Prevalence and drug resistance patterns of Gram-negative enteric bacterial pathogens from diarrheic patients in Ethiopia: A systematic review and meta-analysis

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Abstract

Background

Diarrhoea is the leading cause of morbidity and mortality in the world particularly in developing countries and among vulnerable groups of the population. Gram-negative enteric bacterial pathogens (GNEBPs) are a group of organisms that reside mainly in the intestine and induce diarrhoea. Antimicrobial agents are usually the part of their treatment regimen. The therapeutic effect of antimicrobials is hindered by the emergence and spread of drug-resistant strains. The information regarding the prevalence and antimicrobial resistance patterns of GNEBPs in Ethiopia is limited and found in a scattered form.

Objectives

This study was designed to determine the pooled prevalence and drug resistance patterns of GNEBPs by meta-analysis of data from diarrhoeic patients in Ethiopia.

Method

A comprehensive literature search was conducted through internet searches using Google Scholar, PubMed, Science Direct, HINARI databases, and reference lists of previous studies. Published articles were included in the study based on priorly set inclusion and exclusion criteria. Results were presented in the forest plot, tables, and figures with a 95% confidence interval (CI). The inconsistency index (I²) test statistics was used to assess heterogeneity across studies. The pooled prevalence estimate of GNEBPs and their drug resistance patterns were computed by a random-effects model. Software for Statistics and Data Science (STATA) version 14 statistical software was used for the analysis.
After removing those articles which did not fulfil the inclusion criteria, 43 studies were included in the analysis. Studies were conducted in 8 regions of the country and most of the published articles were from the Amhara region (30.23%) followed by Oromia (18.60%) and Southern Nations, Nationalities, and Peoples’ region (SNNP) (18.60%). The pooled prevalence of GNEBPs was 15.81% (CI = 13.33–18.29). The funnel plot indicated the presence of publication bias. The pooled prevalence of GNEBPs in Addis Ababa, Amhara, SNNP, and Oromia regions were 20.08, 16.67, 12.12, and 11.61%, respectively. The pooled prevalence was 14.91, 18.03, and 13.46% among studies conducted from 2006–2010, 2011–2015, and 2016–2021, respectively and it was the highest (20.35%) in children having age less than or equal to 15 years. The pooled prevalence of *Escherichia coli*, *Campylobacter* spp., *Shigella* spp., and *Salmonella enterica* were 19.79, 10.76, 6.24, and 5.06%, respectively. Large proportions (60–90%) of the isolates were resistant to ampicillin, amoxicillin, tetracycline, and trimethoprim-sulphamethoxazole. The pooled prevalence of multidrug resistance (MDR) was 70.56% (CI = 64.56–76.77%) and MDR in *Campylobacter* spp., *Shigella* spp., *E. coli*, and *S. enterica* were 80.78, 79.08, 78.20, and 59.46%, respectively.

**Conclusion**

The pooled estimate showed a high burden of GNEBPs infections and a high proportion of drug resistance characters to commonly used antimicrobial agents in Ethiopia. Therefore, performing drug susceptibility tests, establishing an antimicrobial surveillance system and confirmation by molecular techniques are needed.

**Introduction**

World Health Organization (WHO) defines diarrhoea as the passage of three or more loose or liquid stools per day (24 hours). During diarrhoea, the water content and volume of stool and defecation frequency will usually increase. The syndrome may be accompanied by other illnesses like vomiting, fever, dysentery, nausea, and abdominal cramps. It is the leading cause of morbidity and mortality in the world and contributes about 4% of all deaths and 5% of health loss to disability [1–3]. Diarrhoea is the fifth leading cause of death and it contributes to one in nine deaths among children younger than 5 years [4,5]. The problem is severe among the vulnerable population such as children, people with HIV, the elderly, and other individuals having weak immunity. Many factors contribute to diarrhoea; however, childhood wasting (low weight–for-height score), unsafe water, and unsafe sanitation are the leading risk factors [5]. The incidence of diarrhoea is different among the regions or continents of the world. It is highly prevalent in Sub-Saharan Africa and South Asia. The report from WHO showed that these countries account for about 78% of all diarrheal deaths among children in the developing world [2,4]. Ethiopia is one of the top three countries with very high child mortality due to diarrhoea in Africa [5–7].

Diarrhoea can be induced by a variety of causes. However, infectious agents like viruses and bacteria are among the leading causes. Bacteria, particularly Gram-negative enteric bacterial pathogens (GNEBPs) are the common causes of the syndrome. The group includes bacteria that reside mainly in the intestine. Genera such as *Escherichia*, *Shigella*, *Campylobacter*, *Salmonella*, *Enterobacter*, *Klebsiella*, *Yersinia*, *Serratia*, *Proteus*, and others are included in the group.
However, the most common and significant pathogens are *S. enterica, E. coli, Campylobacter,* and *Shigella* spp. [8].

Antimicrobial agents are usually part of the treatment regimen, particularly on diarrhoea caused by bacteria. Due to the widespread and indiscriminate use of antimicrobials, several resistant strains are emerging which tend to spread globally [9,10]. Hence, antimicrobial resistance (AMR) is a global health threat and was recognized in the 2016 United Nations (UN) General Assembly [11]. It is one of the top challenges in achieving the 2030 UN sustainable development goals [10]. Infections caused by resistant organisms affect treatment outcomes, treatment costs, disease spread, and duration of illness, posing a challenge to the future of chemotherapy [12]. Some pathogenic strains are also developing resistance not only to one but to several agents, i.e., multidrug resistance [13,14].

Information regarding the prevalence and antimicrobial resistance patterns of GNEBPs in Ethiopia is limited, and available information is found in scattered forms. Hence, there is an interest to conduct a nationwide study. To fill this significant gap, this systemic review and meta-analysis was prepared. The review focused on the prevalence and antimicrobial resistance patterns of GNEBPs isolated from diarrheic patients in Ethiopia. The output of this systematic review and meta-analysis can be used by clinicians, policymakers, and researchers to make evidence-based decisions.

**Methods**

**Literature search and selection**

The published articles were searched based on preferred reporting items for systematic reviews and meta-analyses (PRISMA) guideline [15]. The search was performed from June to August 2021 using Google Scholar, PubMed, Science Direct, and HINARI databases. The search queries were set based on medical subject headlines (MESH) and Boolean logic. Relevant MeSH terms and keywords were used to retrieve all relevant articles from the databases listed above. The keywords and MeSH terms used were “enteric bacteria AND diarrhoea AND drug resistance AND Ethiopia”, “*Salmonella* AND diarrhoea, AND Ethiopia AND drug resistance”, “*Shigella* AND diarrhoea AND Ethiopia AND drug resistance”, “*Escherichia coli* AND diarrhoea AND Ethiopia AND drug resistance”, “*Campylobacter* AND diarrhoea AND Ethiopia AND drug resistance” “*Yersinia* AND diarrhoea AND Ethiopia AND drug resistance”. Each bacterial genus was searched separately, and a search was also conducted on reference lists of previous studies to increase the chance of getting more articles. Only those articles which fulfil the selection criteria were used to analyse the information.

**Inclusion and exclusion criteria**

Research conducted on GNEBPs from the diarrhoeic patient or their antimicrobial susceptibility in Ethiopia and full-length published articles in the English language were included in the analysis. To get updated information on the issue, articles published from 2010 to August 2021 were considered. Studies that did not focus on GNEBPs from the diarrhoeic patient or their antimicrobial susceptibility, anonymous reports, abstracts (incomplete information), and published articles before 2010 and unpublished information were not included in the study. Studies that were conducted to assess the knowledge, attitude, and practice (KAP) of the community or the professionals were not also included.

**Data extraction**

The selected articles were coded, and data were collected using a format prepared in Microsoft Excel. The format consists of the author’s name, study period, year of publication, study
design, study region, study population, sample size, sample type, age, gender, isolated bacteria species, their prevalence, resistance patterns of the isolates, and prevalence of multidrug resistance. The extracted data were checked at least twice for their accuracy.

**Quality control**

The quality of eligible studies was checked using a set of criteria based on Joanna Briggs Institute critical appraisal tools including appropriateness of the research design to address the target population, adequate sample size, quality of paper, completeness of the information, and appropriateness of methods for isolation of the bacteria and appropriate statistical analysis [16]. The eligibility of selected articles was also assessed and approved by experts in the discipline.

**Data analysis**

The data were compiled in Excel 2010 (Microsoft, Redmond, WA, USA) spreadsheet and summarized by descriptive statistics. A random-effect model was used to determine the pooled prevalence and the 95% confidence interval (CI). All statistical analysis was achieved by using Software for Statistics and Data Science (STATA; https://www.stata.com/company/our-sites/) version 14. The data were described using forest plots, figures, and tables. The presence of publication bias was assessed by funnel plot. Sub-group analysis was performed based on the regions in the country, age group; (children, adults, and all age groups), and year of study (2006–2010, 2011–2015, and 2016–2021). Statistical heterogeneity was evaluated by the inconsistency index ($I^2$) test. The $I^2$ provides an estimate of the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error or chance differences. Hence, the $I^2$ test measures the level of statistical heterogeneity among studies [17,18].

**Results**

**Characteristics of published articles**

Of 7,349 identified studies, 6,680 articles were excluded upon reviewing the titles and abstracts because they were irrelevant (were not focusing on GNEBPs, diarrhoea, and drug resistance or were outside Ethiopia or duplicates). The remaining 669 articles were assessed for eligibility; of these, 626 articles were excluded since they were review, KAP, or meta-analysis studies. Finally, 43 studies meeting the inclusion criteria were included in this study. Selected articles were focusing on one or more GNEBPs. Fig 1 shows a flow diagram of the selection of articles for the analysis.

Table 1 shows the overall characteristics of articles included in the analysis, type and prevalence of Gram-negative isolates recovered from diarrheic patients. Studies were conducted in 8 regions of the country and most of the published articles were from the Amhara region (30.23%) followed by the Oromia region (18.60%) and South Nation and Nationalities Region (SNNP) (18.60%). Published articles were not found in other regions of the country (Afar, Somali, and Benishangul Gumuz regions) (Fig 2).

All studies were cross-sectional; conducted from 2006 to 2020 and published online from 2010 to August 2021. Almost all studies (97.67%) were institution-based (conducted on patients visiting health facilities). The stool samples were the specimen used to isolate the bacterial species. Isolates were characterized and their identities were confirmed by cultural and conventional biochemical tests, but molecular techniques were not used. Patients suffering from diarrhoea were used as the population of the studies and three studies were conducted on diarrhoeic patients with HIV. More than half of the studies (55.81%) were focusing on
children less than equal to fifteen years of age. However, 39.53% of studies were considering all age groups (Fig 3 and Table 3).

Prevalence of Gram-negative enteric bacterial pathogens

To isolate GNEBPs, in each study, 24 to 1,225 stool samples were collected. Totally, 13,350 stool samples were examined from 3,688 male and 3,822 female diarrheic patients and 1,962 (14.70%) samples were positive for GNEBPs. The minimum and maximum prevalence of GNEBPs in Ethiopia from diarrhoeic patients were 3.57% [27] and 55.83% [21]. The estimated pooled prevalence of GNEBPs in diarrheic patients from 43 studies was 15.81% (95% CI = 13.33–18.29) (Fig 4).

The distribution of the studies using a funnel plot (Fig 5) showed the asymmetrical distribution of effect estimates; hence, there was a publication bias. To minimize the effect of the bias, subgroup analysis was used. Regionally, the pooled prevalence of GNEBPs from diarrheic patients in Addis Ababa, Amhara, SNNPs and Oromia were 20.08, 16.67, 12.12, and 11.61%, respectively. The pooled prevalence based on the study period was 14.91, 18.03 and 13.46% among studies from 2006–2010, 2011–2015 and 2016–2021, respectively. The pooled prevalence was the highest (20.35%) in children having age less or equal to 15 years, followed by all age groups (10.83%) and adults greater than 15 years (8.51%) (Table 2).

Table 3 shows the types of bacterial isolates reported by published articles from diarrheic patients. *Shigella* spp. were the most frequent isolate (41.67%), followed by *S. enterica* (38.09%). The pooled estimate of *E. coli* was the highest (19.79%) among enteric bacterial isolates. The pooled prevalence of *Campylobacter* spp., *Shigella* spp. and *Salmonella enterica* were 10.76, 6.24 and 5.06%, respectively.
## Table 1. Characteristics, quality, and the number of Gram-negative isolates recovered from diarrheic patients.

| References | Year of publication | Study period | Region | Study population | Age category | Gender | Number examined | No. Positive | Prevalence E. coli | Salmonella | Shigella | Klebsiella | Proteus | Enterobacter | Campylobacter | Citrobacter |
|------------|---------------------|--------------|--------|------------------|--------------|--------|-----------------|--------------|---------------------|------------|----------|------------|---------|-------------|-------------|------------|
| [1]        | 2011                | Jan to March 2018 | Oromia | Diarrheic patient | HIV+ <15 yrs | Male 163 | 191 | 354 | 24 | 6.78 | 16 | 10 | 3 | 6 |
| [2]        | 2012                | Jan to July 2014 | Oromia | Diarrheic patient | HIV+ <15 yrs | Male 125 | 114 | 239 | 9 | 3.77 | 3 | 6 | 1 | 3 |
| [3]        | 2013                | Jan to Sept 2017 | SNNP   | Diarrheic patient | <15 yrs | Male 101 | 103 | 204 | 19 | 9.31 | 3 | 17 |
| [4]        | 2014                | Feb to May, 2014 | Amhara | Diarrheic patient | <15 yrs | Male 125 | 90 | 215 | 32 | 14.88 | 32 |
| [5]        | 2015                | Nov 2015 and Aug 2016 | Amhara | Diarrheic patient | <15 yrs | Male 163 | 191 | 354 | 24 | 6.78 | 17 | 10 | 3 | 6 |
| [6]        | 2016                | Oct 2015 to March 2016 | Amhara | Diarrheic patient | <15 yrs | Male 125 | 114 | 239 | 9 | 3.77 | 3 | 6 | 1 | 3 |
| [7]        | 2017                | Jan to March 2018 | Oromia | Diarrheic patient | HIV+ <15 yrs | Male 101 | 103 | 204 | 19 | 9.31 | 3 | 17 |
| [8]        | 2018                | Nov 2015 and Aug 2016 | Amhara | Diarrheic patient | <15 yrs | Male 163 | 191 | 354 | 24 | 6.78 | 17 | 10 | 3 | 6 |
| [9]        | 2019                | Jan to March 2018 | Oromia | Diarrheic patient | HIV+ <15 yrs | Male 101 | 103 | 204 | 19 | 9.31 | 3 | 17 |
| [10]       | 2020                | May 2019 to Nov 2019 | SNNP   | Diarrheic patient | Adult >15 yrs | Male 125 | 90 | 215 | 32 | 14.88 | 32 |
| [11]       | 2021                | Oct 2015 to March 2016 | Amhara | Diarrheic patient | <15 yrs | Male 125 | 90 | 215 | 32 | 14.88 | 32 |
| [12]       | 2022                | Jan to March 2018 | Oromia | Diarrheic patient | HIV+ <15 yrs | Male 101 | 103 | 204 | 19 | 9.31 | 3 | 17 |

**yrs = years, SNNP = Southern Nations, Nationalities, and Peoples’ Region.**

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Escherichia coli was the most common (15.95%) isolate among children less than or equal to fifteen years of age whereas Salmonella enterica and Shigella spp. were common among studies that were focused on all age groups (Tables 1 and 4).

Drug resistance patterns of Gram-negative enteric bacterial pathogens

Drug resistance in Shigella spp. Twenty-six antimicrobial panels were used to assess the drug resistance pattern of Shigella spp. The highest percentage of resistance was reported among members of the penicillin group such as ampicillin (85.01%) and amoxicillin (82.07%). Resistance against the tetracycline group was also very common (67.01%). A considerable proportion of resistance was also reported among cephalosporin groups, particularly on the first-generation agents and erythromycin. Resistance was not reported against carbapenems (Table 5).
Drug resistance of *Salmonella enterica*. Twenty-five antimicrobial panels were used to assess the drug resistance patterns of *S. enterica*. The highest percentage of resistance was reported among members of the penicillin group such as ampicillin (64.98%) and amoxicillin (82.89%). Resistance against tetracycline and trimethoprim-sulphamethoxazole were also

![Forest plot of pooled prevalence estimates of Gram-negative enteric bacterial pathogens among diarrheic patients.](https://doi.org/10.1371/journal.pone.0265271.g004)
common. A considerable proportion of resistance was also reported against erythromycin and cephalosporin groups. Resistance was not reported against doxycycline, meropenem and azithromycin (Table 6).

**Drug resistance of *Escherichia coli***. Sixteen antimicrobial panels were used to assess the drug resistance pattern of *E. coli*. The highest percentage of resistance was reported on agents like ampicillin (77.97%). Resistance against tetracycline (76.87%) and trimethoprim-sulphamethoxazole (66.97%) were also common. A considerable proportion of resistance was also reported among cephalosporin groups. Resistance was not reported against meropenem (Table 7).

**Drug resistance of *Campylobacter* spp.** Eighteen antimicrobial panels were used to assess the drug resistance patterns of *Campylobacter* spp. The highest percentage of resistance was

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**Table 3. Bacterial isolates reported by published articles from diarrheic patient.**

| Bacterial isolates        | No of Studies | Studies reporting the agent (%) | No of sample | No positive | Positives (%) | Prevalence (%) |
|---------------------------|---------------|---------------------------------|--------------|-------------|---------------|----------------|
| **Shigella spp.**         | 35            | 41.67                           | 10,026       | 632         | 5.61          | 1.03–37.50     |
| **Salmonella enterica**   | 35            | 38.09                           | 11,360       | 644         | 5.67          | 0.38–62.50     |
| **Escherichia coli**      | 9             | 7.1                             | 2392         | 514         | 21.49         | 0.93–51.65     |
| **Campylobacter spp.**    | 5             | 6.0                             | 1079         | 123         | 11.40         | 4.12–19.76     |
| **Citrobacter spp.**      | 1             | 1.2                             | 253          | 10          | 3.95          | -              |
| **Enterobacter spp.**     | 1             | 1.2                             | 163          | 2           | 1.23          | -              |
| **Klebsiella spp.**       | 1             | 1.2                             | 163          | 11          | 6.75          | -              |
| **Proteus spp.**          | 1             | 1.2                             | 163          | 7           | 4.29          | -              |
| **Total**                 | 88*           |                                 |              |             |               |                |

*An article may report one or more bacterial species from diarrheic patients; No = Number; % = Percent; CI = confident interval.*

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Table 4. Type bacterial isolates among different age groups.

| Age category (years) | Type of bacterial isolates | No of studies | No of Sample | No Positive | Pooled prevalence ((95% CI)) |
|----------------------|-----------------------------|---------------|--------------|-------------|-----------------------------|
| < 15                 | Campylobacter spp.          | 3             | 670          | 102         |                             |
|                      | *E. coli*                   | 8             | 2177         | 524         | 15.95 (14.52–17.38)         |
|                      | Salmonella enterica         | 19            | 5893         | 296         | 2.95 (2.52–3.37)            |
|                      | Shigella spp.               | 20            | 5767         | 344         | 3.95 (3.45–4.44)            |
| Adult >15            | Campylobacter spp.          | 1             | 180          | 8           |                             |
|                      | *Salmonella* spp.           | 2             | 458          | 20          |                             |
|                      | *Shigella* spp.             | 2             | 458          | 11          |                             |
| All age groups       | Campylobacter spp.          | 1             | 215          | 13          |                             |
|                      | *E. coli*                   | 1             | 215          | 2           |                             |
|                      | Salmonella enterica         | 14            | 5067         | 381         | 3.21 (2.74–3.69)            |
|                      | Shigella spp.               | 13            | 3859         | 221         | 3.14 (2.59–3.68)            |

No = Number; % = Percent; CI = confident interval.

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Table 5. Prevalence of *Shigella* spp. resistance to different antimicrobial agents in Ethiopia.

| Antimicrobial Agents | The Main group of antimicrobial agents | No of studies | The total no of isolates tested | No of resistant isolate | Resistant isolate (%) | Pooled prevalence (%) (95% CI) | I²% (p-value) |
|----------------------|----------------------------------------|---------------|--------------------------------|-------------------------|-----------------------|------------------------------|---------------|
| Ampicillin           | Penicillins                            | 30            | 519                            | 452                     | 87.09                 | 85.01 (79.79–90.22)           | 61.4 (0.00)  |
| Amoxicillin          | Penicillins                            | 14            | 175                            | 153                     | 87.43                 | 82.07 (74.05–89.65)           | 0.00 (0.47)  |
| Augmentin (Amoxicillin and clavulinate potassium) | Penicillins and β-lactamase inhibitors | 10            | 196                            | 91                      | 46.43                 | 43.87 (22.5–65.24)           | 93.1 (0.00)  |
| Tetracycline         | Tetracyclines                          | 22            | 404                            | 309                     | 76.49                 | 67.01 (55.83–78.36)           | 89.9 (0.00)  |
| Doxycycline          | Tetracyclines                          | 2             | 20                             | 16                      | 80.00                 | -                            | -             |
| Cephalothin          | 1st G cephalosporins                   | 4             | 57                             | 40                      | 70.18                 | 70.18 (60.56–100.65)          | 100(-)       |
| Cefoxitin            | 2nd G cephalosporins                   | 1             | 20                             | 6                       | 30.00                 | -                            | -             |
| Cefuroxime           | 2nd G cephalosporins                   | 1             | 20                             | 13                      | 65.00                 | -                            | -             |
| Cefaclor             | 2nd G cephalosporins                   | 1             | 17                             | 11                      | 64.71                 | -                            | -             |
| Ceftriaxone          | 3rd G cephalosporins                   | 14            | 151                            | 16                      | 10.60                 | 29.53 (7.80–51.25)           | 79.5 (0.001) |
| Cefazidime           | 3rd G cephalosporins                   | 6             | 62                             | 7                       | 11.29                 | 8.24 (0.42–16.03)            | 0.00 (0.46)  |
| Cefotaxime           | 3rd G cephalosporins                   | 2             | 20                             | 4                       | 20.00                 | -                            | -             |

(Continued)
reported for Cephalothin (81.52%). Resistance against ampicillin (65.61%) and trimethoprim-sulphamethoxazole (52.6%) were also common. Resistance was not reported against meropenem and azithromycin (Table 8).

**Drug resistance of other enteric bacterial species.** The number of published articles on other enteric bacterial species from diarrheic patients was very limited and impossible to summarize. However, one study conducted by Zenebe et al. [21] reported the presence of *Klebsiella* spp., *Proteus* spp., *Enterobacter* spp. in under-five children with diarrhoea. These bacteria were showing antimicrobial resistance character as indicated in Table 9.

**Multidrug resistance**

Out of 43 published articles on enteric bacterial pathogens, 32 (74.42%) reported multidrug-resistant (MDR) characters among the isolates. Among 1470 bacterial isolates, 1104 (75.52%) with a pooled prevalence of 70.56% (CI = 64.56–76.77%) were resistant to three or more antimicrobial agents (multidrug resistance). The report showed that the pooled prevalence of MDR in *Campylobacter* spp., *Shigella* spp., *E. coli* and *S. enterica* were 80.78, 79.08, 78.20 and 59.46%, respectively (Table 10).
Table 6. The pooled prevalence of *Salmonella enterica* resistance to different antimicrobial agents in Ethiopia.

| Antimicrobial Agents       | The main group of antimicrobial agents | No of studies | The Total no of isolates tested | No of resistant isolate | Resistant isolate (%) | Pooled prevalence (%) (95% CI) | I²% (p-value) |
|----------------------------|----------------------------------------|---------------|--------------------------------|-------------------------|----------------------|---------------------------------|----------------|
| Ampicillin                 | Penicillins                            | 29            | 588                            | 447                     | 76.02                | 64.98 (45.2–84.76)              | 96.5 (0.00)   |
| Amoxicillin                | Penicillins                            | 12            | 255                            | 223                     | 87.45                | 82.89 (70.58–95.21)             | 62.0 (0.072)  |
| Augmentin (Amoxicillin and clavulanate potassium) | Penicillins and β-lactamase inhibitors | 8             | 185                            | 75                      | 40.54                | 45.34 (19.11–71.56)             | 95.2 (0.00)   |
| Tetracycline               | Tetracycline                           | 24            | 555                            | 287                     | 51.71                | 54.59 (41.28–67.90)             | 90.03 (0.00)  |
| Doxycycline                | Tetracycline                           | 2             | 34                             | 0                       | 0.00                 | -                               | -              |
| Cephalothin, 1st G cephalexins | Penicillins                            | 2             | 9                              | 1                       | 11.11                | -                               | -              |
| Cefaclor, 2nd G cephalexins | Penicillins                            | 1             | 4                              | 4                       | 100.00               | -                               | -              |
| Cefoxitin, 2nd G cephalexins | Penicillins                            | 1             | 33                             | 9                       | 27.27                | -                               | -              |
| Ceftizoxime, 2nd G cephalexins | Penicillins                            | 1             | 21                             | 5                       | 23.81                | -                               | -              |
| Cefuroxime, 2nd G cephalexins | Penicillins                            | 2             | 55                             | 16                      | 29.09                | -                               | -              |
| Ceftriaxone, 3rd G cephalexins | Penicillins                            | 16            | 384                            | 109                     | 28.39                | 33.1 (7.88–58.33)               | 98.0 (0.00)   |
| Ceftaridine, 3rd G cephalexins | Penicillins                            | 5             | 27                             | 4                       | 14.81                | 29.22 (22.42–8086)              | 81.7 (0.02)   |
| Cefotaxime, 3rd G cephalexins | Penicillins                            | 2             | 7                              | 2                       | 28.57                | -                               | -              |
| Chloramphenicol, Penicillins | Penicillins                            | 29            | 629                            | 260                     | 41.34                | 42.39 (27.39–57.38)             | 96.1 (0.00)   |
| Kanamycin, Aminoglycosides | Penicillins                            | 3             | 73                             | 24                      | 32.88                | 33.7 (22.72–44.69)              | 0.00 (0.67)   |
| Gentamicin, Aminoglycosides | Penicillins                            | 24            | 491                            | 121                     | 24.64                | 17.36 (7.57–27.15)              | 93.4 (0.00)   |
| Amikacin, Aminoglycosides  | Penicillins                            | 3             | 26                             | 1                       | 3.85                 | -                               | -              |
| Norfloxacin, Fluoroquinolones | Penicillins                            | 19            | 462                            | 66                      | 14.29                | 14.60 (9.23–19.97)              | 64.2 (0.00)   |
| Ciprofloxacin, Fluoroquinolones | Penicillins                            | 10            | 200                            | 9                       | 4.50                 | 5.17 (1.79–8.55)                | 0.00 (0.98)   |
| Cefotaxime, Fluoroquinolones | Penicillins                            | 28            | 28                             | 28                      | 5.29                 | 7.66 (2.67–12.66)               | 74.8 (0.00)   |
| Trimethoprim-sulphamethoxazole, Folic acid metabolism inhibitors | Penicillins and β-lactamase inhibitors | 25            | 464                            | 218                     | 46.98                | 46.72 (29.74–61.69)             | 94.4 (0.00)   |
| Meropenem, Carbenemases     | Penicillins                            | 2             | 20                             | 0                       | 0.00                 | -                               | -              |
| Erythromycin, Macrolides    | Penicillins                            | 5             | 45                             | 25                      | 55.56                | 52.97 (37.96–68.72)             | 5.8 (0.364)   |
| Azithromycin, Macrolides    | Penicillins                            | 1             | 5                              | 0                       | 0.00                 | -                               | -              |

(Continued)
Diarrhoea is a common health problem, causing mortality and morbidity for thousands of people around the globe. Both infectious and non-infectious agents can induce the problem, among the infectious agents, enteric bacterial pathogens like diarrheagenic *E. coli*, *S. enterica*, *Shigella* spp., and *Campylobacter* spp. play important roles in the induction or severity of diarrhoea [61]. Determining their burden in a given population is very essential to design strategies.

Table 6. (Continued)

| Antimicrobial Agents | The main group of antimicrobial agents | No of studies | The Total no of isolates tested | No of resistant isolate | Resistant isolate (%) | Pooled prevalence (%) (95% CI) | I²% (p-value) |
|----------------------|----------------------------------------|---------------|-------------------------------|------------------------|-----------------------|-------------------------------|---------------|
| Clindamycin          | Macrolides                             | 1             | 113                           | 1                      | 0.88                  | -                             | -             |

No = Number; % = Percent; CI = confident interval, I = Inconsistency Index.

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Discussion

Diarrhea is a common health problem, causing mortality and morbidity for thousands of people around the globe. Both infectious and non-infectious agents can induce the problem, among the infectious agents, enteric bacterial pathogens like diarrheagenic *E. coli*, *S. enterica*, *Shigella* spp., and *Campylobacter* spp. play important roles in the induction or severity of diarrhoea [61]. Determining their burden in a given population is very essential to design strategies.

Table 7. The pooled prevalence of *Escherichia coli* resistance to different antimicrobial agents in Ethiopia.

| Antimicrobial Agents | The main group of antimicrobial agents | No of studies | The total no of isolates tested | No of resistant isolate | Resistant isolate (%) | Pooled prevalence (%) (95% CI) | I²% (p-value) |
|----------------------|----------------------------------------|---------------|-------------------------------|------------------------|-----------------------|-------------------------------|---------------|
| Ampicillin           | Penicillins                            | 6             | 446                           | 359                    | 80.49                 | 77.97 (70.17–85.76)            | 71.4 (0.00)   |
| Amoxicillin          | Penicillins                            | 1             | 47                            | 5                      | 10.64                 | -                             | -             |
| Augmentin            | Penicillins and B-lactamase inhibitors | 5             | 339                           | 204                    | 60.18                 | 64.78 (42.00–87.57)            | 95.0 (0.00)   |
| Tetracycline         | Tetracyclines                          | 3             | 253                           | 194                    | 76.68                 | 76.87 (71.69–82.05)            | 0.00 (0.563)  |
| Ceftriaxone          | 3rd G cephalosporins                   | 5             | 284                           | 11                     | 3.87                  | 2.91 (0.74–5.08)              | 11.5 (0.34)   |
| Cephalothin          | 1st G cephalosporins                   | 1             | 47                            | 8                      | 17.02                 | -                             | -             |
| Cefotaxime           | 3rd G cephalosporins                   | 1             | 204                           | 50                     | 24.51                 | -                             | -             |
| Gentamicin           | Aminoglycosides                        | 6             | 388                           | 102                    | 26.29                 | 19.72 (7.41–32.03)            | 88.03 (0.00)  |
| Amikacin             | Aminoglycosides                        | 1             | 113                           | 2                     | 1.77                  | -                             | -             |
| Chloramphenicol      | Chloramphenicol                        | 5             | 375                           | 121                    | 32.27                 | 30.39 (20.95–39.84)           | 67.0 (0.016)  |
| Nalidixic acid       | Fluoroquinolones                       | 5             | 224                           | 38                     | 16.96                 | 16.71 (11.81–21.6)            | 0.00 (0.713)  |
| Norfloxacin          | Fluoroquinolones                       | 2             | 206                           | 20                    | 9.71                  | -                             | -             |
| Ciprofloxacin        | Fluoroquinolones                       | 7             | 439                           | 27                     | 6.15                  | 5.57 (3.42–7.71)             | 0.00 (0.063)  |
| Trimethoprim-sulphamerthoxazole | Folic acid metabolism inhibitors | 7             | 428                           | 301                    | 70.33                 | 66.97 (56.21–77.71)           | 80.7 (0.00)   |
| Meropenem            | Carabapenems                           | 1             | 133                           | 0                      | 0                     | -                             | -             |
| Erythromycin         | Macrolides                             | 1             | 2                             | 1                      | 50                    | -                             | -             |

No = Number; % = Percent; CI = confident interval; I = Inconsistency Index.

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for the reduction of the incidence and influences of diarrhoea. The minimum and maximum prevalence of GNEBPs in Ethiopia from diarrhoeic patients were 3.57% [27] and 55.83% [21], respectively. The pooled prevalence of EBP isolates from the stool of diarrheic patients in Ethiopia was 15.81% (CI = 13.33–18.29). In line with this finding, Getie et al. [62] reported 13.2% prevalence of GNEBP in other groups of population (food handlers) in Gondar town, Northwest Ethiopia. On the other hand, Shah et al. [63] reported a 33.62% prevalence of GNEBP in Kenya. The difference may be due to the detection methods since they use molecular techniques in addition to the conventional culturing methods.

Almost all studies (97.67%) were institutional, and samples were collected from patients visiting health facilities. Focusing only on health facilities may not reflect the overall prevalence of GNEBPs and their drug resistance patterns in the country. Since some GNEBP infection cases

| Antimicrobial Agents | The main group of antimicrobial agents | No of studies | The total no of isolates tested | No of resistant isolate | Resistant isolate (%) | Pooled prevalence (%) (95% CI) | I² (p-value) |
|---------------------|---------------------------------------|---------------|-------------------------------|------------------------|-----------------------|-------------------------------|------------|
| Ampicillin          | Penicillins                           | 4             | 110                           | 72                     | 65.45                 | 65.61(44.90–86.32)            | 83.3 (0.000) |
| Amoxicillin         | Penicillins                           | 1             | 20                            | 16                     | 80.00                | -                            | -          |
| Augmentin (Amoxicillin and clavulanate potassium) | Penicillins and B-lactamase inhibitors | 1             | 44                            | 16                     | 36.36                | -                            | -          |
| Tetracycline        | Tetracyclines                         | 5             | 123                           | 60                     | 48.78                | 42.17 (20.30–64.05)           | 85.4 (0.00) |
| Doxycycline         | Tetracyclines                         | 3             | 90                            | 16                     | 17.78                | 18.94 (10.5–27.38)            | 0.00 (0.379) |
| Ceftriaxone         | 3rd G cephalosporins                  | 4             | 85                            | 15                     | 17.65                | 39.43 (0.96–77.91)            | 79.0 (0.029) |
| Ceftazidime         | 3rd G cephalosporins                  | 1             | 8                             | 2                      | 25.00                | -                            | -          |
| Cephalothin         | 1st G cephalosporins                  | 3             | 102                           | 91                     | 89.22                | 81.52 (63.78–99.27)           | 63.2 (0.09) |
| Gentamycin          | Aminoglycosides                       | 5             | 123                           | 29                     | 23.58                | 30.70 (8.04–53.36)            | 88.0 (0.00) |
| Chloramphenicol     | Chloramphenicol                       | 5             | 123                           | 26                     | 21.14                | 28.03 (10.33–45.85)           | 74.4 (0.00) |
| Nalidixic acid      | Fluoroquinolones                      | 4             | 115                           | 13                     | 11.30                | 10.45 (4.89–16.00)            | 0.00 (0.711) |
| Norfloxacin         | Fluoroquinolones                      | 3             | 95                            | 10                     | 10.53                | 12.02 (4.99–19.05)            | 0.00 (0.665) |
| Ciprofloxacin       | Fluoroquinolones                      | 5             | 123                           | 19                     | 15.45                | 13.9 (7.87–19.94)             | 0.00 (0.528) |
| Trimethoprim-       | Folic acid metabolism inhibitors      | 5             | 123                           | 67                     | 54.47                | 52.6 (33.76–71.43)            | 78.4 (0.00) |
| Sulphamethoxazole   |                                       |               |                               |                        |                      |                               |            |
| Meropenem           | Carbapenems                           | 1             | 8                             | 0                      | 0.00                 | -                            | -          |
| Erythromycin        | Macrolides                            | 5             | 123                           | 37                     | 30.08                | 35.72 (18.34–53.10)           | 78.4 (0.001) |
| Azithromycin        | Macrolides                            | 1             | 8                             | 0                      | 0.00                 | -                            | -          |
| Clindamycin         | Macrolides                            | 2             | 82                            | 28                     | 34.15                | -                            | -          |

No = Number; % = Percent; CI = confident interval; I = Inconsistency Index.

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Table 9. Pooled prevalence of other enteric bacterial resistance to different antimicrobial agents in Ethiopia.

| Reference | Isolate | Ampicillin | Chloramphenicol | Gentamicin | Nalidixic acid | Tetracycline | Ciprofloxacin | Trimethoprim-sulphamethoxazole | Ceftriaxone | Amoxicillin | Cephalothin |
|-----------|---------|------------|----------------|------------|----------------|--------------|---------------|--------------------------------|--------------|-------------|------------|
| [21]      | Klebsiella | 11 | 3 | 27.27 | 11 | 2 | 18.18 | 11 | 4 | 36.36 | 11 | 1 | 9.09 | 11 | 9 | 81.82 | 11 | 0 | 0.00 | 11 | 8 | 72.73 | 11 | 0 | 0.00 | 11 | 6 | 54.55 | 11 | 2 | 18.18 |
| [21]      | Proteus | 7 | 2 | 28.57 | 7 | 1 | 14.29 | 7 | 3 | 42.86 | 7 | 2 | 28.57 | 7 | 2 | 28.57 | 7 | 1 | 14.29 | 7 | 0 | 0.00 | 7 | 2 | 28.57 | 7 | 0 | 0.00 | 7 | 0 | 0.00 |
| [21]      | Enterobacter | 2 | 1 | 50.00 | 2 | 0 | 0.00 | 2 | 2 | 100.00 | 2 | 0 | 0.00 | 2 | 0 | 0.00 | 2 | 0 | 0.00 | 2 | 0 | 0.00 | 2 | 0 | 0.00 | 2 | 0 | 0.00 |

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may not arrive at health institutions and widespread use or misuse of antimicrobial drugs in the community may accelerate the occurrence of antimicrobial resistance [64,65].

Sub-grouping of the prevalence of GNEBPs based on the studies conducted in different regions of the country showed that the pooled prevalence was high in Addis Ababa (20.08%). In line with this, a spatial variation across the regions of Ethiopia was reported by Bogale et al. [66]. The difference based on the study period was not significant. However, a declining pattern of diarrhoea at the national level was reported by Bogale et al. [66]. Published articles were from 8 regions of Ethiopia, published articles were not found in Afar, Somali and Benishangul Gumuz regions of the country in this study. Hence, the pooled prevalence was calculated from 8 regions ignoring others. However, the scenario may not be equivalent to the region of the country having no reports.

Grouping of study participants based on their age showed that the pooled prevalence was the highest (20.35%) in children having age below or equal to 15 years which indicated that children are more exposed to the GNEBPs and express severe syndromes to visit health facilities. In line with this, Kotloff [4] and Havelaar et al. [67] reported that children contribute a huge proportion of diarrheal diseases in the world.

Diarrheagenic E. coli, Shigella spp., S. enterica and Campylobacter spp. were the most common isolates among GNEBPs. In line with this, Getie et al. [62] reported that Shigella spp. enterohemorrhagic E. coli (EHEC) and S. enterica were important isolates of GNEBPs among food handlers. In this study, the pooled estimate of E. coli was the highest (19.79%) among enteric bacterial pathogens. The result is very close to the report of Zenebe et al. [68] who reported that the pooled prevalence of E. coli was 25% in Ethiopia. A 33.8% pooled prevalence was reported by Oppong et al. [69] in Sub-Sharan Africa. Oppong et al. [69] also found that E. coli detection was the highest in the East African region and lowest in the middle part of Africa. The difference may be due to the number of studies in the summary and the targeted strain of E. coli. For example, in a single study in Niger, 11.1% of diarrhoeic children were positive for diarrheagenic E. coli [70]. Similarly, the Global enteric multicentre study on infants and children showed that diarrheagenic E. coli was among the four major pathogens responsible for diarrhoea in low-income and middle-income countries [71].

The pooled prevalence of Campylobacter spp. in this analysis was 10.76%. In line with this report, Kassie et al. [72] reported a prevalence of 10.5% among children in Denbia district, Ethiopia and 13.8% prevalence was also reported by Gedlu and Aseffa [73] among children in northwest Ethiopia. Oppong et al. [69] reported a 12.3% pooled prevalence of Campylobacter

| Type bacterial isolate | No of studies | The total no of isolates tested | No of multidrug-resistant isolates | Multidrug-resistant isolate (%) | Pooled prevalence (%) (95% CI) | I² (p-value) |
|------------------------|--------------|--------------------------------|-----------------------------------|-------------------------------|--------------------------------|-------------|
| Shigella spp.           | 24           | 443                            | 363                               | 81.94                         | 79.08 (72.19–85.97)           | 68.2 (0.00) |
| Salmonella enterica     | 23           | 496                            | 317                               | 63.91                         | 59.46 (46.13–72.79)           | 91.1 (0.00) |
| Escherichia coli        | 6            | 410                            | 332                               | 80.98                         | 78.20 (67.46–88.93)           | 84.7 (0.00) |
| Campylobacter spp.      | 4            | 110                            | 87                                | 79.09                         | 80.78 (65.04–96.52)           | 94.6 (0.00) |
| Klebsiella spp.         | 1            | 11                             | 5                                 | 45.45                         | -                              | -           |

No = number, % = percent; CI = confidence interval, I = Inconsistency Index.

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in East Africa. A high rate of Campylobacter infection among children was also reported in Kenya [63]. In contrary to the report of this study, Fletcher et al. [74] reported a pooled prevalence of 2.7% in Sub-Saharan countries. The difference may be related to the area coverage, disease prevention and control practices.

The pooled prevalence of Shigella spp. in this study was 6.24% which is equivalent to the report of Hussen et al. [75]. According to their report, the pooled prevalence of Shigella spp. in Ethiopia was 6.6%. Similarly, Oppong et al. [69] reported a pooled prevalence of 5.6% from children under five and Fletcher et al. [74] 4.3% of children aged less than 12 years in Sub-Saharan countries.

The pooled prevalence of S. enterica was 5.06% which is almost comparable with the reported pooled prevalence by Abate and Assefa [76], which was 4.8% among human stools and animal origin foods in Ethiopia.

Resistance to antimicrobial agents is a natural evolutionary process for the bacteria, however, the process is accelerated by human activities in terms of antimicrobial usage patterns and infection control or prevention practices. The risks are very high in developing countries like Ethiopia where there is a widespread use or misuse of antimicrobial agents with a high burden of infectious diseases [76–79].

In this meta-analysis, Shigella isolates were more resistant to the penicillin group of antimicrobial agents like ampicillin (85.01%) and amoxicillin (82.07%). A high percentage of resistance against ampicillin (83.1%) and amoxicillin (84.1%) were also reported by Hussen et al. [75]. There were also reports of drug resistance among the first-line drugs like ciprofloxacin (11.86%) and ceftriaxone (29.53%) for the treatment of Shigellosis. Resistance development against such types of antimicrobial agents was also reported by Hussen et al. [75]. They reported 8.9 and 9.3% resistance against ciprofloxacin and ceftriaxone, respectively.

In this analysis, high proportions of Salmonella isolates were also resistant against the penicillin group of antimicrobial agents like ampicillin (64.98%) and amoxicillin (82.89%). In line with this Tadesse [80] was also reported a high percentage (86.01%) of resistance of Salmonella against ampicillin and/or amoxicillin. Resistance of Salmonella isolates to fluoroquinolone like ciprofloxacin (2.27%) and third-generation cephalosporin (ceftriaxone 16.68%) were also reported. Similarly, according to Tadesse’s report, the pooled prevalence of ciprofloxacin resistance among Salmonella isolates was 3.61% [80] and a prevalence of 2.9% of resistance against ciprofloxacin was also reported in Iran [81].

Resistance was common among E. coli isolates in this analysis, particularly on antimicrobial agents like ampicillin (77.97%), tetracycline (76.87%) and trimethoprim-sulphamethoxazole (66.97%). Resistance of E. coli against a wide array of antimicrobials was also reported by Pormohammad et al. [82], Zenebe et al. [68] and Tuem et al. [83]. Resistance in non-pathogenic strains of E. coli may not have a direct effect on health, however, non-pathogenic resistant strains may acquire virulence genes and induce disease that may not be treated easily or non-pathogenic strains having resistant character may act as a reserve for the resistant character for other bacteria [82].

Among Campylobacter isolates in this analysis, the highest percentage of resistance was reported on antimicrobial agents like cephalothin (81.52%), ampicillin (65.61%) and trimethoprim-sulphamethoxazole (52.60%). A resistance pattern of 92.3–100% to erythromycin and the β—lactams, 61.5–86.7% to trimethoprim-sulfamethoxazole, 92.3–93.3% to tetracycline, 46.2–80% to chloramphenicol, 0–60% to aminoglycosides and 0% to imipenem were reported among Campylobacter spp. in Ghana [84].

In this study, among 1470 bacterial isolates 1104 (75.52%) with a pooled prevalence of 70.56%, were resistant to three or more antimicrobial agents (multidrug resistance) (MDR). In line with this finding, Alemayehu [85] reported that the pooled prevalence of multidrug resistance was
70.5% among bacterial isolates in Ethiopia. Another, meta-analysis study on multidrug resistance by Abayneh et al. [86] reported the pooled prevalence of 80.5% among Gram-negative bacteria. It was also very close to the reports from India (66.12%) [87] and Egypt (65.5%) [88,89]. In contrast to our finding in Ethiopia, a lower prevalence of MDR has been reported from Germany (60%) [90], Nepal (42.6%) [91], Australia (36%) [92], Indonesia (28.7%) [93], the USA (27%) [94], Spain (34.5%) [95] and France (11.6%) [96]. Several factors may play a role in the difference including the magnitude and style of antimicrobial use and infection prevention practices.

The MDR report among Campylobacter isolates in this analysis (80.78%) was higher than the report from Bangladesh (28.8%) [97] and Kenya 50% [98] but lower than the report from Ghana (97%) [84]. This may be due to differences in the use of antimicrobial agents, the area coverage, sample type and technique of detections. The MDR report of E. coli in this analysis (78.20) was not in line with other reports like 50% prevalence in Nigeria [99], 40% in Spain [95], 22% among human isolates in the world [82], 26% in China [100], 39.8% in Egypt isolates from animals [101], 28% in low and middle-income countries [102]. The MDR report of this meta-analysis among Shigella isolates (79.08) was almost similar to the report by Hussen et al. [75] (83.2%) but it was lower than other reports from Iran (89.4%) [103], and Bangladesh (94%) [104]. However, it was higher than other reports such as 53.8% among migrants in Europe [74], 60% in Kenya [98] and 19% in Somalia [105]. Factors like the magnitude and style of antimicrobial use and infection prevention practices may play roles in the differences.

The development of MDR character among S. enterica is also an important public health concern around the globe [106]. In this analysis, the prevalence of MDR character among Salmonella isolate was 59.46% which is comparable with the MDR report of Garedew et al. [107] (46.2%) among food handlers in Gondar. However, it was lower than the report from Dagnew et al. [108] (76%) and Admassu et al. [109] (100%). The difference may be due to the target population and study methods (single versus pooled meta-analysis reports).

Limitations of the study

Some of the studies included in the analysis were targeting the most common bacterial pathogens that did not rule out the absence of others. Therefore, for bacteria that are thought to be less frequent, the reported prevalence may not accurate. Publication bias and heterogenicity were observed in the analysis, but attempts were made to reduce their impact on the analysis by following the random effect model and subgrouping. However, these may not totally avoid their impact on the interpretation of the pooled results.

Conclusion

According to this analysis, the burden of Gram-negative enteric bacterial pathogens (GNEBPs) was high and may be considered a major cause of diarrhoea in Ethiopia. A significant proportion of the isolates exhibited resistance to the commonly used antibacterial agents which are expected to affect the treatment response and cost, morbidity and progression of the infection. Shigella spp., S. enterica, E. coli and Campylobacter spp. were the commonly isolated GNEBP from diarrheic patients in the country. The pooled estimate of Campylobacter spp. was the highest followed by E. coli, Shigella spp. and S. enterica. Resistance to antimicrobial agents was most common among the penicillin groups, followed by tetracycline, and trimethoprim-sulfamethoxazole. However, there were also resistant strains against very relevant drugs for the treatment of GNEBP such as fluoroquinolones and third-generation cephalosporins. Almost all isolates were susceptible to meropenem.

Since the incidences of these bacterial diseases are related to hygiene, all activities that enhance hygienic practices (clean water and food, handwashing, proper use of latrine) must be
advocated and implemented. Performing drug sensitivity tests for suspected diarrheagenic bacteria is extremely advantageous to select the appropriate antimicrobial drugs for the treatment. The antimicrobial resistance surveillance system must be established to understand the trend of resistance among pathogenic bacteria and to plan and implement mitigating strategies like proper control and prevention of infectious diseases and antimicrobial stewardship programs. Almost all studies were using conventional techniques for confirmation of the isolates, thus, adding molecular methods in the future will increase analysis precision.

**Supporting information**

S1 File. Forest plot of pooled prevalence estimates of Gram-negative enteric bacterial pathogens in different regions of Ethiopia.

(SDOCX)

S2 File. Forest plot of pooled prevalence estimates of Gram-negative enteric bacterial pathogens subgrouping based on the study period.

(SDOCX)

S3 File. Forest plot of pooled prevalence estimates of Gram-negative enteric bacterial pathogens subgrouping-based age of the study subjects.

(SDOCX)

S4 File. Frost plot of the studies on *Shigella* species.

(SDOCX)

S5 File. Frost plot of the studies on *Salmonella enterica*.

(SDOCX)

S6 File. Frost plot of the studies on *Escherichia coli* strains.

(SDOCX)

S7 File. Frost plot of the studies on *Campylobacter* species.

(SDOCX)

S8 File. Frost plot of the studies on multidrug resistance.

(SDOCX)

S9 File. Frost plot of the studies on multidrug resistance of *Shigella* species.

(SDOCX)

S10 File. Frost plot of the studies on multidrug resistance of *Salmonella enterica*.

(SDOCX)

S11 File. Frost plot of the studies on multidrug resistance of *E. coli*.

(SDOCX)

S12 File. Frost plot of the studies on multidrug resistance of *Campylobacter* species.

(SDOCX)

S13 File. Frost plot of the studies on the prevalence of *Escherichia coli* in children less than or equal to 15 years of age.

(SDOCX)

S14 File. Frost plot of the studies on the prevalence of *Escherichia coli* in children less than or equal to 15 years of age.

(SDOCX)
S15 File. Frost plot of the studies on the prevalence of *Shigella* spp in children less than or equal to 15 years of age. (DOCX)

S16 File. Frost plot of the studies on the prevalence of *Salmonella enterica* in all age groups. (DOCX)

S17 File. Frost plot of the studies on the prevalence of *Shigella* species in all age groups. (DOCX)

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**References**

1. Caramia G, Silvi S, Verdenelli MC, Magdalena M. Treatment of acute diarrhoea: past and now. Int J Enteric Pathog. 2015; 3: e28612. https://doi.org/10.17795/ijep28612

2. WHO. WHO estimates of the global burden of foodborne diseases: foodborne disease burden epidemiology reference group 2007–2015, 2015. Available from: https://apps.who.int/iris/bitstream/handle/10665/199350/9789241565165_eng.pdf?sequence=477&isAllowed=y.

3. Girmay AM, Gari SR, Alemu BM, Martin R. Diarrheal disease and associated behavioural factors among food handlers in Addis Ababa, Ethiopia. AIMS Public Heal., 2020: 7:100–113. https://doi.org/10.3934/publichealth.2020010 PMID: 32258193

4. Kotloff KL. The burden and etiology of diarrheal illness in developing countries. Pediatr. Clin North Am. 2017; 64:799–814. https://doi.org/10.1016/j.pclin.2017.03.006 PMID: 28734511

5. Troeger C, Blacker BF, Khullar IA, Rao PC, Cao S, Zimsen SR, et al. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of diarrhoea in 195 countries: A systematic analysis for the global burden of disease study 2016. Lancet Infect Dis. 2018; 18:1211–1228. https://doi.org/10.1016/S1473-3099(18)30362-1 PMID: 30243583

6. Alebel A, Tesema C, Temesgen B, Gebrie A, Petrucka P, Kibret GD. Prevalence and determinants of diarrhoea among under-five children in ethiopia: A systematic review and meta-analysis. PLoS ONE. 2018: 13:e0199684. https://doi.org/10.1371/journal.pone.0199684 PMID: 29953555

7. Ugboko HU, Nwinyi OC, Oranusi SU, Oyewale JO. Childhood diarrhoeal diseases in developing countries. Heliyon, 2020; 6:e03690. https://doi.org/10.1016/j.heliyon.2020.e03690 PMID: 32322707

8. Brooks GF, Morse SA, Carroll KC, Mietzner TA, Butel JS, Jawetz, Melnick, & Adelberg’s Medical Microbiology. 26th ed. MC Graw Hill Medical, New York. 2013.
10. Jassovsky D, Littmann J, Zorzet A, Cars O. Antimicrobial resistance: A threat to the world's sustainable development. Ups J Med Sci. 2016; 121:159–164. https://doi.org/10.1080/03009734.2016.1195900

11. UN. United Nations general assembly. Draft resolution submitted by the president of the general assembly political declaration of the high-level meeting of the general assembly on antimicrobial resistance, Seventy-first session agenda item 127 Global health. 2016.

12. O’Neill J. Antimicrobial resistance: Tackling a crisis for the health and wealth of nations. 2014. https://www.gov.uk/government/publications/antimicrobial-resistance-tackling-a-crisis-for-the-health-and-wealth-of-nations

13. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffman TC, Mulrow CD, et al. The PRISMA 2020 Statement: An updated guideline for reporting systematic reviews. Syst Rev. 2021; 10:89. https://doi.org/10.1186/s13643-021-01626-4 PMID: 33781348

14. Haidich A. Meta-analysis in medical research. Hippokratia. 2010; 14:29–37. PMID: 21487488

15. Teferi SC. Prevalence and antimicrobial resistance patterns of Shigella in Ethiopia from 2000 to 2018: A critical review. Chem Biomol Eng. 2020; 5:51–56.

16. Page MJ, McKenzie JE, Bossuyt PM, Bouton I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 Statement: An updated guideline for reporting systematic reviews. Syst Rev. 2021; 10:89. https://doi.org/10.1186/s13643-021-01626-4 PMID: 33781348

17. JBI. The Joanna Briggs Institute critical appraisal tools for use in JBI systematic reviews; Checklist for systematic reviews and research syntheses. 2017. Available from: https://jbi.global/sites/default/files/2019-05/JBI-Critical-Appraisal-checklist-for-Systematic-Reviews2017-0.pdf

18. Rücker G, Schwarzer G, Carpenter JR, Schumacher M. Undue reliance on I² in assessing heterogeneity may mislead. BMC Med Res Methodol. 2008; 9:79. http://www.biomedcentral.com/1471-2288/8/79.

19. Gebresilasie YM, Tullu KD, Yeshanew AG. Resistance pattern and maternal knowledge, attitude and practices of suspected diarrheagenic Escherichia coli among children under 5 years of age in Addis Ababa, Ethiopia: A cross-sectional study. Antimicrob resist infect control. 2018; 7:110. https://doi.org/10.1186/s13756-018-0402-5 PMID: 30214719

20. Abera K, Anticho T L, Ali MM. Salmonella and Shigella and antimicrobial susceptibility profiles among adult patients with complaints of diarrhea at Hawassa comprehensive specialized. SAGE Open Med. 2021; 9:1–6. https://doi.org/10.1177/20503121211000911 PMID: 33786180

21. Zenebe T, Gebreyyes D, Tesema A, Craddock H, Gishen N. Entero pathogens in under-five children with diarrhea in health facilities of Debre Berhan Town, North Shoa, Ethiopia. Ethiop J Heal Sci. 2019; 29:203. http://dx.doi.org/10.4314/ejhs.v29i2.7, 2019.

22. Belay A, Ashagrie M, Seyoum B, Alemu M, Tsegaye A. Prevalence of entero pathogens, intestinal parasites and resistance profile of bacterial isolates among HIV infected and non-infected diarrheic patients in Dessie Town, Northeast. PLoS One, 2020; 15: e0243479. https://doi.org/10.1371/journal.pone.0243479 PMID: 33320909

23. Tosisa W, Mihret A, Ararsa A, Eguale T, Abebe T. Prevalence and antimicrobial susceptibility of Salmonella and Shigella species isolated from diarrheic children in Ambo town. BMC Pediatr. 2020; 20:91. https://doi.org/10.1186/s12887-020-1970-0 PMID: 32103729

24. Abebe W, Earsido A, Taye S, Assefa M, Eyasu A, Godebo G. Prevalence and antibiotic susceptibility patterns of Shigella and Salmonella species among children aged below five years with diarrhea attending Nigist Eleni Mohammed memorial hospital, South Ethiopia. BMC Pediatr. 2018; 18:241. https://doi.org/10.1186/s12887-018-1221-9 PMID: 30045699

25. Belew GD, Kibret M, Biadglegne F, Abera B. Prevalence and antimicrobial susceptibility patterns of Shigella species at Felege Hiwot Referral Hospital, Northwest Ethiopia. Ethiop Med J. 2011; 49:3.

26. Demissie TA, Wubie MT, Yehuala FM, Fetene DM, Gudeta GA. Prevalence and Antimicrobial susceptibility patterns of Shigella and Salmonella species among patients with diarrhea attending Gondar town health institutions, Northwest Ethiopia. Sci J Public Health. 2014; 2:469–475.

27. Feleke H, Medhin G, Abebe A, Birhan HK, Asrat D. Enteric Pathogens and associated risk factors among under-five children with and without diarrhea in Wegera district, northwestern Ethiopia. Pan Afr Med J. 2018; 29:72. https://doi.org/10.11604/pamj.2018.29.72.13973 PMID: 29675953

28. Beyene G, Tasew H. Prevalence of intestinal parasite, Shigella and Salmonella species among diarrheal children in Jimma health center, Jimma southwest Ethiopia: A Cross Sectional Study. Ann Clin Microbiol Antimicrob. 2014; 13:1–7. https://doi.org/10.1186/1476-0711-13-1 PMID: 24383440
29. Kefyalew S, Kebede G, Keneni A. Prevalence of *Shigella* related diarrhea in Ambo town and antibiotic susceptibility of the isolated strains. Greener J Epidemiol Public Heal. 2015; 3:001–006. http://doi.org/10.15580/GJEPH.2015.1.

30. Ayele AA, Tadesse D, Manilal A, Yohanes T, Seid M, Mekuria MS. Prevalence of enteric bacteria and enteroparasites in human immunodeficiency virus-infected individuals with diarrhea attending antiretroviral treatment clinic, Arba Minch General Hospital, Southern. New Microbes New Infect. 2020; 38:100789. https://doi.org/10.1016/j.nmni.2020.100789 PMID: 33224508

31. Ayenew Z, Biazin H, Gebre-selassie S, Yeshtilla B. Enteric pathogens and antimicrobial susceptibility profile among pediatric patients with diarrhea in Addis Ababa, Ethiopia. Ethiop Med J. 2019; 57–65.

32. Fentaw S, Getahun M, Hussein M, Mamuye Y, Abebe A. Microbial aetiology of gastro-enteritis, antimicrobial susceptibility patterns of *Salmonella* spp. from under-five children with acute diarrhea in Bahir Dar town. Ethiop J Sci Technol. 2015; 8:27–35.

33. Getamesa M, Getenet B, Ahmed Z. Prevalence of *Salmonella* and *Salmonella* spp. from under-five children with acute diarrhea in Bahir Dar. BMC Infect Dis. 2018; 2018:1–6. https://doi.org/10.1186/s12879-019-0079-7.

34. Mekonnen H, Kebede A, Menkir S. Isolation rate and drug resistance patterns of *Shigella* species among diarrheal patients attending at Hiwot Fana Hospital, Harar, Ethiopia. Ethiop J Sci Technol. 2014; 7:15–25.

35. Getamesay M, Getenet B, Ahmed Z. Prevalence of *Salmonella* and *Campylobacter* species and their susceptibility patters among under five children with diarrhea. Ethiop J Health Sci. 2014; 24:101–108. https://doi.org/10.4314/ehjs.v24i2.1 PMID: 24795510

36. Yemane G, Mulaw G, Gaim T. Prevalence and antimicrobial susceptibility of *Salmonella* species in diarrheal children under five-years in Bahir Dar. Int J Integr Sci Innov Technol. 2014; 3:2278–1145.

37. Teshome B, Teklemariam Z, Ayana DA, Marami D, Asaminew N. *Salmonella* and *Shigella* among patients with diarrhea at public health facilities in Adama, Ethiopia: Prevalence, antimicrobial susceptibility pattern, and associated factors. SAGE Open Med. 2019; 7:1–8.

38. Teferi SC. Prevalence, Antibiotic Susceptibility Profile, and associated risk factors of *Salmonella* isolate among diarrheal patients visiting Dessie referral hospital, Northeast Ethiopia. Int J Microbiol., 2020; 2020:8834107. https://doi.org/10.1155/2020/8834107 PMID: 33144860

39. Adugna A, Kibret M, Abera B, Nibret E, Adal M. Prevalence and antibiogram of *Shigella* and *Salmonella* spp. from under-five children with acute diarrhea in Bahir Dar town. BMC Pediatrics. 2013; 13: 82. https://doi.org/10.1186/1471-2431-13-82 PMID: 23694714

40. Mekonnen K, Mengistie B, Sahilu G, Kloos H, Mulat W. Etiologies of diarrhea and drug susceptibility patterns of bacteria isolates among under-five year children in refugee camps in Gambella Region, Ethiopia: A case control study. BMC Infect Dis. 2019; 19:1008. https://doi.org/10.1186/s12879-019-4699-6 PMID: 31779589

41. Gebrekidan A, Dejene TA, Kahsay G, Wasihun AG. Prevalence and antimicrobial susceptibility patterns of *Shigella* among acute diarrheal outpatients in Mekele hospital. BMC Res Notes. 2015; 8: 611. https://doi.org/10.1186/s13104-015-1606-x PMID: 26508303

42. Mengistu G, Mulugeta G, Lema T, Asella A. Microbial and biochemical technology prevalence and antimicrobial susceptibility patterns of *Salmonella* serovars and *Shigella* species. Microb Biochem Technol. 2014; S2. http://dx.doi.org/10.4172/1948-5948.S2-006.
48. Reda AA, Seyoum B, Yimam J, Andualem G, Fiseha S, Vandeweerd JM. Antibiotic susceptibility patterns of *Salmonella* and *Shigella* isolates in Harar, Eastern Ethiopia. J Infect Dis Immun. 2011; 3:134–139.

49. Assefa A, Girma M. Prevalence and antimicrobial susceptibility patterns of *Salmonella* and *Shigella* isolates among children aged below five years with diarrhea attending Robe general hospital and Goba referral hospital, South East. Trop Dis Travel Med Vaccines. 2019; 5:19. https://doi.org/10.1186/s40794-019-0096-6 PMID: 31832223

50. Gebremichael G, Gebregeziabher G, Asrat D, Amanuel YW, Hagos T. Isolation and antimicrobial susceptibility profile of *Shigella* and *Salmonella* species from children with acute diarrhoea in Mekelle hospital and Semen health center, Ethiopia. Ethiop J Sci. 2018; 28: 197. http://dx.doi.org/10.4314/ejhs.v28i2.11, 2018.

51. Huruy K, Kassu A, Mulu A, Worku N, Fetene T, Gebretsadik S, et al. Intestinal parasitosis and shigellosis among diarrheal patients in Gonder teaching hospital, northwest Ethiopia. BMC Res Notes. 2011; 4:472. http://www.biomedcentral.com/1756-0500/4/472. https://doi.org/10.1186/1756-0500-4-472 PMID: 22041102

52. Hayamo M, Alemayehu T, Tadesse B, Mitiku E, Bedawi Z. Magnitude, risk factors and antimicrobial susceptibility pattern of *Shigella* and *Salmonella* among children with diarrhea in southern Ethiopia: A cross-sectional study. SAGE Open Med., 2021; 9:1–10. 2021. https://doi.org/10.1177/20503121211099729 PMID: 33948178

53. Eguale T, Gebreyes WA, Asrat D, Alemayehu H, Gunn JS, Engidawork E. Non-typhoidal *Salmonella* serotypes, antimicrobial resistance and co-infection with parasites among patients with diarrhea and other gastrointestinal complaints in Addis Ababa, Ethiopia. BMC Infect Dis. 2015; 15:497. https://doi.org/10.1186/s12879-015-1235-y PMID: 26537951

54. Abara B, Hailu T, Beza L. Aetiology of acute diarrhoea and antimicrobial usage among children aged under five years at health centres in Bahir Dar, Ethiopia. Trop Doct. 2020; 10:1–4. https://doi.org/10.1177/004707592012558 PMID: 32223540

55. Lamboro T, Ketema T, Bacha K. Prevalence and antimicrobial resistance in *Salmonella* and *Shigella* species isolated from outpatients, Jimma University specialized hospital, southwest Ethiopia. Can J Infect Dis Med Microbiol. 2016. http://dx.doi.org/10.1155/2016/4210760.

56. Mamuye Y, Metaferia G, Birhanu A, Desta K, Fantawe S. Isolation and antibiotic susceptibility patterns of *Shigella* and *Salmonella* among under 5 children with acute diarrhoea: A cross-sectional study. SAGE Open Med., 2021: 6:1. 2021. https://doi.org/10.1177/20503121211099729 PMID: 33948178

57. Kebede A, Aragie S, Shimelis T. The common enteric bacterial pathogens and their antimicrobial susceptibility pattern among HIV-infected individuals attending the antiretroviral therapy clinic of Hawassa University Hospital, Southern Ethiopia. Antimicrob. Resist. Infect. Control. 2017; 6: 128. https://doi.org/10.1186/s13756-017-0288-7 PMID: 29299302

58. Mekonnen M, Geda B, Teklemariam Z, Weldgegebreal F, Balakrishnan S. Prevalence of childhood diarrhoea and associated risk factors in Dire Dawa, Eastern Ethiopia. J Public Heal From Theory to Pract. 2018; 26:29–37.

59. Kebede R, Alemayehu H, Medhin G, Belay T. Prevalence of *Escherichia coli*, *Salmonella* and *Shigella* from children with acute diarrhoea in Mekelle hospital and Semen health center, Ethiopia. J of Public Health From Theory to Pract. 2018; 26:29–37.

60. Admasu DA, Kebede A, Menkir S. Prevalence of antibiotic resistant *Salmonella* isolates, *Enterobacteria histolytica* and *Giardia lamblia* in Harar, Eastern Ethiopia. African J Microbiol Res. 8:2044–2053.

61. Walker CL, Oduro L, Dziffo K, Debrah AY, Aziz QA, Nyarko S, et al. Intestinal parasitoses in children aged below five years at health centres in Bahir Dar, Ethiopia. Trop Doct. 2020; l0:1–4. https://doi.org/10.1186/s13756-016-0004-y PMID: 27398060

62. Shah M, Kathiikoo C, Wada A, Odoyo E, Prata MG, Lima FN, et al. Etiology and severity of diarrheal diseases in infants at the semi-arid region of Brazil: A case- control study. PLoS Neglected Trop Dis. 2019; 13:e0007154. https://doi.org/10.1371/journal.pntd.0007154 PMID: 30735493

63. Giacomini E, Perrone V, Alessandrini Paoli DD, Luca CN, Esposti D. Evidence of antibiotic resistance from population-based studies: A Narrative Review. Infect Drug Resist. 2021; 14: 849–858. https://doi.org/10.2147/IDR.S289741 PMID: 33688220
66. Bogale GG, Gelaye KA, Degef DT, Gelaw YA. Spatial patterns of childhood diarrhea in Ethiopia: data from Ethiopian demographic and health surveys (2000, 2005 and 2011). BMC Infect Dis. 2017; 17:426. https://doi.org/10.1186/s12879-017-2504-8 PMID: 28619051

67. Havelaar AH, Kirk MD, Torgerson PR, Gibb HJ, Hald T, Lake RJ, et al. World Health Organization global estimates and regional comparisons of the burden of foodborne disease in 2010. PLoS Med, 2015; 12:e1001923. https://doi.org/10.1371/journal.pmed.1001923 PMID: 26633896

68. Zenebe T, Mitiku M, Alem Y. Prevalence of *Escherichia coli* in under-five children with diarrhea in Ethiopia: a systematic review and meta-analysis. Int J Microbiol. 2020; 2020:1–7. https://doi.org/10.1155/2020/8844294 PMID: 32963539

69. Oppong B, Yang H, Amponsem-Boateng C, Kyere EK, Abdulai T, Duan G, Opolot G. Enteric pathogens associated with gastroenteritis among children under 5 years in Sub-Saharan Africa: A systematic review and met-analysis. Epidemiol Infect. 2020; 148:1–9.

70. Langendorf C, Le Hello S, Moumouni A, Gouali M. Enteric Bacterial pathogens in children with diarrhea in Niger: diversity and antimicrobial resistance. PLoS One, 2015; 10:e0120275. https://doi.org/10.1371/journal.pone.0120275 PMID: 25799400

71. Kotloff KL, Nasrin D, Blackwelder WC, Wu Y, Farag T, Panchalingham S, et al. The incidence, aetiology, and adverse clinical consequences of less severe diarrhoeal episodes among infants and children residing in low-income and middle-income countries: a 12-month case-control study as a follow-on to the global enteric multicenter study. Lancet Glob Heal. 2019; 7:e658–e684.

72. Kassie GM, Kassu A, Bayih AG. *Campylobacter enteritis* among children in Dembia District, Northwest-East Afr Med J. 2000; 77:654–657.

73. Gedlu E. *Campylobacter enteritis* among children in north-west ethiopia a one-year prospective study. Ann Trop Paediatr. 1996; 16:207–212. https://doi.org/10.1080/02724936.1996.11747828

74. Fletcher SM, McLaws M, Ellis JT. Prevalence of gastrointestinal pathogens in developed and developing countries: Systematic review and meta-analysis. J Public Health Sci. 2013; 2:e9. https://doi.org/10.4081/jphsr.2013.e9 PMID: 25170480

75. Hussien S, Mulatu G, Kassa ZY. Prevalence of *Salmonella* species and its drug resistance pattern in ethiopia: a systematic review and meta-analysis. Ann Clin Microbiol Antimicrob. 2019; 1:22. https://doi.org/10.1186/s12941-019-0321–1.

76. Abate D, Assefa N. Prevalence and antimicrobial resistance patterns of *salmonella* isolates in human stools and animal origin foods in Ethiopia: A Systematic review and meta-analysis. Int J Health Sci. 2021; 13: 43–55. PMID: 33456442

77. Misganaw D, Abtew K. Evaluation of antibiotic utilization pattern during acute diarrheal disease at chefa-robii health. Drug Healthc Patient Saf, 2020; 12:169–175. https://doi.org/10.2147/DHPS.S256330 PMID: 33061654

78. Moges F, Endris M, Mulu A, Tessema B, Belyhun Y, Shiferaw Y, et al. The growing challenges of antibiotic use and resistance pattern in Ethiopia. J Glob Antimicrob Resist. 2014; 2: 148–154. https://doi.org/10.1016/j.jgar.2014.02.004 PMID: 27873721

79. Muhie OA. Antibiotic use and resistance pattern in Ethiopia: Systematic review and meta-analysis. Int J Microbiol. 2019; 2019:2489063. https://doi.org/10.1155/2019/2489063 PMID: 31467550

80. Tadesse G. A meta-analysis of the proportion of antimicrobial resistant human *Salmonella* isolates in Ethiopia. BMC Pharmacol Toxicol. 2014; 15:51. http://www.biomedcentral.com/2050-6511/15/51. https://doi.org/10.1186/2050-6511-15-51 PMID: 25213011

81. Khademi F, Vaez H, Ghanbari F, Arzaniou M, Sahebkar A. Prevalence of fluoroquinolone-resistant *Salmonella* serotypes in Iran: A meta-analysis. Pathog Glob Health. 2020; 114:16–29. https://doi.org/10.1080/20477724.2020.1719701 PMID: 32013798

82. Pormohammad A, Nasiri MJ, Azimi T. Prevalence of antibiotic resistance in *Escherichia coli* strains simultaneously isolated from humans, animals, food, and the environment: A systematic review and meta-analysis. Infect Drug Resist. 2019; 12:1181–1197. https://doi.org/10.2147/IDR.S201324 PMID: 31190907

83. Tuem KB, Gebre AK, Atey TM, Bitew H, Yimer EM, Berhe DF. Drug resistance patterns of *Escherichia coli* in Ethiopia: A meta-analysis. Biomed Res Int. 2018; 2018:4536905. https://doi.org/10.1155/2018/4536905 PMID: 29854757

84. Karikari AB, Obiri-danso K, Frimpong EH, Krogfelt KA. Antibiotic resistance in *Campylobacter* isolated from patients with gastroenteritis in a teaching hospital in Ghana. Open J Med Microbiol. 2017; 7:1–11.

85. Alemayehu T. Prevalence of multidrug-resistant bacteria in Ethiopia: A systematic review and meta-analysis. J Glob Antimicrob Resist. 2021; 26:133–139. https://doi.org/10.1016/j.jgar.2021.05.017 PMID: 34129993
86. Abayneh M, Hailemariam S, Asnake M. Bacterial profile and multi-drug resistance pattern of bacterial isolates among septicemia suspected cases: A meta-analysis report in Ethiopia. J Lab Med. 2021; 45:167–178.

87. Pattnaik D, Panda SS, Singh N, Sahoo S, Mohapatra I, Jena J. Multidrug resistant, extensively drug resistant and pan drug resistant gram negative bacteria at a tertiary care centre in Bhubaneswar. Int J Community Med Public Heal. 6: 567–572.

88. Elsalam MA, Garmal D, El Said M, Salen D, Atta AA, El Gamal MS. Prevalence of plasmid-mediated quinolone resistance in multidrug-resistant gram negative bacilli in Egypt. Biomed Pharmacol J. 2018; 11:1927–1936.

89. Melake NA, Eissa NA, Keshk TF, Sleem AS. Prevalence of multidrug-resistant bacteria isolated from diarrhoeic children at Kapsabet County referral hospital, Kenya. BMC Infect Dis. 2021. 21: 109. https://doi.org/10.1186/s12879-021-05788-3 PMID: 33485326

90. Awasthi TR, Pant ND, Dahal PR, Prevalence of Multidrug resistant bacteria in causing community acquired urinary tract infection among the patients attending outpatient department of Seti zonal hospital, Dhangadi, Nepal. Nepal J Biotechnol. 2015; 3:55–59.

91. Lim CJ, Cheng AC, Kenna J, Spelman D, Hale D, Mcilican G et al. Prevalence of multidrug-resistant organisms and risk factors for carriage in long-term care facilities: a nested case–control study. J Antimicrob Chemother. 2014; 69:1972–1980. https://doi.org/10.1093/jac/dku077 PMID: 24710025

92. Adrizain R., Suryaningrat F, Alam A, Setiabudi D. Drug-resistant bacteria in children hospitalized at Dr. Hasan Sadikin general bandung hospital Indonesia. IOP Conf Ser Earth Environ Sci. 2018; 125: 012077. https://doi.org/10.1088/1755-1315/125/1/012077

93. Sainfer A, Smaldone A, Larson E. Prevalence of Multidrug-Resistant Gram-Negative Bacteria Among Nursing Home Residents- A Systematic Review and Meta-Analysis. Am. J. Infect. Control. 2017; 45:512–518. https://doi.org/10.1016/j.ajic.2017.01.022 PMID: 28456321

94. Rivera-Izquierdo M, Benavente-Fernández A, López-Gómez J, Láinez-Ramos-Bossini AJ, Rodríguez-Camacho M, Valero-Ubierna MC, et al. Prevalence of multi-resistant microorganisms and antibiotic stewardship among hospitalized patients living in residential care homes in Spain. Antibiotics, 2020; 9:324. https://doi.org/10.3390/antibiotics9060324 PMID: 32545738

95. Buke C, Armand-Lefèvre L, Laurence G, Isabelle D, Waafa R, et al. Epidemiology of multidrug-resistant bacteria in patients with long hospital stays infection control and hospital epidemiology Cambridge Core. Infect Control Hosp Epidemiol. 2007; 28: 1255–1260. https://doi.org/10.1088/1755–1315/125/1/012077

96. Rahman A, Paul PR, Hoque N, Islam SS, Ziaul Haque AKM, Sikder MH, et al. Prevalence and antimicrobial resistance of Campylobacter species in diarrheal patients in Mymensingh, Bangladesh. Biomed Res Int. 2021; 2021: 9229485. https://doi.org/10.1155/2021/9229485 PMID: 34395627

97. Zachariah OH, Lizzy MA, Rose K, Angela MM. Multiple drug resistance of Escherichia coli isolates in neonatal ward. Front Pediatr. 2021. 9:670470. https://doi.org/10.3389/fped.2021.670470 PMID: 34113589

98. Aworh MK, Adewusi OA, Mba N, Helwigh B, Hendriksen RS. Prevalence and risk factors for faecal carriage of multidrug-resistant Escherichia coli among slaughterhouse workers. Sci Rep. 2021; 11:133362. https://doi.org/10.1038/s41598-021-92819-3 PMID: 34172803

99. Wu D, Ding Y, Yao K, Gao W, Wang Y. Antimicrobial resistance analysis of clinical Escherichia coli isolates in neonatal ward. Front Pediatr. 2021, 9:670470. https://doi.org/10.3389/fped.2021.670470 PMID: 34113589

100. Suárez-Pérez A, Corbera JA, Tejedor-Junco MT, González-Martín M. Multidrug-resistant phenotypes of Escherichia coli isolates. Anim Artic. 2021; 11:1682. https://doi.org/10.3390/an11061692 PMID: 34204084

101. Nkansa-gyamfi NA, Kazibwe J, Nji E. Prevalence of multidrug, extensive drug, and pandrug-resistant commensal Escherichia coli isolated from healthy humans in community settings in low and middle-income countries: a systematic review and meta-analysis. Glob Health Action. 2021; 12:1815272. https://doi.org/10.1080/16549716.2020.1815272 PMID: 32909519

102. Abbasi E, Abtahi H, Van Belkum A. Multidrug-resistant Shigella infection in pediatric patients with diarrhea from central Iran. Infect Drug Resist. 2019; 12:1535–1544. https://doi.org/10.2147/IDR.S203654 PMID: 31239729

103. Ud-din AI, Wahid UH, Latif HA, Shahnaj J, Akter M, Azmi UJ et al. Changing trends in the prevalence of Shigella species: Emergence of multi-drug resistant Shigella sonnei biotype—in Bangladesh. PLoS One, 2013; 8:e82601. https://doi.org/10.1371/journal.pone.0082601 PMID: 24367527
105. Sheikh B, Nor A, Menza NC, Musyoki AM. Multidrug-resistant shigellosis among children aged below five years with diarrhea at Banadir hospital in Mogadishu, Somalia. Can J Infect Dis Med Microbiol. 2021; 2021:6630272. https://doi.org/10.1155/2021/6630272 PMID: 34211618

106. Wang X, Biswas S, Paudyal N, Pan H, Li X. Antibiotic resistance in Salmonella Typhimurium isolates recovered from the food chain through national antimicrobial resistance monitoring system between 1996 and 2016. Front Microbiol. 2019; 10:985. https://doi.org/10.3389/fmicb.2019.00985 PMID: 31134024

107. Garedew L, Wondafrash N, Feleke A. Identification of drug-resistant Salmonella from food handlers at the University of Gondar, Ethiopia. BMC Res Notes. 2014; 7:1–6. https://doi.org/10.1186/1756-0500-7-1 PMID: 24382056

108. Dagnew B, Alemayehu H, Medhin G, Eguale T. Prevalence and antimicrobial susceptibility of Salmonella in poultry farms and in-contact humans in Adama and Modjo Towns, Ethiopia. Microbiologyopen. 2020; 9: e1067. https://doi.org/10.1002/mbo3.1067 PMID: 32510864

109. Admassu D, Egata G, Teklemariam Z. Prevalence and antimicrobial susceptibility pattern of Salmonella enterica serovar Typhi and Salmonella enterica serovar Paratyphi among febrile patients at Karimara Hospital, Jigjiga, Eastern Ethiopia. SAGE Open Med. 2019; 7:1–7. https://doi.org/10.1177/2050312119837854 PMID: 30906553