive bacteria and 13 from gram-negative bacteria. *S. aureus* 53% (95%CI: 42–64%), Coagulase negative *Staphylococci* 68% (95%CI:53–82), *Pseudomonas* spp. 73%(95%CI:48–93%), *E. coli* 70% (95%CI:61–78%), *Citrobacter* spp. 71%(95%CI:54–87%), *Klebsiella* spp. 68% (54–80%), *Enterobacter* spp. 67% (48–83%) and *Salmonella* spp. 65% (95%CI:48–81%) were the common multidrug-resistant species of bacteria from two or more sources.

**Conclusion:** In Ethiopia, the pooled prevalence of MDR is high in most bacterial species from humans, animals, food, and environmental sources. *Staphylococcus*, most members of the Enterobacteriaceae and *Pseudomonas*, are the standard MDR bacterial population involving all sources. Therefore, integrated policy and intervention measures should be implemented to reduce the emergence and spread of MDR bacteria for better animal and human health outcomes.

### 1. Introduction

The emergence of antimicrobial resistance (AMR) is a major global health challenge and becoming an urgent priority for policymakers [1]. Despite the natural factors, repeated exposure to antimicrobial agents in human and veterinary medicine is driving the emergence of antimicrobial resistance [2]. This widespread availability and misuse of antimicrobials and escalating AMR jeopardise the modern health care system

[1,3]. Besides, there is a lack of new drug products due to economic shortcomings and challenges related to the regulatory requirements [4]. Because antimicrobials used to treat human infections are often used in animals, and exposed organisms have been transferred to humans through food and released into the environment through human and animal excretions, livestock and the ecosystem play a significant role in changing the resistance profile of microorganism [3]. Furthermore, the global mobility of people, food, and animals adds to the problem [5].

**Abbreviations:** CI, Confidence interval; CoNS, Coagulase-negative *Staphylococci*; ES, Estimate; MDR, Multidrug resistance.

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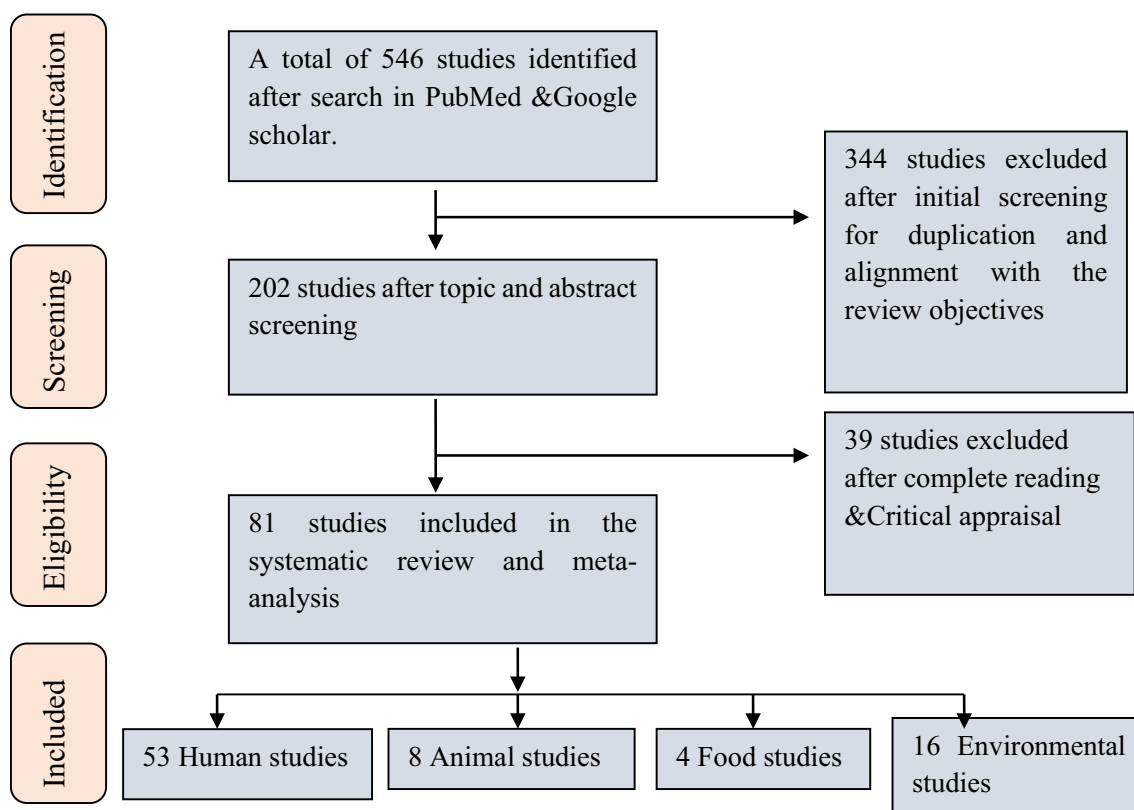


Fig. 1. Prisma flow chart showing the selection process of articles on antimicrobial resistance in Ethiopia.

Infection due to resistant organisms leads to increased morbidity, hospital stay, and mortality [6]. Antimicrobial resistance organisms affect the outcome of patients due to enhanced virulence and delay in the administration of antimicrobial therapies [7]. The changes in regimens may also lead to two-fold higher adverse drug effects, increased disease severity, and unintended surgical procedures [7,8]. The prescription is syndrome-biased and rarely correlated with the specific etiologic agent [3]. Hence, this misleads physicians for inappropriate prescription of antimicrobials, ultimately ending with sub-inhibitory drug exposure and genetic rearrangement within the pathogen; the genetic rearrangement leads to altered gene expression and increased virulence spread of antimicrobial resistance [9].

Antimicrobial resistance also has a significant impact on the health care system. Infections and admissions associated with drug-resistant organisms lead to much higher health care costs; these increased costs are associated with complicated conditions that demand increased resource utilisation and therapeutic alterations [8]. The inflated health care costs may also be attributed to the cost of isolation, infection control, and wastage due to cancelled procedures [5].

In developing countries, the burden of antimicrobial resistance is much higher due to several reasons. The common causes include inadequate patient education, inappropriate medications or unregulated dispensing, limited facilities, and poor regulatory mechanisms [10]. The increased burden of infectious disease, shortfalls in infection control, and public health accelerate the rate of antimicrobial resistance [11]. Overall, poverty was the driving factor for multidrug resistance problems in developing countries [4].

Antibiotic-resistant bacteria infections are more complicated and, in some cases, impossible to treat with currently available medications. Such conditions result in increased morbidity and mortality and a significant increase in healthcare costs [12]. As a result of evolutionary pressure or horizontal gene transfer, microorganisms have become resistant to two or more kinds of antibiotics in recent years. Several studies have been done on the antimicrobial resistance of common

pathogens such as *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella* species, *P. aeruginosa*, *Acinetobacter baumannii*, and *Enterobacter* species [13]. Antibiotic resistance trends among widely encountered bacterial etiologies in Ethiopia have previously been characterised [14]. Antibiotic resistance in bacteria is also recognised to be a dynamic phenomenon. Because of the close association between antibiotic efficiency and antibiotic resistance, resistance patterns reported in the past may not accurately reflect the current situation. As a result, understanding the dynamic and trend of resistance requires knowledge about bacteria's current antibiotic resistance pattern. Therefore, the systematic review and meta-analysis aimed to determine the pooled prevalence of multi-drug resistance in bacteria from human, animal, food, and environmental sources.

## 2. Methods

### 2.1. Search strategy

This systematic review and meta-analysis did an electronic search in PubMed & Google scholar. The search strategy on PubMed was made using different keywords and corresponding Mesh words, including "Food Microbiology" or "Environmental Microbiology", "Microbial sensitivity" or "Drug resistance", and "Ethiopia". Furthermore, the searching process was filtered by year of publication to include full-length research articles published from 2015 to 2020. According to our search, we accessed a total of 546 studies.

### 2.2. Inclusion criteria and screening strategy

The studies conducted in all areas of Ethiopia, published from 2015 to 2020 in peer-reviewed journals, English full-length papers were included in this study. Studies that use human clinical samples and samples from animals, food, and environmental sources were included in the review. Studies isolated and tested for antimicrobial susceptibility

**Table 1**  
Description of included studies based on the study area: clustered into regions.

Description	Number of studies	Percentage
Study area		
Addis Ababa area	19	23.5
Eastern Ethiopia	5	6.5
Southern Ethiopia	11	13.6
Oromia region	13	16
Amhara region	21	25.9
Tigray region	12	14.8
Total	81	100

N: indicates the number of studies.

**Table 2**  
Description of human studies (n = 53).

Disease condition (n)	Type of sample taken (n)
Multiple infections (14)	Multiple clinical samples (14)
Nasal/nasopharyngeal Colonization (11)	Nasal/nasopharyngeal swab (12)
Skin colonization (1)	Skin swab (1)
Intestinal infection/colonization (11)	Stool (14)
Sepsis (4), Enteric fever (2)	Blood (4)
Genital colonization/infection (6)	Viginal swab & rectal swab/urethral discharge/cervical swab (6)
UTI (5)	Urine (5)
Ocular infection (5)	Eye discharge or swab (5)
Ear infection (2)	Ear discharge (2)
Nosocomial infection (2)	Multiple clinical samples (2)

N: indicates the number of studies.

using standard microbiological methods were included; the studies that did not indicate the prevalence of MDR isolates based on the commonly accepted MDR definition have been excluded from the systematic review and meta-analysis. Two members made the screening process independently with the fixed inclusion criteria to ensure double-checking. The Joanna Briggs Institute (JBI) checklist for critical appraisal was used for quality assessment and to enrol each article in this systematic review and meta-analysis [15–17]. The selection process is presented based on the preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines [18] (Fig. 1). *Mycobacterium tuberculosis* has been excluded from systematic review and meta-analysis because it is extensively addressed in a recent study [19].

### 2.3. Data extraction process

The data extraction was made by a carefully designed excel data extraction sheet. The data extraction sheet recorded the author, year of publication, study area, study design, source (human source, animal source, food, or environment), and the type of specimen taken. Additionally, we have extracted the kind of bacterial isolates, the number of each isolate, and the number of multidrug-resistant isolates. We have also extracted the type of infection or type of anatomical colonization considered in each study for human studies.

### 2.4. Statistical analysis and synthesis

The data extracted was cleaned for any legibility errors, and the meta-analysis was done on STATA version 14. The pooled prevalence of MDR for each bacteria combination was analysed using the random-effects model; Cochran Q statistics and the  $I^2$  statistic was used to analyse heterogeneity and considered significant at  $p < 0.01$  [18,20]. A forest plot was done for each bacterial and MDR combination. The results were narrated in words and plotted in terms of tables and forest plots that best suit readers. For the studies on Animals and the environment, MDR estimates were pooled if reported in at least three studies, whereas, in the case of Human sources, the point estimates were pooled

**Table 3**  
Description of Animal, food, and environmental studies.

Animal studies (8)	
Type of animal (n)	Type of sample taken (n)
Cattle (3)	Feces (1), Milk (1), Feces & surface swab (1)
Chicken (1)	Visceral organ samples (1)
Dog (1)	Rectal swab (1)
Goat (1)	Different clinical samples (1)
Cockroaches (2)	External and internal body samples (2)
Food & Environment studies (n = 16)	
Type of food/Environment (n)	Type of sample taken (n)
Meat (3), Milk (2), Egg (1)	Meat or carcass swabs (3) Raw milk (2), Egg (1)
Hospital environment (6)	Surface swab (4), Air (2), wastewater (1)
Wastewater from urban rivers (2)	Water sample (2)
Abattoir/butcher shops/retailer houses (5)	A swab from meat & surfaces (4)
Poultry industry (1)	Surface swab (2)
Dairy farm (1)	Carcass swab & excretes (1)
Transport buses (1)	A swab from hand surfaces (1)
Mobile phones (1)	Surface swab (1)

N: indicates the number of studies associated with that particular description.

if the bacterium-MDR combinations were reported in at least four studies [18]. The Begg and Mazumdar rank correlation ( $P < 0.05$ ) was used to test publication bias.

## 3. Results

### 3.1. Description of the included studies

In this review, 81 studies were included in the systematic review and meta-analysis; 81 of the studies were cross-sectional studies, and one study was retrospective. The different features of the included studies are summarised below in Tables 1, 2 & 3. The studies were grouped into regions based on the study area; the higher percentage of the studies were from the Amhara region (25.9%), followed by the Addis Ababa area (23.5%) area (Table 1). On the other hand, few studies were included from eastern Ethiopia due to limited published articles on MDR.

### 3.2. Characteristics of studies that involved humans

In this data extraction, we have considered studies involving various medical conditions; multiple infections, anatomical colonization, hospital-acquired (nosocomial) infections, UTIs, and other types of diseases described in Table 2. Out of the 53 included studies on humans, 14 studies have isolated bacteria from patients with multiple infections and tested organisms isolated from various clinical samples. The nasopharyngeal area, intestine, genitalia, and skin were the commonly studied anatomical sites for the presence of drug-resistant bacteria isolates (Table 2).

### 3.3. Characteristics of studies on animals, food, and environment

Eight studies on different animals have reported MDR bacteria, and three out of the eight animal studies have isolated MDR bacteria from dairy cattle. Hospital environment, abattoir, and meat establishments were the most frequent categories of the environment associated with MDR isolates (Table 3).

**Table 4**

The type of bacterial isolates considered for the meta-analysis.

Type of bacteria	Number of studies from each source				Reference
	Humans	Animals	Environment/Food	Total	
<i>S. aureus</i>	25	3	9	37	[21–56]
CoNS	12	1	7	8	[21–23,25–28,31,33–35,38,42–44,46–48,52,53]
<i>S. agalactae</i>	5	–	–	5	[40,53,57–59]
<i>Streptococcus pyogenes</i>	8	–	–	8	[33,38,40,42,43,52,53,56]
<i>Streptococcus pneumoniae</i>	8	–	–	8	[20,35,40,42,53,56,60,61]
<i>Enterococcus</i> spp.	6	–	–	6	[35,38,41,62–64]
<i>E. coli</i>	19	4	14	37	[21,22,24–31,33–35,38,40,42–46,48,52,53,65–78]
<i>Klebsiella</i> spp.	18	1	7	26	[21,26–28,31,33–35,38,40,42–48,52,53,67–69,74,76–78]
<i>Enterobacter</i> spp.	15	1	3	19	[24,31,33–35,38,40,42,43,45–47,53,67,69,74,76–78]
<i>Citrobacter</i> spp.	14	1	5	20	[25,26,31,33–35,38,40,42,43,45,47,53,67–69,74,76–78]
<i>Salmonella</i> spp.	12	5	6	23	[21,30,31,35,38,40,53,69,75,77,79–91]
<i>Shigella</i> spp.	11	2	–	13	[30,31,35,40,53,75,87–89,91–93]
<i>Proteus</i> spp.	11	1	2	14	[21,28,31,33–35,38,40,42,44,47,53,74,76]
<i>Serratia</i> spp.	7	1	1	9	[28,31,33,38,43,45,52,53,77]
<i>Acinetobacter</i> spp.	7	–	1	8	[22,35,36,38,44,45,48,77]
<i>Pseudomonas</i> spp.	11	–	5	16	[21,22,26–28,35,36,38,40,42,45,47,52,53,76,77]
<i>N. gonorrhoea</i>	4	–	–	4	[35,38,40,94]
<i>Neisseria meningitidis</i>	4	–	–	4	[35,40,53,95]
<i>Haemophilus influenzae</i>	4	–	–	4	[38,42,52,53]

**Table 5**

A summary of the pooled proportion of MDR for each gram-positive bacterium included in the meta-analysis, 2015–2020.

Type of bacteria	Estimate (95%CI) for bacterial isolates from each source			Overall pooled proportion	Heterogeneity between groups
	Humans	Animals	Environment/Food		
<i>S. aureus</i>	0.57 (0.44, 0.70)	0.32(0.00, 0.97)	0.49 (0.31, 0.68)	0.53 (0.42, 0.64), I <sup>2</sup> = 96.10% p = 0.000	P = 0.677
CoNS	0.78(0.62–0.91)	–	0.51(0.28–0.74)	0.68 (0.53–0.82), I <sup>2</sup> = 93.35% p = 0.00	P = 0.062
<i>Streptococcus pyogenes</i>	0.42(0.07–0.80)	–	–	I <sup>2</sup> = 83.07% p = 0.00	NA
<i>S. agalactae</i>	0.51(0.15–0.89)	–	–	I <sup>2</sup> = 92.83% p = 0.00	NA
<i>S. pneumoniae</i>	0.27(0.10–0.47)	–	–	I <sup>2</sup> = 88.26% p = 0.01	NA
<i>Enterococcus</i> spp.	0.65(0.41–0.85)	–	–	I <sup>2</sup> = 88.69% p = 0.000	NA

**Table 6**

A summary of the pooled proportion of MDR for each gram-negative bacteria included in the meta-analysis, 2015–2020.

Type of bacteria	Estimate (95%CI) for bacterial isolates from each source			Overall pooled proportion: ES (95%CI), I <sup>2</sup> = % p = value	Heterogeneity between groups
	Humans	Animals	Environment/ Food		
<i>E. coli</i>	0.81(0.70–0.90)	0.72 (0.57–0.86)	0.53(0.35–0.70)	0.70(0.61–0.78) I <sup>2</sup> = 89.4% p = 0.000	No, p = 0.035
<i>Klebsiella</i> spp.	0.81 (0.70–0.90)	–	0.37(0.20–0.57)	0.68(0.54–0.80) I <sup>2</sup> = 89.92% p = 0.00	Yes, P = 0.0000
<i>Enterobacter</i> spp.	0.64 (0.43–0.84)	–	0.73(0.43–0.98)	0.67(0.48–0.83) I <sup>2</sup> = 69.95% p = 0.00	No, P = 0.622
<i>Citrobacter</i> spp.	0.73 (0.54–0.90)	–	0.69(0.32–0.97)	0.71(0.54–0.87)	No, P = 0.849
<i>Salmonella</i> spp.	0.70 (0.50–0.87)	0.64 (0.43–0.83)	0.56(0.13–0.94)	0.65(0.48–0.81) I <sup>2</sup> = 91.88% p = 0.000	No,0.068
<i>Shigella</i> spp.	0.69 (0.54–0.82)	–	–	I <sup>2</sup> = 58.13% p = 0.01	NA
<i>Proteus</i> spp.	0.54 (0.34–0.75)	–	–	I <sup>2</sup> = 57.50% p = 0.01	NA
<i>Serratia</i> spp.	0.42 (0.12–0.74)	–	–	I <sup>2</sup> = 25.00% p = 0.24	NA
<i>Acinetobacter</i> spp.	0.86 (0.46–1.00)	–	–	I <sup>2</sup> = 77.69% p = 0.00	NA
<i>Pseudomonas</i> spp.	0.82 (0.52–1.00)	–	0.53(0.13–0.92)	0.73 (0.48–0.93) I <sup>2</sup> = 89.18% p = 0.00	No, P = 0.312
<i>N. gonorrhoea</i>	0.74 (0.51–0.92)	–	–	I <sup>2</sup> = 20.80% p = 0.29	NA
<i>N. Meningitidis</i>	0.44 (0.00–0.95)	–	–	I <sup>2</sup> = 81.29% p = 0.00	NA
<i>Haemophilus influenzae</i>	0.10 (0.00–0.39)	–	–	I <sup>2</sup> = 0.00% p = 0.99	NA

NA: not applicable.

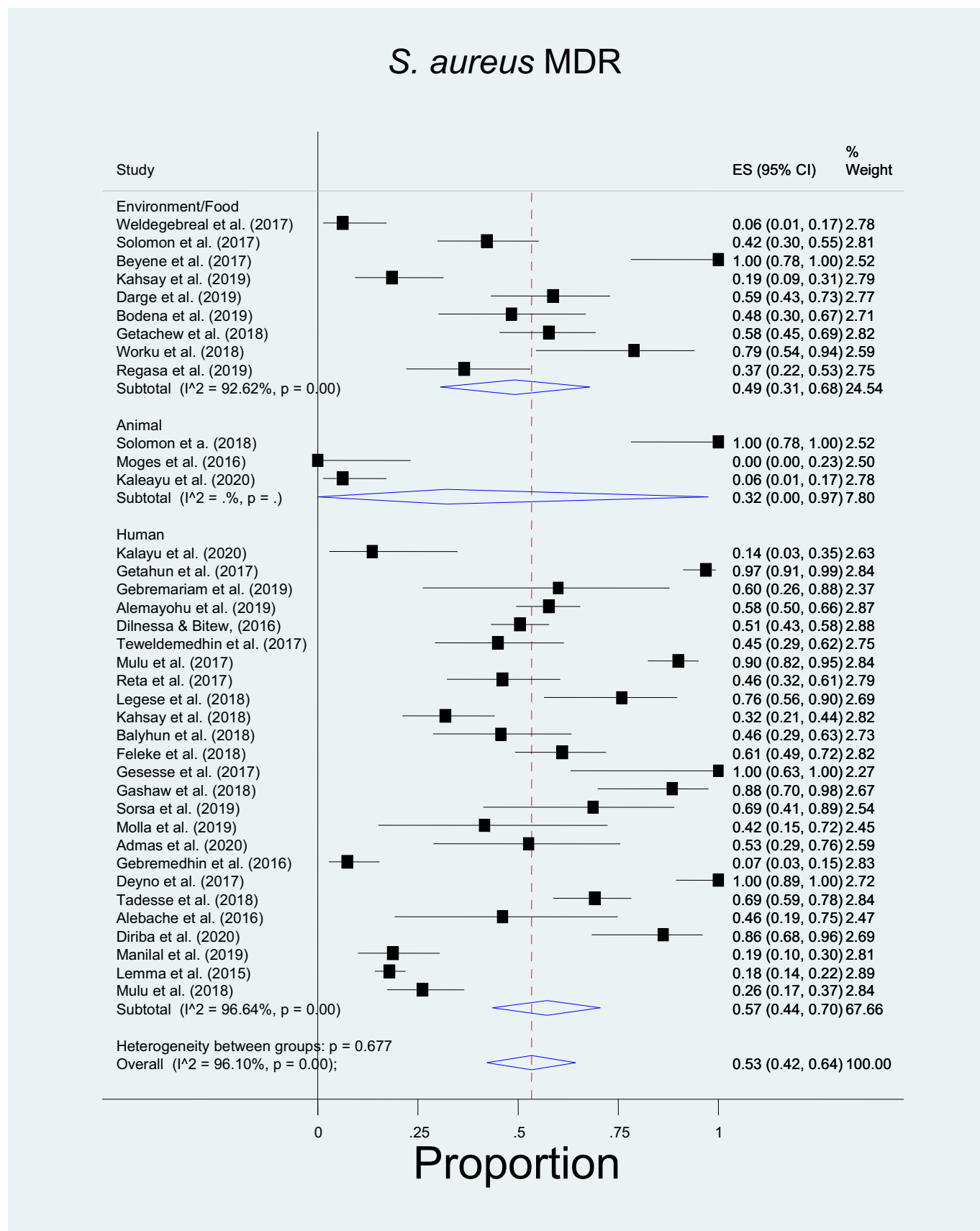
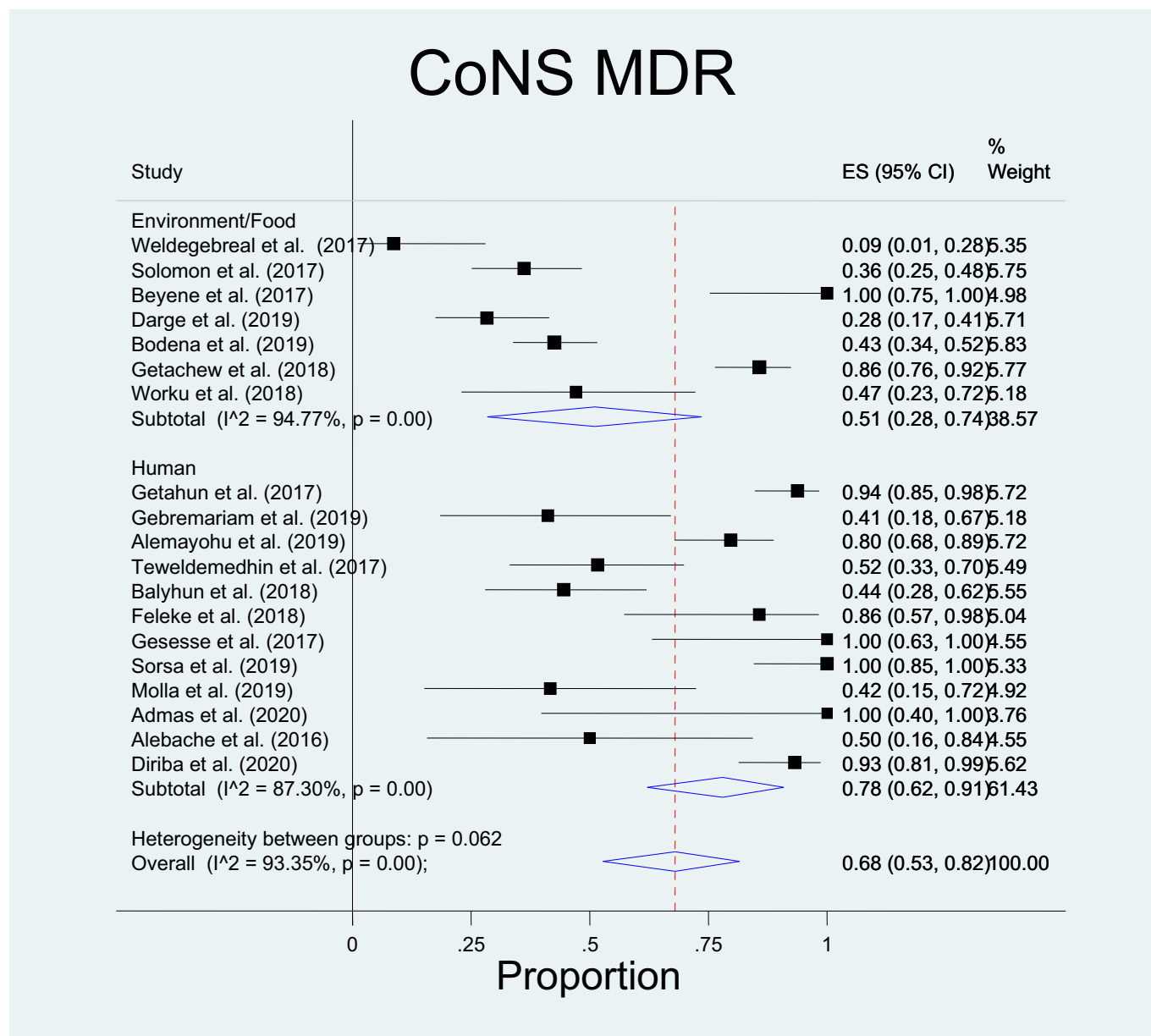


Fig. 2. The Forest plot shows the pooled prevalence of multidrug-resistant (MDR) *S. aureus* in humans was 0.57(0.44, 0.70), 0.32(0.00, 0.97) in animal studies, and 0.49(0.31, 0.68) for isolates from the environment or food. There was no significant heterogeneity between the three sources; p = 0.677.



**Fig. 3.** Forest plot of the pooled proportion of Coagulase-negative Staphylococci (CoNS) Multidrug-resistant (MDR) was 0.78(0.62–0.91) in human studies, 0.51 (0.28–0.74) in environment or food with an overall estimated MDR of 68% and has no significant heterogeneity between the two sources.

### 3.4. The pooled proportion of MDR for commonly reported bacterial isolates

This review extracts the type of bacterial isolate, the number of isolates tested for antimicrobial resistance, and the number of isolates reported as MDR. A total of 6 species of gram-positive bacteria and 13 species of gram-negative bacteria were included in the meta-analysis (Table 4). Among all, different studies found that *S. aureus*, *E. coli*, and *Klebsiella* spp. were the top three frequently reported species. The pooled proportion of MDR was computed for each bacterium from all categories (animal studies, human studies, environment, and food) as summarised below (Tables 5 & 6). Organisms were included in the meta-analysis if reported by at least four human studies and at least three animal studies, food & environmental studies.

### 3.5. Multidrug resistance in gram-positive bacteria

In this study, bacterial isolates that belong to three genera (genus

*Staphylococcus*, genus *Streptococcus*, and *Enterococci*) have been included in the meta-analysis because reports from other genera did not fulfil the criteria for meta-analysis. Among the included species, the pooled proportion of MDR for *S. aureus* was found to be 0.57(0.44, 0.70) for isolates from humans, 0.32(0.00, 0.97) in animal studies, and 0.49(0.31, 0.68) for isolates from the environment or food (Table 5). This study has yielded an overall estimated MDR of 53%. The meta-analysis indicated no significant heterogeneity between the three sources;  $p = 0.677$  (Fig. 2). In the case of Coagulase-negative *Staphylococci* (CoNS), the pooled proportion of MDR was 0.78(0.62–0.91) in human studies, 0.51 (0.28–0.74) in environment or food with an overall estimated MDR of 68%. There was no significant heterogeneity between the two sources (Fig. 3). However, group heterogeneity has been explained by study area and year in both species. Concerning CoNS, a single animal study reported the proportion of MDR CoNS as 0.29 [31].

All reported isolates of *S. pyogenes*, *S. agalactiae*, *Streptococcus pneumoniae*, and *Enterococcus* species were from human sources. Hence, the pooled proportion of MDR *S. pyogenes* and GBS in humans were 0.42



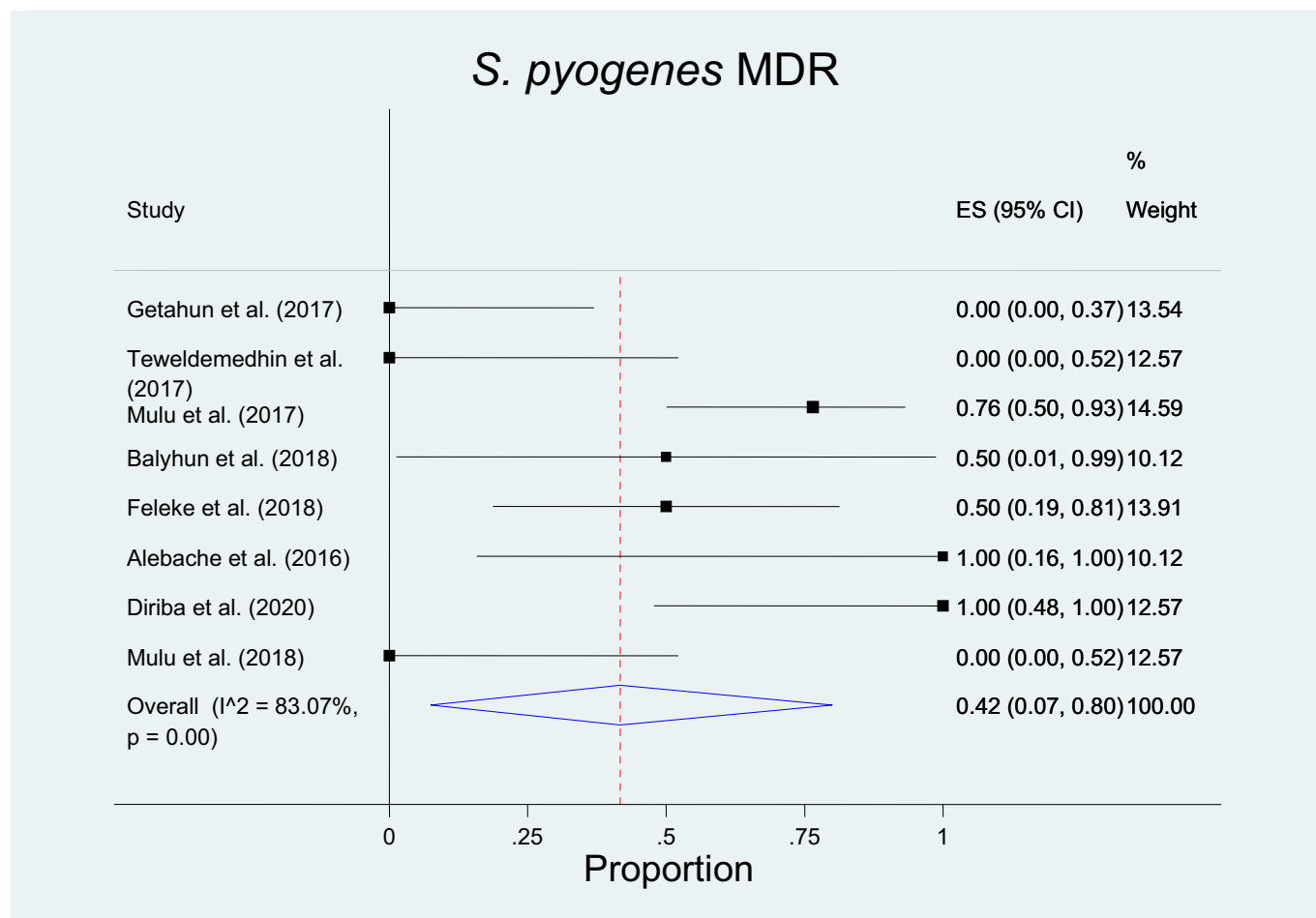


Fig. 4. The pooled prevalence of Multidrug-resistant (MDR) *S. pyogenes* in humans was 0.42(0.07–0.80), I<sup>2</sup> = 83.07%, and p = 0.

(0.07–0.80), I<sup>2</sup> = 83.07% p = 0.00 and 0.51(0.15–0.89), I<sup>2</sup> = 92.83% p = 0.00 respectively (Figs. 3-6; Table 5).

### 3.6. Multidrug resistance in gram-negative bacteria

As summarised in Table 6, pooled MDR was computed for 13 species of gram-negative bacteria. Accordingly, the highest pooled MDR in human sources was for *Acinetobacter* species 86% (95% CI: 46–100%) followed by *Pseudomonas* species 82% (95% CI: 52–100%), *E. coli* 81% (95% CI: 70–90%) and *Klebsiella* species 70% (95% CI: 50–87%). In the case of animal sources, *E. coli* and *Salmonella* species were frequently reported with a pooled MDR proportion of 0.72 (0.57–0.86) and 0.64 (0.43–0.83), respectively.

Among the isolates from environment or food sources, the highest pool of MDR was found in *Enterobacter* species (0.73(0.43–0.98)), *Citrobacter* species (0.69 (0.32–0.97)), and *Salmonella* species (0.56 (0.13–0.94) (Table 6). Overall, for the species that involved all sources, there was no significant heterogeneity between the subgroups (Human source, Animal source, Environment, or food sources) except for *Klebsiella* species (Table 6). The pooled proportion of MDR and group differences can be compared from the forest plots for each bacterium.

## 4. Discussion

Multidrug-resistant organisms pose a significant burden worldwide [96]. Mitigation of the problem needs to determine its magnitude from the perspective of human infections and the animals, food, and the environment from a health perspective. Hence, this systematic review and meta-analysis determined the prevalence of MDR for commonly

reported bacteria from humans, animals, environment, and food studies in Ethiopia.

From the perspective of human studies, CoNS (78%), *Enterococcus* spp. (65%) and *S. aureus* (57%) had the highest pooled percentage of MDR among the gram-positive bacteria. In gram-negative bacteria, *Acinetobacter* spp. (86%), *Pseudomonas* spp., *E. coli* and *Klebsiella* spp. (81%) were the top MDR bacteria. Various mechanisms contribute to the emergence of drug resistance in human pathogens. One mechanism is the carriage state in various anatomical sites, as *Staphylococcus*, *Enterococci*, and *E. coli* results in frequent suboptimal exposure to antimicrobials used for the treatment and prophylactic measures. The other scenario is prolonged hospitalisation [97], prolonged use of prophylaxis, and predispositions to hospital-acquired infections, a common scenario in *S. aureus*, *E. coli*, *Klebsiella*, and *Pseudomonas* spp. [98]. These MDR organisms could pose a triple burden because humans take the highest share of releasing MDR organisms to the environment and animals through direct contact, faecal pollution, mucosal secretion, and recreational activities. Compared to other studies, the pooled prevalence of MDR for *Klebsiella* spp. and *E. coli* is higher than the findings in Cameroon through the consistent finding was found for *Proteus* spp. and *Staphylococcus* spp. [18].

Out of the eight species of bacteria extracted from environmental or food studies, the pooled prevalence of MDR was above 50% for seven of the species, specifically, *Enterobacter* spp. (73%), *Citrobacter* spp. (69%), *Salmonella* spp. (56%), *E. coli* (53%) and *Pseudomonas* spp. (53%) were the top MDR bacteria. Almost half of the staphylococcal isolates from environment/food studies were also MDR. As stated in the results section, most of the included studies from the environment domain were from the hospital environment and wastewater. Hence, the selective

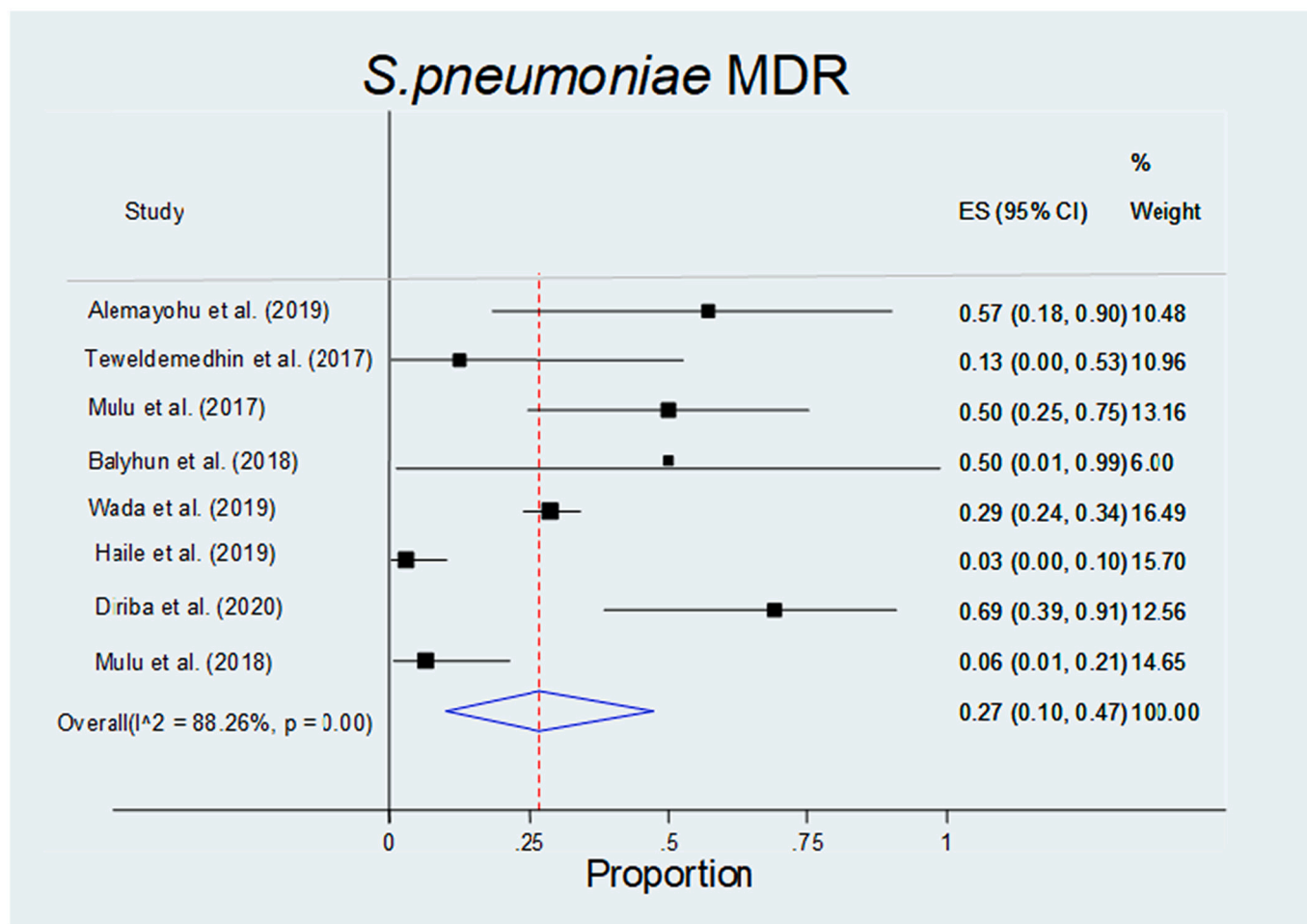


Fig. 5. The pooled prevalence of multidrug-resistant (MDR) *Streptococcus pneumoniae* in humans was 0.27 (0.10–0.47),  $I^2 = 88.26\%$ , and  $p = 0$ .

pressure of nosocomial pathogens such as *Pseudomonas*, *E. coli*, *Enterobacter*, *Citrobacter* species, and *S. aureus* might have contributed to the high degree of MDR because the stress response, adaptation, and gene transfer events in the hospital environment favour the emergence of multidrug resistance foci within the bacterial genome [99]. Furthermore, the mixed release of organisms and antimicrobials in the health care wastes and urban rivers may contribute to the development and acquisition of drug resistance [100], which may sound specifically for common water contaminants such as *E. coli* and *Enterococci* [101]. Hence, the released drug-resistant bacteria pollute drinking water sources, which may affect human health [102].

On the other hand, many studies were from the abattoir, butcher shops, meat chains, and milk chains. In this case, firstly, there might be contamination with skin and mucosal floras such as MDR *Staphylococcus* from the food handlers; secondly, there might also be surface contamination with faecal matter, animal excreta, and water sources which may also be true for *E. coli*, *Enterococci*, and *Salmonella* spp. It may allow the transmission of drug resistance determining genes between bacterial populations from raw meat, carcasses, surfaces/soil, water, and humans [100]. Hence, the habitual consumption of raw meat and raw milk may be a potential risk of these MDR bacteria.

In the case of animal studies, *E. coli* (72%), *Salmonella* spp. (64%) and *S. aureus* (32%) were the common MDR bacteria. Animals have direct and indirect contributions to the spread of MDR bacteria to the environment and humans [103]. This may be explained by direct contact with the environment (soil, water), faecal contamination, and manure associated spread of antibiotic resistance genes in agricultural fields [104]. The frequent contact between humans, dairy cattle, and poultry

may also be a good opportunity for the bidirectional transmission of MDR bacteria such as *S. aureus* and *E. coli*. Lastly, small animals such as cockroaches may contribute to the spread of MDR bacteria between humans, animals, and the environment [72]. Overall, the spread of multidrug-resistant bacteria is a cyclic process between the environment, animals, and the environment. It is also evidenced that MDR bacteria are associated with excess morbidity, mortality, and cost [96]. Therefore, understanding the nature of the problem from one health perspective has paramount importance.

Various environmental routes are essential avenues for human exposure to resistant bacteria and their genes coming from animal and plant reservoirs and opportunities for improved antimicrobial resistance regulation [105]. The transmission of bacteria and resistance genes from agricultural sources is largely foodborne. In the developed countries with good sewage and drinking water treatment, most people have little to no direct contact with food-producing animals. Bacteria and resistance genes are transmitted directly from contaminated meat and poultry during slaughter and processing or indirectly from contaminated fruit and vegetables from manure or irrigation water [106]. In countries with inadequate sewage and water treatment, drinking water is expected to significantly transmit resistant germs and genes from animals [107,108].

Furthermore, poor sanitation allows for indirect person–person waterborne transmission of enteric germs among residents and international tourists, who return home colonised with resistant bacteria [109]. Globalised trade in animals and food, and long-distance migratory patterns of wildlife, are used to spread antimicrobial-resistant bacteria worldwide. Among the broad actions to prevent antibiotic



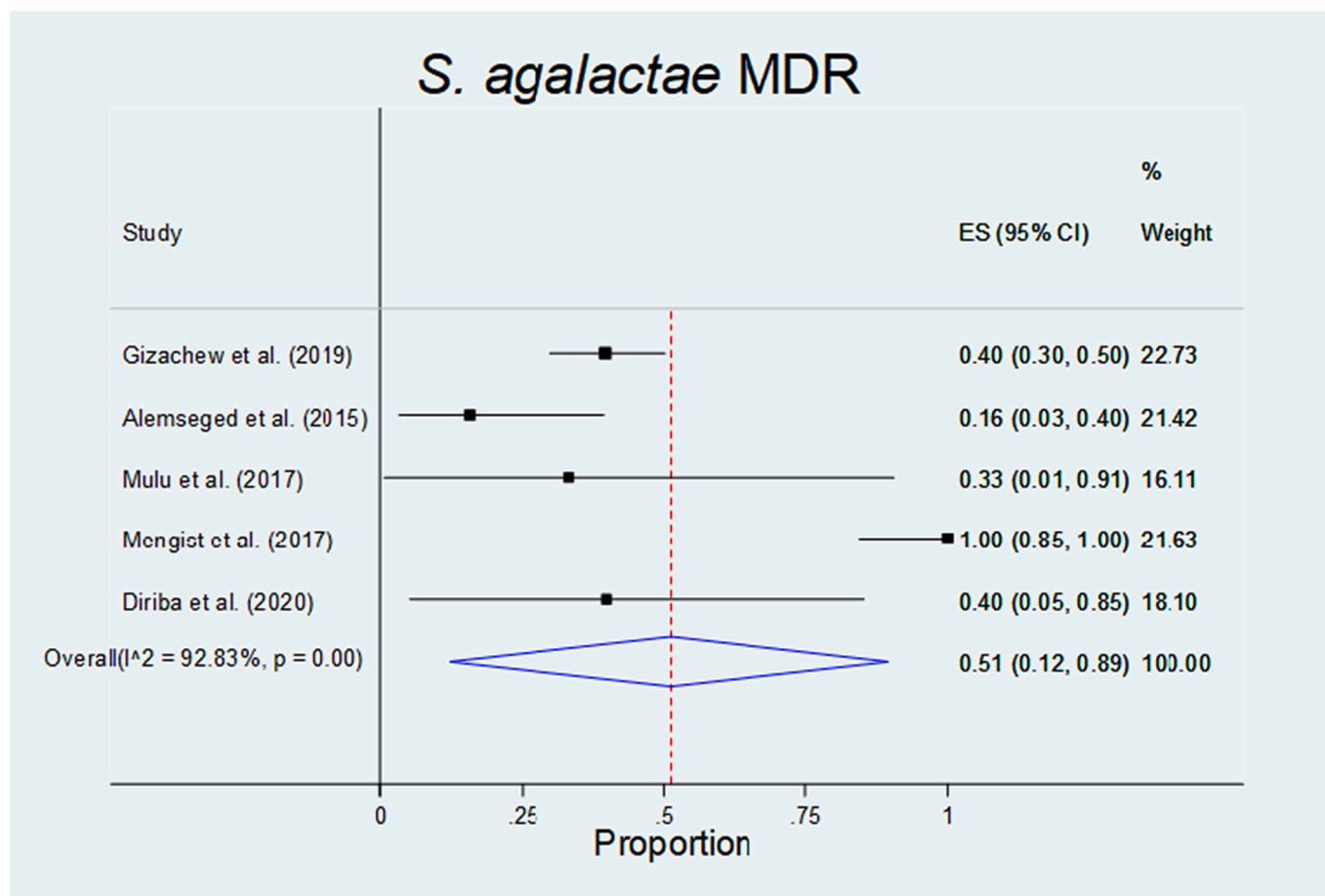


Fig. 6. The pooled prevalence of multidrug-resistant (MDR) *S. agalactiae* in humans was 0.51(0.12–0.89),  $I^2 = 92.83\%$ , and  $p = 0$ .

resistance in the wider environment are improved pollution controls from industrial, residential, and agricultural sources. More research and environmental monitoring and risk assessment are needed to understand better the role of the environment in the selection and spread of antimicrobial resistance and create more specialised approaches to combat resistance in this area [110]. The WHO Global Plan is supported by five pillars: 1. Reduce the Incidence of Infection via Effective Sanitation, Hygiene, and Infection Prevention Measures; 2. Strengthen the Knowledge and Evidence Base through Surveillance and Research; 3. Optimise Antimicrobial Medicine Use in Human and Animal Health; 4. Develop an Economic Case for Long-Term Investment.

The One Health approach of the WHO Global Action Plan is appropriate and consistent with remarks made in other international and national action plans [111]. However, until a fully integrated One health plan to combat antibiotic resistance is adopted at the national and global levels, there is still a long way to go. Multiple sectors (including animals, humans, and the environment) and organisations have competing interests, and there are gaps in antimicrobial resistance surveillance, antimicrobial use regulation, and infection control in many regions of the world. History has proven that it is impossible to clearly divide antimicrobial classes into those used solely in the human or non-human sectors, except for novel antimicrobial types. As long as there are few or no options, they should probably be reserved for use in humans. On the other hand, most classes will be offered in both sectors, and One health's goal would be to ensure their utilisation is efficient collectively. It is more likely to happen if antimicrobials used in both industries are only used for therapy, never for prophylaxis, not for improving plant growth, and if we effectively manage the types and amounts of antimicrobials we allow into the environment, as well as the frequency of resistant bacteria.

There are several obstacles to enhancing antibiotic management in One health, including a lack of knowledge, limited awareness, antibiotic misuse, and insufficient regulatory approaches in various countries. Excessive antibiotic usage in food-producing animals has been shown to have hostile public and animal health consequences. However, the poor world has been sluggish to integrate scientific development and accept the findings. Advanced molecular approaches, including whole genome sequencing, metagenomics, metadata analysis, and phylogenetic research, are required for a deeper understanding of global antibiotic resistance. These cutting-edge tools will help us better understand how resistant superbugs and antibiotic resistance spread among humans, animals, insects, plants, water, and soil. One health is a topic that improves health via multidisciplinary collaboration by gathering data from multiple areas of One health to understand how antibiotic resistance spreads at the human-animal-environment interface. Microbiome study of the various regions of One health will be broad and challenging in the future. Plans for antibiotic stewardship must be feasible to reduce antibiotic usage.

## 5. Conclusion

In Ethiopia, the pooled prevalence of MDR is high in most bacterial species from humans, animals, food, and environmental sources. *Staphylococcus* species, most members of the Enterobacteriaceae, and *Pseudomonas* species are the standard MDR bacterial population involving all sources. To reduce the human, animal, and environmental health hazards, the global emergence and spread of antibiotic resistance need the implementation of a harmonised and multidisciplinary One Health approach. The proliferation of antibiotic resistance infections worldwide due to antibiotic abuse, poor sanitation, and ineffective

control mechanisms has a significant influence on global public health. Therefore, this demands integrated policy and intervention measures should be implemented to reduce the emergence and spread of MDR bacteria for better animal and human health outcomes.

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Not applicable.

## CRediT authorship contribution statement

**Mebrahtu Tweldemedhin:** Writing – original draft, Conceptualization. **Saravanan Muthupandian:** Supervision. **Tsega Kahsay Gebremeskel:** Data curation, Investigation. **Kibrati Mehari:** Formal analysis. **Getahun Kahsay Abay:** Methodology, Validation. **Teklay Gebrecherkos Teklu:** Resources. **Ranjithkumar Dhandapani:** Visualization, Validation. **Ragul Paramasivam:** Software, Formal analysis. **Tsehaye Asmelash:** Validation.

## Declaration of Competing Interest

The author reports no conflicts of interest in this work.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.onehlt.2022.100390>.

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