Review Article

Drug Resistance Patterns of *Escherichia coli* in Ethiopia: A Meta-Analysis

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Background. Antimicrobial drug resistance is a global threat for treatment of infectious diseases and costs life and money and threatens health delivery system’s effectiveness. The resistance of *E. coli* to frequently utilized antimicrobial drugs is becoming a major challenge in Ethiopia. However, there is no inclusive countrywide study. Therefore, this study intended to assess the prevalence of *E. coli* resistance and antimicrobial-specific resistance pattern among *E. coli* clinical isolates in Ethiopia.

Methods. Articles were retrieved from PubMed, Embase, and grey literature from 2007 to 2017. The main outcome measures were overall *E. coli* and drug-specific resistance patterns. A random-effects model was used to determine pooled prevalence with 95% confidence interval (CI), using DerSimonian and Laird method. In addition, subgroup analysis was conducted to improve the outcome. The study bias was assessed by Begg’s funnel plot. This study was registered in PROSPERO as follows: PROSPERO 2017: CRD42017070106. Results. Of 164 articles retrieved, 35 articles were included. A total of 19,235 study samples participated in the studies and 2,635 *E. coli* strains were isolated. Overall, *E. coli* antibacterial resistance was 45.38% (95% confidence interval (CI): 33.50 to 57.27). The resistance pattern ranges from 62.55% in Addis Ababa to 27.51% in Tigray region. The highest resistance of *E. coli* reported was to ampicillin (83.81%) and amoxicillin (75.79%), whereas only 13.55% of *E. coli* isolates showed resistance to nitrofurantoin.

Conclusion. *E. coli* antimicrobial resistance remains high with disparities observed among regions. The bacterium was found to be highly resistant to aminopenicillins. The finding implies the need for effective prevention strategies for the *E. coli* drug resistance and calls for multifaceted approaches with full involvement of all stakeholders.

1. Background

*Escherichia coli* (*E. coli*) is one of the most widespread bacteria throughout the world. Some strains of *E. coli* can cause serious illness for humankind [1] including urinary tract infections [2–4], bloodstream infections [5], skin infection, otitis media [6, 7], and diarrhea [8].

*E. coli* resistance to antimicrobials is creating trouble to the healthcare system worldwide [9, 10]. This complicates treatment outcomes, increases the cost of treatment, and limits the therapeutic options that contribute to the global spectra of a postantimicrobial age in which some of the most effective drugs lose their efficiency [11]. The bacterium is becoming highly resistant to conventionally used antibiotics (to both the newer and older medicines) as evidenced by many previous studies [12–16]. Adaptive resistance was supposed to be the main mechanism for the development of resistance including that to lethal doses of the antimicrobials [17].

Antimicrobial resistance of *E. coli* in developing countries including Ethiopia is reported to be one major reason for failure of treatment of infectious diseases [18]. A number of studies conducted in Ethiopia from various clinical settings show increments in the prevalence of antimicrobial resistance patterns of *E. coli* [6, 19, 20]. However, there is no comprehensive and aggregated nationwide study to show the pattern
of antimicrobial resistance in E. coli. Hence, the purpose of this meta-analysis was to sum up the available data and to establish the pooled prevalence and antimicrobial resistance of E. coli in Ethiopia.

2. Methods

This study was conducted in a similar approach to Eshetie et al. (2016) [21] and according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Checklist [22] (additional SI file).

2.1. Study Selection. A systematic literature search was conducted in PubMed and Embase, and also manual search for articles potentially relevant to our study was identified. We built our search strategy by combining the three main arms (Table 1): E. coli, drugs-related terms, and Ethiopia.

Among the citations extracted, abstracts were reviewed to retrieve the clinical studies on E. coli colonization. Articles that were relevant, by title and abstract, were accessed in full text to determine those that provided sufficient information to be included in our meta-analysis. Finally, the references cited by each eligible study were screened to identify additional articles.

2.2. Inclusion and Exclusion Criteria. Studies included in this meta-analysis were those that had extractable data on the prevalence of drug resistance of E. coli on a human in Ethiopian hospitals or research centers and were only published from 2007 to 2017 and were only in English language.

2.3. Outcome of Interest. The main outcome of interest was the prevalence of drug resistance or antimicrobial susceptibility of E. coli among the total E. coli clinical isolates. The prevalence was calculated by dividing the numbers of resistant E. coli isolates by the total number of clinically isolated E. coli. As a secondary outcome of interest, we had also calculated the pooled resistance pattern of E. coli isolates to specific antibiotics.

2.4. Data Extraction and Assessment of Quality of Study. Screening by title, abstract, and full text and data extraction were done independently by two authors (Kald Beshir Tuem and Abadi Kahsu Gebre) at each step and Derbew Fikadu Berhe was involved in consensus for discrepancies (if any) between the two authors (Kald Beshir Tuem and Abadi Kahsu Gebre). In cases of insufficient data, the authors reviewed the full text of the article for further information and clarification. The extracted data from each article were summarized into a spreadsheet. References and data for each study were carefully cross-checked to ensure that no overlapping data were present and to maintain the integrity of the meta-analysis. Information extracted from each paper was region, study area, study design, study population, culture specimens, number of E. coli isolated, the average percentage of resistant E. coli, antimicrobial resistance rate of E. coli, and references. With all the articles used in this study being cross-sectional, the score for the quality of the study was assessed using the modified Newcastle-Ottawa scale for the representativeness of sample, appropriateness of sample size, response rate, validity of method, strategy to control confounding factors, reliability of outcome determination, and appropriate statistical analyses. The quality score (Table 2) disagreements were resolved by consensus and a final agreed-upon rating was assigned to each study (S2 file) [58].

2.5. Quality Control. The quality of eligible studies was checked independently by two authors (Kald Beshir Tuem and Abadi Kahsu Gebre) using a set of predetermined criteria such as research design quality of paper, completeness of extractable information, and employed methods for E. coli isolation. The study bias was measured by Begg’s funnel plot [59]. This study was registered in PROSPERO as follows: PROSPERO 2017: CRD42017070106.

2.6. Data Analysis. A random-effects model was used to determine pooled prevalence, subgroup analysis, and 95% confidence interval (CI) by employing the approach of Der-Simomian and Laird [60]. Variances and CIs were stabilized using Freeman-Tukey arc-sine methodology [61]; the reason is that using the standard approach of inverse variance method to calculate pooled prevalence does not work well in meta-analysis of single-arm study because, for studies with small or large prevalence, the inverse variance method causes the variance to become small and the calculated CI may be outside of the range [62]. Heterogeneity of study results was assessed using I² test and significant heterogeneity was considered at p < 0.10 and I² > 50% [60, 63]. Statistical analyses were performed using Open Meta- Analyst (version 3.13) and Comprehensive Meta-Analysis (version 3.1). In addition, we performed subgroup analyses according to the region of the country and the mechanism of action.

Table 1: Searching strategies including search arm and terms used in the study.

| Search arm | Search terms |
|------------|--------------|
| 1 E. coli  | “Escherichia coli” OR “E. coli” |
|            | “antibiotic resistance” OR “drug resistance” OR “drug resistance, microbial” OR “drug resistance, microbial” OR “antibacterial resistance” OR “antibiotic resistance” OR “antimicrobial resistance” |
| 2 Drug and/or resistance | |
| 3 Ethiopia | “Ethiopia” |

The word “OR” was used to combine search terms within each arm and the word “AND” was used to connect the three search arms (#1 AND #2 AND #3).
Table 2: Summary of 35 studies reporting the prevalence and resistance pattern of *E. coli* in different parts of Ethiopia.

| References                  | Region          | Study area     | Study period                  | Study design | Study population                                      | Culture specimens | Study samples | Number of *E. coli* isolated | Average % resistant *E. coli* | NOS quality score out of 7 |
|-----------------------------|-----------------|----------------|-----------------------------|--------------|--------------------------------------------------------|-------------------|---------------|-----------------------------|-----------------------------|---------------------------|
| Abejew et al., 2014 [23]    | Amhara          | Dessie         | January to March 2012       | RCS          | Test results of patients diagnosed with UTI           | Urine             | 2486          | 400                         | 51.8                        | 6                         |
| Kibret and Abera, 2014 [24] | Amhara          | Dessie         | —                           | R            | Patients                                               | Mid-stream morning urine, Urine, ear discharge, pus swab from wounds, and eye discharge | 1404          | 203                         | 53.2                        | 6                         |
| Kibret and Abera, 2011 [25] | Amhara          | Dessie         | —                           | R            | Patients                                               | Wound swab        | 3149          | 446                         | 44.2                        | 6                         |
| Azene and Beyene, 2011 [26] | Amhara          | Dessie         | —                           | R            | Patients with wound infections                        | Wound swab        | 599           | 82                          | 49.8                        | 6                         |
| Alebachew et al., 2016 [27] | Amhara          | Gondar         | March 1 to May 2, 2013      | CS           | HIV patients                                           | Blood             | 100           | 01                          | 44.4                        | 7                         |
| Alemu et al., 2012 [28]     | Amhara          | Gondar         | March 22 to April 30, 2011  | CS           | Pregnant women attending ANC                          | Urine             | 385           | 19                          | 29.2                        | 7                         |
| Wondimeneh et al., 2014 [29]| Amhara          | Gondar         | January to May 2013         | CS           | Fistula patients                                      | “Clean-catch” mid-stream urine specimen | 53            | 6                           | 59.3                        | 6                         |
| Wondimne et al., 2013 [30]  | Amhara          | Gondar         | December 2011 to June 2012  | CS           | Blood donated from donors at blood bank               | blood             | 137           | 2                           | 0.7                         | 7                         |
| Eshetie et al., 2015 [31]   | Amhara          | Gondar         | February to May 2014        | CS           | UTI-suspected patients                                | Urine             | 442           | 112                         | 48.0                        | 4                         |
| Tiruneh et al., 2014 [32]   | Amhara          | Gondar         | September 1, 2011, to June 30, 2012 | CS       | UTI-suspected patients                                | Urine             | 284           | 120                         | 68.0                        | 4                         |
| Eshetie et al., 2016 [33]   | Amhara          | Gondar         | February to June 2014       | CS           | Patients with UTI                                     | Urine             | 446           | 112                         | 38.8                        | 6                         |
| Mulu et al., 2017 [34]      | Amhara          | Debre Markos   | January 2015                | R            | Patients                                               | Urine             | 575           | 39                          | 31.5                        | 6                         |
| Abera and Kibret, 2014 [35] | Amhara          | West Gojam     | November 2009 to February 2010 | CS           | Adult patients who underwent trachomatous trichiasis surgery | Conjunctival swabs | 1413          | 20                          | 26.5                        | 5                         |
| Adugna et al., 2015 [36]    | Amhara          | Bahir Dar      | December 2011 to February 2012, October 2010 to January 2011 | CS           | Children below five years of age with acute diarrhea | Stool sample      | 422           | 204                         | 42.8                        | 7                         |
| Demtie et al., 2012 [37]    | Amhara          | Bahir Dar      | —                           | CS           | Pregnant women                                         | Clean-catch urine | 367           | 16                          | 41.7                        | 4                         |
| Derbie et al., 2017 [38]    | Amhara          | Bahir Dar      | —                           | R            | Patients                                               | Urine             | 446           | 72                          | 55.3                        | 5                         |
| Melaku et al., 2012 [39]    | Amhara          | Bahir Dar      | January to March 2012       | CS           | Patients                                               | Urine             | 1254          | 33                          | 87.8                        | 6                         |
| Mulu et al., 2012 [40]      | Amhara          | Bahir Dar      | May to November 2013        | CS           | Patients                                               | Wound swab and venous blood samples | 294           | 8                           | 53.1                        | 6                         |
| Wondemagegn et al., 2015 [41]| Amhara          | Bahir Dar      | —                           | CS           | Women of reproductive age                              | Vaginal swab      | 409           | 105                         | 50.5                        | 7                         |
| References | Region | Study area | Study period | Study design | Study population | Culture specimens | Study samples | Number of E. coli isolated | Average % resistant E. coli | NOS quality score out of 7 |
|------------|--------|------------|--------------|--------------|------------------|-------------------|--------------|---------------------------|-----------------------------|---------------------------|
| Dereje et al., 2017 [42] | Addis Ababa | Central Ethiopia | February to May 2015 | CS | Fistula patients | Clean-catch mid-stream urine | 210 | 65 | 38.2 | 7 |
| Dessie et al., 2016 [43] | Addis Ababa | Addis Ababa | October 2013 and March 2014 | CS | Surgical site infected patients | Wound swab | 107 | 24 | 68.4 | 6 |
| Desta et al., 2016 [44] | Addis Ababa | Addis Ababa | December 2012 to January 2014 | CS | All age groups patients | Fecal samples/swabs | 267 | 235 | 83.0 | 7 |
| Mamuye, 2016 [45] | Addis Ababa | Addis Ababa | January to March 2014 | CS | Outpatient and inpatient and pregnant women | Mid-urine samples | 424 | 53 | 52.2 | 5 |
| Legese et al., 2017 [46] | Addis Ababa | Addis Ababa | January to March 2014 | CS | Septicemia and UTI-suspected patients | Blood and urine | 322 | 6 | 72.9 | 6 |
| Ramos et al., 2014 [47] | West Ahsi | Addis Ababa | July to December 2013 | CS | Leprosy patients | Pus produced by ulcer | 68 | 17 | 35.8 | 5 |
| Derese et al., 2016 [48] | Dire Dawa | Addis Ababa | February 18, 2015 | CS | Pregnant women | Urine specimens | 186 | 9 | 34.4 | 6 |
| Beyene and Tsegaye, 2011 [49] | Jimma | Addis Ababa | April to June 2010 | CS | UTI cases patients | Urine | 228 | 7 | 217 | 5 |
| Debalki et al., 2014 [50] | Oromia | Jimma | September to December 2012 | CS | HIV/AIDS patients | Urine | 481 | 31 | 36.6 | 7 |
| Mama et al., 2014 [51] | Jimma | Addis Ababa | May to September 2013 | CS | Patients with wound infection | Wound swab | 150 | 29 | 61.6 | 6 |
| Muhalem, 2012 [52] | Jimma | Jimma | February to March 2007 | CS | Inpatients and outpatients | Urine, sputum, stool, and wound | 359 | 67 | 45.7 | 6 |
| Zenebe et al., 2011 [53] | Jimma | Jimma | October 27, 2009, to March 26, 2010 | CS | Febrile patients | Venous blood | 260 | 4 | 25.0 | 6 |
| Nigussie and Amsalu, 2017 [54] | Hawassa | SNNP | June to October 2014 | CS | Diabetic patients | Mid-stream urine | 240 | 11 | 47.7 | 7 |
| Amsalu et al., 2016 [55] | Hawassa | SNNP | January 2012 to December 2014 | RCS | Patients registered at microbiology lab book | Pus, ear discharge, nasal swab, urine, genital swab, CSF, and stool | 510 | 35 | 64.0 | 7 |
| Tadesse et al., 2014 [56] | Hawassa | SNNP | March to September 2012 | CS | Pregnant women attending ANC | Mid-stream urine | 244 | 16 | 56.3 | 6 |
| Wasihun et al., 2015 [57] | Tigray | Mekelle | March to October 2014 | PCS | Febrile patients | Venous blood | 514 | 16 | 27.5 | 6 |
| **Total** | | | | | | | **19,235** | **2,635** | | |
of the tested drugs to improve the specificity of the assessment.

3. Results

From Embase, PubMed, and manual searching, we found 164 potentially relevant studies, of which 35 were included for analysis (Figure 1).

The study design of all included articles (35) was cross-sectional study. In these studies, a total of 19,235 study samples participated, from which 2,635 E. coli strains were isolated. The published studies were from four regions in Ethiopia (Table 2) which include the federal capital city of Ethiopia, Addis Ababa. No report was obtained from other regions in the country (Afar, Benishangul-Gumuz, Gambella, and Somali). Most of the studies indicated that various specimens had been utilized for screening of E. coli; particularly multisite swabbing was performed from different parts of the body, including skin, nasal, eye, ear, urethra, throat, vagina, or genital area (Table 2), and other biological fluids like blood, urine, pus, stool, and cerebrospinal fluid (CSF) were taken for test. A total of 2,635 E. coli strains were isolated from these various sites. The lowest and highest proportions of E. coli resistance were reported, respectively, from Bahir Dar (55.20%) and Mekelle (27.50%) cities. The average prevalence of E. coli resistance was also noted in different regions of Ethiopia; Addis Ababa region was ranked first (62.55%, 95% CI: 38.28–6.83%), followed by Southern Nations, Nationalities, and Peoples of Ethiopia (58.14%, 95% CI: 48.69–67.58%), Amhara (47.83%, 95% CI: 39.77–55.89%), and Oromia (42.86%, 95% CI: 32.77–52.95%), whereas relatively low magnitude of E. coli resistance was reported from Tigray region (27.51%, 95% CI: 16.14–38.88%) (Figures 2 and 3).

Subgroup analyses (Figure 3) were carried out based on the region (Addis Ababa, Amhara, Oromia, SNNP, and Tigray) and the mechanism of action of the drugs (cell wall synthesis inhibitors, protein synthesis inhibitors, DNA synthesis inhibitors, and antimetabolites). A paper-based analysis in our study showed that the overall E. coli resistance in Ethiopia was 48.87% (95% CI: 42.17–55.57%) with highest prevalence in the capital city, Addis Ababa, 62.55% (95% CI: 38.28–86.83%) (Figure 3).

As presented in Figure 4 and Table 3, the pooled prevalence of E. coli resistance was 45.38% (95% CI: 33.50–57.27%), and high resistance rates were observed to ampicillin, 83.81% (95% CI: 76.95–90.67%), amoxicillin, 75.79% (95% CI: 64.26–87.32%), tetracycline, 67.18% (95% CI: 58.89–75.47%), trimethoprim-sulfamethoxazole, 57.47% (95% CI: 58.89–75.47%), and cephalothin, 56.69% (95% CI: 33.74–79.64%). A relatively low level of nitrofurantoin resistance was observed, 13.55% (95% CI: 5.83–21.27%).

Comparing the prevalence of E. coli resistance among the antibacterial drugs, subgroup analysis (Figure 5) revealed that the cell wall synthesis inhibitors account for the greatest resistance percentage, 59.37% (95% CI: 36.21–82.53%), and DNA synthesis inhibitors account for the lowest resistance percentage, 26.14% (95% CI: 33.50–57.27%).

There was a high level of heterogeneity by random model methods ($I^2 = 97.89\%$; $p < 0.01$). Hence, the included studies have been conducted in different study settings, study periods, and study populations, which could have an effect on the heterogeneity of the included studies. The symmetry of funnel plot showed small study bias, which yielded insignificant effect.

4. Discussion

Antibiotic resistance continues to be a major global challenge in the management of bacterial infection. The trouble behind antibiotic resistance is highly marked in undeveloped or developing countries, including Ethiopia, where infectious
### Table 3: Percentage of pooled antibacterial resistance rates of *E. coli* in Ethiopia, 2007–2017.

| Studies | Antibacterial |
|---------|---------------|
|         | AML | AMP | AMC | KF | CRO | TE | DO | C | E | CN | K | CIP | NA | F | NOR | SXT |
| Abejew et al., 2014 [23] | 84.6 | 80.0 | — | 42.3 | 46.9 | 82.2 | 64.5 | 49.0 | 94.4 | — | — | 34.0 | 20.0 | 28.3 | 13.3 | 10.4 | — | 75.8 |
| Abera and Kibret, 2014 [35] | — | — | — | 40 | 25 | — | 35 | — | 40 | — | — | 4 | — | — | — | 15 |
| Adugna et al., 2015 [36] | 86.8 | 475 | — | 76 | — | 36.2 | — | 37.2 | — | 6.9 | — | — | 9.3 | — | — | — | 9.3 |
| Alebachew et al., 2016 [27] | 100 | 100 | 100 | 100 | 100 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 100 |
| Alemu et al., 2012 [28] | 100 | 100 | 36.8 | 0 | 52.6 | 0 | 0 | 5.3 | 0 | — | 0 | — | 0 | 26.3 |
| Beyene and Tsegaye, 2011 [49] | 100 | 100 | — | 0 | 28.6 | 0 | 0 | 0 | 14.3 | 0 | 0 | 0 | 28.6 |
| Debakey et al., 2014 [50] | 100 | 100 | — | — | 21.6 | — | 24.6 | — | 32.2 | — | — | 53.8 | — | — | 56.9 | 40 | — | — |
| Demilie et al., 2012 [37] | 75 | 81.7 | 37.5 | — | 68.8 | — | 375 | — | 31.2 | 18.8 | 18.8 | 43.8 | 6.3 | 25 | 27 | 64.5 |
| Derbie et al., 2017 [38] | 89.1 | 78.6 | — | 66.1 | — | — | 276 | — | 64.4 | — | — | 72 | — | — | — | 64.5 |
| Dereje et al., 2017 [42] | 100 | 100 | 36.8 | 0 | 52.6 | 0 | 0 | 5.3 | 0 | — | 0 | — | 0 | 26.3 |
| Derese et al., 2016 [48] | 77.8 | 77.8 | — | 0 | 66.7 | 0 | 0 | 11.1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Dessie et al., 2016 [43] | 95.8 | 70.8 | — | 83.3 | 83.3 | — | 25 | — | 54.2 | — | 6.7 | — | — | — | — | — |
| Desta et al., 2016 [44] | — | 93 | 98 | — | — | — | — | — | — | 63 | — | 78 | — | — | — | — |
| Eshetie et al., 2015 [31] | 92.9 | 60.7 | 179 | 53.6 | — | 64.3 | — | 57.1 | — | 10.7 | 25 | — | 50 |
| Kibret and Abera, 2014 [24] | 87.3 | 56.9 | 33.9 | 80.1 | 61 | 374 | 93.7 | 24.5 | — | 34.1 | 3.8 | — | 72.1 |
| Kibret and Abera, 2011 [25] | 86 | 59.5 | 37.4 | 72.4 | — | 35.3 | 89.4 | 13 | — | 19.9 | 3.6 | 6.5 | 62.9 |
| Azene and Beyene, 2011 [26] | 85.0 | 54.7 | 66.7 | 71.4 | 33.3 | 37.1 | 11.1 | 14.4 | — | 7.7 | — | — | — | 67.1 |
| Mama et al., 2014 [51] | 100 | 100 | 62 | 79 | 44.8 | 65.5 | — | 51.7 | — | 34 | 41 | — | 44.8 | 55 |
| Mamuye, 2016 [45] | 75.5 | 79.2 | 32.1 | 45.3 | 83.0 | 71.7 | 30.2 | 22.6 | — | 54.7 | 73.6 | 20.8 | 67.9 | 22.6 |
| Melaku et al., 2012 [39] | 85.7 | 100 | — | 81.6 | 83.7 | — | — | 63 | — | 78 | — | — | — | — |
| Melaku et al., 2017 [34] | 25 | 33.3 | — | 3.3 | 75 | 75 | 13 | 0 | 69.6 | — | 18.2 | — | 23.1 | 11.1 |
| Mullalem et al., 2012 [52] | 86 | 86 | 70.1 | 9 | 73.1 | 75 | 75 | 0 | 44.4 | 44.4 | 44.4 | 66.7 | 22.2 | 44.4 | 67 |
| Mulu et al., 2012 [40] | 90 | 78 | — | 55.6 | 66.7 | 66.7 | 0 | 44.4 | 44.4 | 44.4 | 66.7 | 22.2 | 67.9 | 22.6 |
| Nigussie and Amsalu, 2017 [54] | 64.7 | 70.6 | 5.9 | 5.9 | 41.2 | 29.4 | 35.3 | 41.2 | 11.8 | — | 29.4 | — | — | 58.8 |
| Ramos et al., 2014 [47] | 100 | 36.4 | 63.6 | — | — | — | — | 72.7 | 18.2 | 0 | 9.1 | 81.8 |
| Wasihun et al.2015 [57] | 50 | 66.7 | — | 50 | 100 | — | 16.7 | — | 66.7 | — | 50 | — | 66.7 | 66.7 |
| Wondimeneh et al., 2014 [29] | 80 | 73.3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Wondimun et al., 2013 [30] | 33.3 | 0 | 45.7 | 64.3 | — | 60.6 | 56.2 | — | 68.8 | 90 |
| Zenebe et al., 2011 [53] | 0 | 100 | 0 | 0 | 75 | 100 | 75 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Amsalu et al., 2016 [54] | 100 | 26.1 | 45.7 | — | 64.3 | — | 60.6 | 56.2 | — | 68.8 | 90 |
| Tadesse et al., 2014 [56] | 68.8 | — | — | — | — | — | 43.8 | — | — | — | — | 18.8 | 81.2 |
| Tiruneh et al., 2014 [32] | 87.5 | 83.3 | — | 79.2 | 58.3 | — | 44.2 | 46.7 | — | — | — | 76.7 |
| Legesse et al., 2017 [46] | 100 | 100 | 83.3 | 66.7 | 66.7 | — | — | 0 | 66.7 | 100 |
| Eshetie et al., 2016 [33] | 98.2 | 42 | — | 43.8 | 54.5 | 52.7 | — | 0.9 | 17 | — | — | — | 64.3 |
| Wondagemgen et al., 2015 [41] | 80 | 73.3 | — | 73.3 | — | 26.7 | — | 20 | — | 20 | 60 |

AMC: amoxicillin-clavulanic acid, AML: amoxicillin, AMP: ampicillin, C: chloramphenicol, CIP: ciprofloxacin, CN: gentamicin, CRO: ceftriaxone, DO: doxycycline, E: erythromycin, F: nitrofurantoin, K: kanamycin, KF: cephalothin, NA: nalidixic acid, NOR: norfloxacin, SXT: trimethoprim/sulfamethoxazole, TE: tetracycline, —: not done.
diseases are highly prevalent [64]. Factors responsible for an increase in rates of antimicrobial resistance include misuse/overuse of antibiotics by healthcare professionals and general public and inadequate surveillance systems due to lack of reliable microbiological techniques leading to the inappropriate prescription of antibiotics [33]. Antimicrobial resistance in \( E. \text{ coli} \) has increased worldwide and its susceptibility patterns show substantial variation in different geographical locations [5]. To date, the overall epidemiology and burden of multidrug resistance (MDR) bacteria have not been fully understood, especially in resource-limited countries including Ethiopia [64, 65]. To the best of our knowledge, this is the first meta-analysis study conducted to determine the pooled prevalence of \( E. \text{ coli} \) prevalence and resistance in Ethiopia. Our result revealed that \( E. \text{ coli} \) strains displayed diverse resistance patterns, with percentages varying slightly based on sample type and geographical distribution. Based on the tested antimicrobials, the overall \( E. \text{ coli} \) resistance in Ethiopia was nearly 50% (45.38% (95% CI: 33.50–57.27%)).

Developing countries have comparatively higher risk factors associated with MDR strains than the developed ones [64, 66]. Resistance to antibacterial agents is a normal evolutionary process for microorganisms, but it is highly aggravated by continuous deployment of antimicrobial drugs in treating infections [67, 68]. It is claimed that more than half of drugs are prescribed, sold, or dispensed without following standard protocols, and the situation is more pronounced in developing countries including Ethiopia [69]. Sosa et al. (2010) reported that antibiotic usage in most of the low-income countries is generally unregulated, which is a prime factor for the occurrence of resistant bacterial strains [64]. This implies that antibiotics are being used widely and inappropriately in resource-limited countries including Ethiopia. This may lead to an increase in the occurrence of drug-resistive bacterial strains such as \( E. \text{ coli} \).

In our study, the regional prevalence of \( E. \text{ coli} \) resistance was estimated, and the subgroup analysis showed that the highest prevalence of \( E. \text{ coli} \) resistance (62.55%) was noted in Addis Ababa city, which was almost two times higher than Tigray region (27.51%). The observed variation might be due to differences in study location, hospital setup, and antimicrobial utilization.
Subgroup analysis also showed that *E. coli* strains exhibited higher resistance with cell wall inhibitors, specifically aminopenicillins (ampicillin and amoxicillin), followed by protein synthesis inhibitors, mainly to tetracycline, and lesser resistance prevalence to nitrofurantoin. In line with our data, globally, *E. coli* strains were reported to be highly resistant to the above-mentioned antibiotics, mainly to aminopenicillins [70, 71]. Sândulescu (2016) reported that *E. coli* showed low
### Table: E. coli antimicrobial resistance % (95% CI)

| Antimicrobial Drugs                  | E. coli antimicrobial resistance % (95% CI) |
|-------------------------------------|--------------------------------------------|
| Ampicillin                          | 83.81 (76.95, 90.67)                       |
| Amoxicillin                         | 75.79 (64.26, 87.32)                       |
| Tetracycline                        | 67.18 (58.89, 75.47)                       |
| Trimethoprim+sulfamethoxazole       | 57.47 (46.86, 68.08)                       |
| Cephalaxin                          | 56.69 (33.74, 79.64)                       |
| Erythromycin                        | 52.94 (22.02, 83.86)                       |
| Amoxicillin+Clavulanic acid         | 49.04 (33.60, 64.48)                       |
| Doxycycline                         | 48.64 (34.01, 63.27)                       |
| Gentamycin                          | 35.78 (27.50, 44.06)                       |
| Chloramphenicol                     | 35.28 (25.49, 45.07)                       |
| Nalidixic acid                      | 34.25 (19.39, 49.11)                       |
| Norfloxacin                         | 32.81 (21.70, 43.92)                       |
| Ceftriaxone                         | 30.20 (19.70, 40.70)                       |
| Kanamycin                           | 27.73 (11.38, 44.08)                       |
| Ciprofloxacin                       | 27.59 (19.70, 35.48)                       |
| Nitrofurantoin                      | 13.55 (5.83, 21.27)                       |
| **Overall**                         | 45.38 (33.50, 57.27)                       |

*Figure 4: Forest plot of the pooled percentage and confidence interval of E. coli resistance to antibacterial drugs in Ethiopia from 2007 to 2017.*

Furthermore, our finding indicated the higher magnitude of E. coli resistance. This may imply the need for intervention in prescribing and using antibacterial against E. coli infections. Interventional strategies may include creating public awareness, maintaining hand hygiene, applying infection prevention protocols, and maintaining environmental sanitation, which are encouraged for preventing infection. In addition to these, promoting health education, maintaining continuous professional educations, and advocating rational prescribing habits are evidently effective in the minimization of the unwanted use of antibiotics, which in turn decrease selective pressure of resistant strains.

#### 5. Conclusion

In this meta-analysis, the pooled E. coli resistance is considerably high. E. coli strains were highly resistant to ampicillin but showed lesser resistance to nitrofurantoin. Adopting safety protocols and implementing proper antibiotic prescription policies could be potential interventional strategies to address the emerging resistance of E. coli.

#### Abbreviation

- ANC: Antenatal clinic
- AMC: Amoxicillin-clavulanic acid
- AML: Amoxicillin
- AMP: Ampicillin
- C: Chloramphenicol
- CI: Confidence interval
- CIP: Ciprofloxacin
- CN: Gentamicin
- CRO: Ceftriaxone
- CS: Cross-sectional
- CSF: Cerebrospinal fluid
- DO: Doxycycline
- E: Erythromycin
- E. coli: Escherichia coli
- F: Nitrofurantoin
- K: Kanamycin
- KP: Cephalothin
- MDR: Multidrug resistance
- NA: Nalidixic acid
- NOR: Norfloxacin
- PCS: Prospective cross-sectional
- R: Retrospective review of culture
- RCS: Retrospective cross-sectional
- SNNP: Southern Nations, Nationalities, and Peoples
- SXT: Trimethoprim/sulfamethoxazole
- TE: Tetracycline
- UTI: Urinary tract infection.
Antimicrobial Drugs | *E. coli* antimicrobial resistance % (95% CI)
---|---
Ampicillin | 83.81 (76.95, 90.67)
Amoxicillin | 75.79 (64.26, 87.32)
Cephalexin | 56.69 (33.74, 79.64)
Amoxicillin+Clavulanic acid | 49.04 (33.60, 64.48)
Ceftriaxone | 30.20 (19.70, 40.70)
**Subgroup Cell wall Synthesis Inhibitors** | **59.37 (36.21, 82.53)**
(I² = 94.9%, p = 0.00)
Tetracycline | 67.18 (38.89, 75.47)
Erythromycin | 52.94 (22.02, 83.86)
Doxycycline | 48.64 (34.01, 63.27)
Gentamycin | 35.78 (27.50, 44.06)
Chloramphenicol | 35.28 (25.49, 45.07)
Kanamycin | 27.73 (11.38, 44.08)
**Subgroup Protein Synthesis Inhibitors** | **44.32 (30.34, 58.31)**
(I² = 89.67%, p = 0.00)
Trimethoprim+sulfamethoxazole | 57.47 (46.86, 68.08)
**Subgroup Anti-metabolite** (I² = NA, p = NA)
Nalidixic acid | 57.47 (46.86, 68.08)
Norfloxacin | 34.25 (19.39, 49.11)
Ciprofloxacin | 32.81 (21.70, 43.92)
Nitrofurantoin | 27.59 (19.70, 35.48)
**Subgroup DNA Synthesis Inhibitors** | **26.14 (16.23, 36.06)**
(I² = 75.17%, p = 0.01)
**Overall** (I² = 94.89%, p = 0.00) | 45.38 (33.50, 57.27)

**Figure 5:** Subgroup analysis of pooled percentage and confidence interval of *E. coli* resistance to antibacterial drugs according to drug mechanism of action.

**Ethical Approval**

Ethical clearance was not required and was not necessary for this study.

**Conflicts of Interest**

The authors declare that they have no conflicts of interest.

**Authors’ Contributions**

Kald Beshir Tuem contributed to conception of the research protocol and study design. Kald Beshir Tuem, Abadi Kahsu Gebre, Tesfay Mehari Atey, and Derbew Fikadu Berhe contributed to literature review, data collection, data extraction, data analysis and interpretation, and drafting the manuscript. Kald Beshir Tuem, Abadi Kahsu Gebre, Tesfay Mehari Atey, Helen Bitew, Ebrahim M. Yimer, and Derbew Fikadu Berhe contributed to drafting and reviewing the manuscript. All authors have read and approved the manuscript.

**Supplementary Materials**

*Supplementary 1.* S1 file: PRISMA 2009 Checklist. We have conducted the meta-analysis according to Moher et al. (2009), “Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement.” We included all the criteria on the checklist, except in the discussion part; we did not include the limitations of the study related to incomplete retrieval of articles, as we did not face such a problem.

*Supplementary 2.* S2 file: Modified Newcastle-Ottawa Scale. This scale had been adapted from Wells et al. (2009), “The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomized Studies in Meta-Analyses.” We considered...
the comparability to be controlled if the standard laboratory procedure is described in the articles. Since the outcome of the bacterial sensitivity test is obtained after full growth of the bacterial strains, we assigned one star for the assessment outcomes of all studies.

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