Global prevalence and risk factors of multidrug resistance Escherichia coli in human and animal samples (2015-2023): A systematic review and meta-analysis

Sema Tirusew

tirusewsema29@gmail.com

Bahir Dar University

Damtie Destaw

Bahir Dar University

Mohammad Abas

Jigjiga University

Systematic Review

Keywords: Global prevalence, Meta-analysis, Multidrug-resistant Escherichia coli, Risk factors, Systematic review

Posted Date: November 5th, 2024

DOI: https://doi.org/10.21203/rs.3.rs-5287484/v1

Additional Declarations: No competing interests reported.

Abstract

Antimicrobial resistance has emerged as a critical global concern. *Escherichia coli*, a prominent Gram-negative bacterium, present significant challenges in infection management due to its adaptive resistance mechanisms. Found naturally in the gastrointestinal tracts of humans and animals, *E. coli* strains are increasingly resistant to antibiotics worldwide, necessitating urgent intervention strategies. This study aimed to assess the global prevalence and risk variables linked to multidrug-resistant *E. coli* in human and animal samples via systematic review and meta-analysis. We searched databases like Google Scholar, Scopus and Medline (PubMed) for relevant publications from January 2015 to April 2023. These studies reported on multidrug-resistant *E. coli* prevalence and associated risk factors. Articles were selected based on predefined criteria. Results were presented with 95% confidence intervals in forest plots, tables, and figures. Heterogeneity was assessed using the inconsistency index (I^2). Random-effects model Comprehensive meta-analysis software calculated pooled prevalence and risk factor estimates. The combined prevalence of multidrug-resistant *E. coli* was estimated at 36.5% (95% CI: 24.6–50.3), showing significant heterogeneity (I^2 = 99.13%). Risk variables like length of hospital stay and past history of antibiotic usage have been linked to increased multidrug resistance in *E. coli*, according to a pooled study of 23 researches that satisfied the meta-analysis eligibility criteria. The pooled odds ratio for risk factors was 1.266 (95% CI: 0.804–1.992), with notable heterogeneity (I^2 = 85.92%). Additionally, the odds ratio for prior antibiotic usage was 1.326 (95% CI: 0.837–2.102), and for length of hospital stay, it was 1.162 (95% CI: 0.340–3.973). This study and meta-analysis highlight global concerns regarding antibiotic resistance, particularly the increasing prevalence of multidrug-resistant *E. coli*. Key-independent risk factors identified include the duration of hospital stays and prior antibiotic use. Effective management and prevention strategies for drug resistance in *E. coli* and other bacteria should depend on identifying and addressing these risk factors.

Introduction

Antimicrobial resistance in bacteria represents a critical global public health challenge, significantly impacting the treatment and management of infectious diseases [1, 2]. Resistance typically arises when antibiotics fail to inhibit critical bacterial survival pathways, such as protein synthesis, nucleic acid replication, cell wall synthesis, or foliate metabolism, which are vital to the survival of bacteria. Despite their importance in treatment the rate at which antibiotic resistance outpaces the development of new antibiotics. Proactive measures are crucial to curb its spread. The World Health Organization predicts a stark rise in global fatalities due to antibiotic resistance, potentially reaching 10 million annually by 2050 [3].

Certain drug-resistant Gram-negative bacteria within the *Enterobacteriaceae* family, including *E. coli* have been classified as "urgent threats" or "priority 1" infections by esteemed bodies such as the Centers for Disease Control and Prevention (CDC) and the WHO [4]. *Escherichia coli* is prominently featured on the WHO's critical priority list for intensive research, antibiotic discovery, and development [1, 2]. According to WHO research spanning 2015 to 2020, the emergence of antimicrobial resistance has emerged as a pervasive concern, profoundly impacting global human, animal, and ecological health [5].

Gram-negative *Enterobacteriaceae* bacteria, such as *Escherichia coli*, are frequently isolated from variety infection sites in both human and animal hosts. This bacterial species encompasses several pathotypes including Shiga toxin-producing *E. coli* (STEC), enteroinvasive *E. coli* (EIEC), enteropathogenic *E. coli* (EPEC), enterotoxigenic *E. coli* (ETEC), enterohemorrhagic *E. coli* (EHEC), enteroaggregative *E. coli*, and diffusely adherent *E. coli* (DAEC) [6]. Key virulence genes, like stx1, stx2, eaeA, and hlyA play a significant roles in *E. coli* pathogenicity and are closely

associated with diarrheal diseases in both human and animal hosts [6]. Careful selection of appropriate antimicrobials is critical to effectively treat these infections and minimize the risk of antimicrobial resistance in commensal and pathogenic *E. coli* [7].

The primary sources of drug-resistant Gram-negative bacteria are contaminated water, food (especially meat and vegetables), and healthcare settings [8]. Antimicrobial resistance genes are often acquired from drug-resistant bacteria found in the colon, with horizontal gene transfer, facilitating the spread of resistance among different bacterial species, including *E. coli* and other Gram-negative pathogens entering the digestive system through contaminated sources. Widespread and indiscriminate antibiotic use has contributed significantly to the proliferation of resistant strains globally [9].

The escalating prevalence of antibiotic resistance in diverse *E. coli* strains worldwide is a major concern, emphasizing the urgent need for effective measures to impede its spread [10]. Moreover, as the efficacy of current antibiotics diminishes, the rise of multidrug-resistant (MDR) bacteria poses a serious threat to public health [10]. Superbugs, defined as bacteria resistant to multiple drugs, can enzymatically degrade a broad spectrum of medicines. Precisely quantifying their prevalence and identifying associated risk factors are crucial for guiding prevention and control strategies. Hence, this systematic review and meta-analysis aims to elucidate factors contributing to the emergence of multidrug-resistant *E. coli* strains and comprehensively assess their global prevalence in human and animal samples.

Method

Literature search and selection

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline was followed during the search for published articles to guarantee a logical and exhaustive approach to information retrieval [11]. The primary sources for the search, which took place between February and April 2023, were the Google Scholar, Scopus and PubMed databases. To increase search precision, Boolean logic and medical subject headings (MeSH) were utilized to construct the search queries. Comprehensive and pertinent articles were gathered from the selected databases using MeSH terms and keywords like "*Escherichia coli*," OR "*E. coli*," "antimicrobial resistance," OR "AMR," OR "antibiotic resistance," OR "multidrug resistance," OR "MDR," and "Worldwide." To ensure that only articles meeting the standards were included in the information analysis that followed strict selection criteria were applied.

Inclusion and exclusion criteria

A comprehensive assessment of studies on the global prevalence and risk factors of multidrug-resistant *E. coli* was included in the analysis. Only full-length, published English-language articles were included to guarantee the availability of substantial material. We considered studies published between 2015 and 2023 to obtain the most recent and relevant conclusions. Studies that did not explicitly examine the prevalence and risk factors of multidrug resistance in *E. coli* were excluded from the analysis. Furthermore, unpublished data, studies published before 2015, incompletely described abstracts, and anonymous reports were also excluded from this analysis.

Data extraction

The chosen articles were subjected to an organized coding procedure, and the data were painstakingly gathered in Microsoft Excel using a specific format. The format comprised discrete sections for documenting relevant data, including the name of the author, the length of the study, the year it was published, the study design, the location of the study population, the sample size, the total number of isolates, and the number of isolates of a particular strain of *E. coli*. A stringent validation process was used to preserve data integrity, entailing several exhaustive checks to guarantee the dependability and correctness of the retrieved data.

Data analysis

After being assembled into an Excel 2010 spreadsheet, the gathered data was put through a descriptive statistical analysis. The Comprehensive Meta-Analysis a version 2 program was used to objectively examine the prevalence estimate and pinpoint the risk factors connected to multidrug-resistant *E. coli*. When two or more studies were available, the odds ratio (OR) and its matching 95% confidence interval (CI) were used to create a forest plot, which allowed for the estimation of the pooled odds ratio.

A narrative review technique was used when risk factors were only covered in a single article or when there was significant heterogeneity among several papers that made meta-analysis difficult. Using the random effects model, pooled estimates of prevalence and risk variables were obtained. To illustrate the extracted data, visual aids including tables, figures, and forest plots were used. A funnel plot was used to assess publication bias, and the inconsistency index (I^2) test was used to gauge the level of statistical heterogeneity among the included papers. The I^2 test yields an estimate of the percentage of variation in effect estimates that may be ascribed to heterogeneity as opposed to chance or random error. It therefore functions as a gauge for the degree of statistical heterogeneity amongst the included research [12, 13].

Results

Selection of articles

Upon identifying 2,325 records in the first pool, 475 publications were deemed redundant and eliminated. An additional 637 publications that did not pertain to the examination of multidrug resistance, prevalence, and risk factors in *E. coli* were excluded after reviewing abstracts and titles. A thorough evaluation of the eligibility criteria was conducted on the remaining 576 items, resulting in the exclusion of 548 studies. Reasons for exclusion included the presence of review papers, inadequate information about multidrug resistance in *E. coli*, and lack of data on prevalence and risk factors. Consequently, 28 studies that satisfied the inclusion criteria were selected for qualitative analysis, 23 articles were chosen for the prevalence meta-analysis, and 17 articles were included for calculating the odds ratios of risk factors from the 23 studies. These selected studies focused specifically on investigating the prevalence and risk factors associated with multidrug resistance in *E. coli.* Figure 1 shows the flow diagram of study selection for the analysis, providing a visual depiction of the article selection procedure.

Global Trends in MDR Research (2015–2023)

Global Trends in MDR *E. coli* Research (2015–2023)
Table 1 provides a concise overview of the features and findings from the quality evaluation of each of the 28 investigations. Interestingly, 23 of these articles were deemed appropriate for the prevalence study meta-analysis.

Geographically, the studies exhibited a global distribution, with eight conducted in Asia, seven in Africa, two in America, and six in Europe.

There were a total of five studies with two different study designs: four cross-sectional studies (n = 4) and one prospective cohort study (n = 1) that were excluded from the prevalence study meta-analysis. These studies were excluded because the research population was non-human and did not meet the meta-analysis's homogeneity requirements. One study was conducted in America, one in Europe, two in Africa, and one in Asia. Of the five investigations, two involved dogs, two involved poultry, and one involved cows and farms. According to two studies, the use of antibiotics within the preceding month is a substantial risk factor for *E. coli* that is resistant to multiple drugs.

A higher risk of multidrug-resistant *E. coli* has been linked to a number of risk factors, including being a farmer, not using patient isolation precautions, having liver cirrhosis, recently undergoing digestive surgery, eating organic food, having had a urinary tract infection within the previous year, acquiring the infection in a medical facility, sex, age, and having metastases. However, these factors were only examined in one study each and lacked the required consistency and replication, so they were excluded from the meta-analysis. In contrast, the risk factor study's odds ratios were determined using a meta-analysis that included risk factors evaluated by several studies, such as length of hospital stay and past history of antibiotic use.

Table 1
Global Distribution and Characteristics of Studies on MDR *E. coli* (2015–2023)

Autor	Country	Study period	Study design	Study population	Sample size	# Total isolates	# *E. coli* isolates
[14]	Morocco	February 2013 to July 2015	Prospective study	Neonatal intensive care unit	455	641	261
[15]	Thailand	April 2018 to October 2020	Prospective case-control	Patients with UTIs	284	309	267
[16]	Ethiopia	March to May 2017	Cross-sectional study	Pregnant women	384	61	30
[17]	Zambia	2019	Cross-sectional study	Children under-five years	1287	1020	1020
[18]	Morocco	March 2015 to March 2016	Case-control study	Adult intensive care unit	479	305	45
[19]	Spain	November 2018 to 31 October 2019	Case-control study	Adult patients admitted to ICU	1342	101	58
[20]	Spain	January 2013 and December 2014	Retrospective cohort study	Hospitalized patients with UTIs	948	1074	559
[21]	USA	June and October 2018	Cross-sectional study	A college community	103	103	93
[22]]	Korea	January 2009 to April 2013	Retrospective cohort study	Cancer surgery patients	143	232	25
[23]	Taiwan	January 2010 to December 2017	Retrospective cohort study	Adults with surgical surgery	364	594	176
[24]	Bangladesh	December 2018 to April 2019	Cross-sectional study	Broiler chickens & environment	150	114	114
[25]	Ethiopia	Undefined	Cross-sectional study	Dairy cows and farms	408	408	19
[26]	Egypt	January 2017 to December 2020	Retrospective cohort study	Cancer patients in ICUs	497	748	136

Autor	Country	Study period	Study design	Study population	Sample size	# Total isolates	# *E. coli* isolates
[27]]	Algeria	January 2015 to February 2017	Cross-sectional study	Inpatients/outpatients with UTIs	426	363	215
[28]	Spain	January and October 2015	Prospective cohort study	Dogs attended at a veterinary hospital	44	32	22
[29]	USA	July 2013 and July 2014	Retrospective cohort study	Adults patients	177	177	69
[30]	German	2005 to 2014	Retrospective analysis	Children admitted to the Pediatric ICU	123	167	47
[31]	Poland	January 2018 and December 2019	Cross-sectional study	Children undergoing hematopoietic cell transplantation	175	175	7
[32]	Brazil	August and December 2018	Cross-sectional study	Dogs	130	130	35
[33]	Czech Republic	January 2013 to 31 December 2020	Retrospective cohort study	Urine samples from spinal cord injury or disorder	246	829	232
[34]	Ethiopia	November 2015 to April 2016	Cross-sectional study	Backyard chicken	191	694	62
[35]	Indian	March 2013 to February 2014	Retrospective study	Hospitals	346	346	93
[36]	Iran	February 2012 to June 2013	Cross-sectional study	Hospitalized Patients	250	250	134
[37]	Ethiopia	April to May 2017	Cross-sectional study	Children under five	269	264	224
[38]	China	2015 to 2019	Cross-sectional study	Residents of long term care facilities	385	71	39
[39]	Taiwan	April 2016 to August 2019	Retrospective study	Patients with multi-drug resistant Enterobacterales	91	91	17
[40]	China	August 2021 to	Prospective study	Children	510	510	12

Autor	Country	Study period	Study design	Study population	Sample size	# Total isolates	# *E. coli* isolates
		September 2021					
[41]	Morocco	February 2013 to July 2015	Cross-sectional and case-control study	Human gut micro-biota	782	149	147

Meta-analysis of the prevalence estimates of multidrug-resistant

Meta-analysis of the prevalence estimates of multidrug-resistant *E. coli*
The results of the meta-analysis showed that the overall prevalence of *E. coli* in human and animal samples, after combining 23 studies, was 36.5% with a 95% confidence interval (CI: 24.6–50.3%); I^2: 99.13%; P: 0.055. The heterogeneity percentage of these studies was 99.13%, indicating high heterogeneity in this estimate (Fig. 2).

Random effects model: I^2 = 99.13; Q = 2533.107; df = 22. The diamond indicates the overall pooled estimate.

Publication Bias in Prevalence Estimates of Multidrug-Resistant *E. coli*

The funnel plots, as well as Egger's linear regression test, revealed that there is publication bias in the prevalence estimate of multidrug-resistant *E. coli* analyses; (Fig. 3, Z = -1.922, P = 0.055, Random effects model: I^2 = 99.13; Q value = 2533.107; df = 22). The distribution of the studies using a funnel plot showed an asymmetrical distribution of effect estimates, indicating publication bias. To minimize the effect of the bias, subgroup analysis was used.

Subgroup analysis by publication year

According to the publishing year, the subgroup analysis showed a result of 36.2% (95% CI: 33.2–39.4%) (Fig. 4). Based on pooled estimate prevalence data, the lowest result was found in three studies from 2019 (18.7%) (95% CI: 4.2–54.6%), followed by two studies from 2015 and 2023 (22.3%) (95% CI: 14.4–3.3%) and one study in 2019 (27.4%) (95% CI: 23.6–31.5). The study conducted in 2016 yielded the highest pooled estimate prevalence result (53%) (95% CI: 47.4–59.7%), followed by four studies from 2021 (52.6%) (95% CI: 15.8–86.8%), two studies from 2018 (49.2%) (95%CI: 30.5–68.2%), one study from 2017 (38.2%) (95% CI: 30.1–47.1%), and nine studies from 2022 (36.9%) (95% CI: 33.2–39.4%).

Subgroup analysis by country

Based on national distribution, the total pooled prevalence estimate of multidrug-resistant *E. coli* was 46% (95% CI: 44–47.7%) (Fig. 5). Poland had the lowest estimated prevalence (4%; 95% CI: 1.9–8.2%), followed by Taiwan (13.2%; 95% CI: 0.4–84.6%), the Netherlands (10.1%; 95% CI: 7.5–13.6%), Korea (17.5%; 95% CI: 12.1–24.6%), and China (18.8%; 95% CI: 16.3–21.5%). The Czech Republic had the highest prevalence estimate at 94.3% (95% CI: 90.6–96.6%). Thailand, Zambia, the USA, and Algeria followed with estimates of 94% (95% CI: 90.6–96.2%), 79.3%

(95% CI: 77.3–81.4%), 70.6% (95% CI: 14.8–97.1%), and 50.5% (95% CI: 45.7–55.2%), respectively. The remaining estimates ranged from 20.1 to 39.4%.

Subgroup analysis by continent

According to the continent, the overall prevalence of multidrug-resistant *E. coli* was 41.7% (95% CI: 29.5–55.0%) (Fig. 6). Europe exhibited the lowest estimated prevalence of multidrug-resistant *E. coli*, at 29.3% (95% CI: 27.7–30.9%). The highest estimated prevalence was observed in the Americas, at 57.9% (95% CI: 52–63.5%). In Africa and Asia, the prevalence rates were 50.9% (95% CI: 49.3–52.4%) and 31.4% (95% CI: 29.7–33.2%), respectively.

Meta-analysis of Risk Factors

Risk factors such as length of hospital stay and past history of antibiotic usage have been associated with increased multidrug resistance in *E. coli*, based on a pooled study of 23 research articles that met the eligibility criteria for meta-analysis. This analysis was part of the Comprehensive Meta-study involving more than two studies. Following the meta-analysis, forest plots and funnel plots were generated to represent the odds ratios of risk factors associated with multidrug resistance. According to eleven studies, the development of multidrug-resistant *E. coli* is significantly correlated with prior antibiotic use. Accordingly, six studies indicate that longer hospital stays significantly increase the likelihood of *E. coli* developing antibiotic resistance.

The forest plot revealed a high degree of heterogeneity at 85.92% and a pooled estimate of the odds ratio for risk factors associated with multidrug resistance in *E. coli* of 1.266 (OR = 1.266; 95% CI: 0.804–1.992) (Fig. 7).

Random effects model: I^2 = 85.92%; Q value = 113.64; df = 16. The diamond at the base indicates the pooled estimate from all studies.

Publication bias

The funnel plots, along with Egger's linear regression test, indicated publication bias among the odds ratios of risk factors associated with multidrug-resistant *E. coli*, (Fig. 8, Z = 1.019, P = 0. 308). Random effects model I^2 = 85.921%; Q value = 113.642; df = 16.

The pooled estimate of odds ratio of previous antibiotic use

According to the study's pooled odds ratio estimate for prior antibiotic use, a history of antibiotic use was the primary risk factor associated with increased likelihood of multidrug resistance in *E. coli*. The forest plot revealed that the odds ratio for prior antibiotic use averaged 1.326 (OR = 1.326; 95%CI: 0.837–2.102) (Fig. 9).

The pooled estimate of odds ratio of length of hospital stay

According to the forest plot, the odds ratio for length of hospital stay was estimated to be 1.162 (OR = 1.162; 95%CI: 0.340–3.973) (Fig. 10).

Discussion

For the qualitative evaluation, a total of 28 papers involving *E. coli* isolates from various samples were chosen, while 23 studies were selected for the quantitative prevalence study. The meta-analysis of these 23 publications revealed that the overall prevalence of multidrug-resistant *E. coli* in the human population was 36.5% (95% CI:

24.6–50.3), with high heterogeneity at 99.13%. Compared to the study conducted by [42] on water samples in Africa, where 71.7% (95% CI: 56.2–83.3) was observed, our findings indicate a lower outcome. Additionally, [43] reported a combined prevalence of antibiotic resistance in *E. coli* from urinary tract infections in Iran at 49.9%, showing a higher prevalence compared to our study. The estimated prevalence of *E. coli* among pregnant women in Iran, based on polling data, was 29% (95% CI: 23–36%), according to the study by [44]. Our meta-analysis revealed a significantly higher prevalence compared to the study by [45], which reported a prevalence of 5% in meat samples from Ethiopia. Additionally, a study by [46] indicated an overall 15.3% of *E. coli* in cervical secretions of mothers in India.

A different study by [47] reported that 15% of Ethiopian meals with animal origin had a pooled prevalence of *E. coli.* In another study by [48], the combined prevalence of *E. coli* in urine samples from Ethiopia was 41% (95% CI: 38–45%). Furthermore, [49] found that 24.7% of pregnant women had *E. coli*, which was lower than our findings. Several factors such as differences in antibiotic prescribing practices, number of included studies, geographical location, publication year, social and personal health statuses of communities, sample sizes, source and detection methods (employing molecular techniques in addition to traditional culturing methods) may contribute to these discrepancies. Our study revealed a comparatively high prevalence of *E. coli* when compared to many of these results, suggesting a global increase in antibiotic resistance among *E. coli* strains. Specifically, samples from children and pregnant women exhibited higher prevalence rates of *E. coli* isolates in our investigation.

The subgroup analysis results based on continents in this study indicate that 41.7% (95% CI: 29.5–55.0%) of the population had *E. coli*. In Europe, the lowest estimated prevalence of *E. coli* resistant to drugs was 29.3% (95% CI: 27.7–30.9%). The usage of antibiotics, accessibility of medical services, or other relevant factors may be contributing factors. America had the highest estimated prevalence of the outcome, at 57.9% (95% CI: 52–63.5%). This increase may result from the recent development of new and advanced detection techniques and the growing awareness among specialists of the threat posed by *E. coli* strains, particularly in industrialized nations.

The risk factors associated with multidrug-resistant *E. coli* isolated from human and animal samples are identified in 28 investigations conducted across various nations. The study results revealed that several independent risk factors increase the likelihood of multidrug resistance in *E. coli*: sex, age, metastasis, liver cirrhosis, and recent digestive surgery within the last year, consumption of organic food, urinary tract infection within the previous year, acquisition in a medical facility, and farming. A comprehensive meta-analysis was performed on a hospital stay duration and prior antibiotic treatment across more than two studies. The pooled estimate of the odds ratio for risk factors linked to multidrug resistance in *E. coli* was 1.266 (OR = 1.266; 95% CI: 0.804–1.992), with a high heterogeneity of 85.92% according to the meta-analysis results.

Eleven studies yielded an odds ratio (OR) of 1.266 (95% CI: 0.804–1.992) for antimicrobial resistance in *E. coli*, highlighting antibiotic use as the primary risk factor for this increase. Supporting this finding, a study on community-dwelling children in the Asia-Pacific region conducted in China [50] reported an OR of 2.65 (95% CI: 1.70–4.12). Horizontal gene transfer is a crucial mechanism facilitating the rapid spread of antibiotic-resistance genes among gram-negative bacteria, including *E. coli* strains [51], [52]. Accurately describing drug resistance patterns in *E. coli* is essential for reducing its global spread.

Efflux pump systems likely contribute to multidrug resistance, with multidrug efflux systems being the most prevalent mechanism of bacterial resistance to antimicrobial medications is multidrug efflux systems, [53], [54]. These efflux pumps facilitate increased antibiotic diffusion, identified as a significant factor in the development of antibiotic resistance within bacterial biofilm structures [55]. The widespread use of antibiotics, particularly broad-

spectrum ones, promotes the evolution of specialized drug defense mechanisms in microorganisms [53], [56]. Antibiotic resistance has become one of the most important public health concerns of the twenty-first century, having escalated rapidly in recent years [53]. There is compelling evidence that overusing or misusing antibiotics in farm animals leads to an increase in antibiotic-resistant bacteria [57]. Both innate and acquired resistance pathways contribute to *E. coli'*s resistance to antibiotics [58].

With an odds ratio (OR) of 1.162 (95% CI: 0.340–3.973), our investigation indicated that the duration of hospital stay is the second risk factor for the emergence of multidrug resistance in *E. coli*. This finding aligns with the results from [50], conducted in China, which reported an OR of 3.43 (95% CI: 2.13–5.51). Hospitals, due to extensive antibiotic usage in treating illnesses, are major environments where antimicrobial resistance can develop. During antibiotic treatment, patients' resistant strains can proliferate, potentially spreading to medical staff or other patients in confined hospital settings [59].

Limitations of the study

This research focused on multidrug-resistant *E. coli*, providing valuable insights into this significant health concern. Although this study primarily addressed *E. coli*, it highlights the need for further investigation into less common germs, which may have different prevalence rates. Future research could build on our findings to mitigate some limitations, such as the limited number of combined risk factors. Expanding the assessment to include more risk factors in future studies will enhance our understanding and improve the robustness of the conclusions drawn.

Conclusion

The study's findings indicate that the years with the lowest and highest occurrences of multidrug-resistant *E. coli* were 2019 and 2016, respectively. Poland had the lowest incidence estimate, while the Czech Republic had the highest prevalence estimate. This systematic review and meta-analysis confirmed several critical risk factors associated with an increased capacity for germs to become resistant to multiple drugs. Notably, routine use of antibiotics significantly contributes to antimicrobial resistance in humans and animals, with effects persisting for up to six months after an antibiotic prescription. Addressing these risk factors is essential to mitigate the problem of antibiotic resistance and improve the future use of antibiotics, it is important to take into account these risk factors. Implementing strategies to reduce multidrug resistance in harmful organisms, such as *E. coli*, will improve future antibiotic use and reduce the burden of resistance on public health.

Declarations

Authors Contribution

TS, DD and AM conceived the idea and designed the study. TS and AM collected data and reviewed the literature. TS and DD extracted data and appraised the studies. TS and AM participated in data analysis, interpreted the results, and drafted the manuscript. DD reanalyzed the data. All authors reviewed, discussed, provided critical comments, approved the final manuscript, and accepted responsibility for publication. The corresponding author had full access to all the data in the study.

Funding

This work is not financially supported any project

Ethics approval

The conducted review is not related to either human or animal use.

Consent for publication

Not applicable.

Competing interests

The authors declare that there are no conflicts of interest.

Clinical trial number

Not applicable.

Data availability statement

All data used to support the findings are included within the article

Author's detail

[1] Department of Biology, College of Sciences, Bahir Dar University, Bahir Dar, Ethiopia, [2]Department of Biology, College of Sciences, Bahir Dar University, Bahir Dar, Ethiopia, [3]Department of Medical Laboratory Science, College of Medicine and Health Science, Jigjiga University, Jigjiga, Ethiopia.

References

1. WHO. World Health Organization. Global action plan on antimicrobial resistance. Accessed from https://www.who.int/publications/i/item/9789241509763 on 19 March 2024 2016.
2. WHO. World Health Organization. Global Antimicrobial Resistance and Use Surveillance System (GLASS) report. Accessed from https://www.who.int/publications/i/item/9789240005587 on 19 March 2024 2020.
3. Adam RD. Antimicrobial resistance at a community level. The Lancet Planetary Health. 2018;2(11):e473-e4.
4. De Oliveira DM, Forde BM, Kidd TJ, Harris PN, Schembri MA, Beatson SA, *et al*. Antimicrobial resistance in ESKAPE pathogens. Clinical microbiology reviews. 2020;33(3):10.1128/cmr. 00181-19.
5. Organization WH. World Health Organization Ten threats to global health in 2019. Retrieved on September. 2019;22:2021.
6. Kaper JB, Nataro JP, Mobley HL. Pathogenic *Escherichia coli.* Nature reviews microbiology. 2004;2(2):123-40.
7. Weese J, Giguère S, Guardabassi L, Morley P, Papich M, Ricciuto D, et al. ACVIM consensus statement on therapeutic antimicrobial use in animals and antimicrobial resistance. Journal of Veterinary Internal Medicine. 2015;29(2):487-98.
8. Collignon P, Beggs JJ. Socioeconomic enablers for contagion: factors impelling the antimicrobial resistance epidemic. Antibiotics. 2019;8(3):86.
9. Saliu E-M, Vahjen W, Zentek J. Types and prevalence of extended–spectrum beta–lactamase producing *Enterobacteriaceae* in poultry. Animal Health Research Reviews. 2017;18(1):46-57.

10. Sapkota S, Adhikari S, Pandey A, Khadka S, Adhikari M, Kandel H, *et al.* Multi-drug resistant extended-spectrum beta-lactamase producing *E. coli* and *Salmonella* on raw vegetable salads served at hotels and restaurants in Bharatpur, Nepal. BMC Res Notes. 2019;12(1):516. Epub 20190816. doi: 10.1186/s13104-019-4557-9. PubMed PMID: 31420003; PubMed Central PMCID: PMCPMC6697966.
11. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, *et al.* The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Bmj. 2021;372.
12. Haidich A-B. Meta-analysis in medical research. Hippokratia. 2010;14(Suppl 1):29.
13. Hadifar A, Bitew SK, Deleu J, Develder C, Demeester T. Eduqg: A multi-format multiple-choice dataset for the educational domain. IEEE Access. 2023;11:20885-96.
14. Arhoune B, El Fakir S, Himri S, Moutaouakkil K, El Hassouni S, Benboubker M, *et al.* Intense intestinal carriage and subsequent acquisition of multidrug-resistant enterobacteria in neonatal intensive care unit in Morocco. PLoS One. 2021;16(6):e0251810.
15. Assawatheptawee K, Treebupachatsakul P, Luangtongkum T, Niumsup PR. Risk factors for community-acquired urinary tract infections caused by multidrug-resistant enterobacterales in Thailand. Antibiotics. 2022;11(8):1039.
16. Biset S, Moges F, Endalamaw D, Eshetie S. Multi-drug resistant and extended-spectrum β-lactamases producing bacterial uropathogens among pregnant women in Northwest Ethiopia. Annals of clinical microbiology and antimicrobials. 2020;19:1-9.
17. Bumbangi FN, Llarena A-K, Skjerve E, Hang'ombe BM, Mpundu P, Mudenda S, *et al.* Evidence of community-wide spread of multi-drug resistant *Escherichia coli* in young children in Lusaka and Ndola districts, Zambia. Microorganisms. 2022;10(8):1684.
18. Zahlane K, Ouafi AT, Barakate M. The clinical and epidemiological risk factors of infections due to multi-drug resistant bacteria in an adult intensive care unit of University Hospital Center in Marrakesh-Morocco. Journal of infection and public health. 2020;13(4):637-43.
19. Fernández-Martínez NF, Cárcel-Fernández S, De la Fuente-Martos C, Ruiz-Montero R, Guzmán-Herrador BR, León-López R, et al. Risk factors for multidrug-resistant gram-negative bacteria carriage upon admission to the intensive care unit. International Journal of Environmental Research and Public Health. 2022;19(3):1039.
20. Gomila Grange A, Shaw Perujo E, Carratalà J, Leibovici L, Tebé C, Wiegand I, *et al.* Predictive factors for multidrug-resistant gram-negative bacteria among hospitalised patients with complicated urinary tract infections. Antimicrobial Resistance and Infection Control, 2018, vol 7, num 111. 2018.
21. Hu Y, Rubin J, Mussio K, Riley LW. Risk factors for faecal carriage of multidrug-resistant *Escherichia coli* in a college community: A penalised regression model. Journal of Global Antimicrobial Resistance. 2021;26:166-73.
22. Lee D-S, Ryu J-A, Chung CR, Yang J, Jeon K, Suh GY, *et al.* Risk factors for acquisition of multidrug-resistant bacteria in patients with anastomotic leakage after colorectal cancer surgery. International journal of colorectal disease. 2015;30:497-504.
23. Lin T, Chang P, Chen I, Lai W, Chen Y, Li W, *et al.* Risk factors and mortality associated with multi-drug-resistant Gram-negative bacterial infection in adult patients following abdominal surgery. Journal of Hospital Infection. 2022;119:22-32.
24. Mandal AK, Talukder S, Hasan MM, Tasmim ST, Parvin MS, Ali MY, *et al.* Epidemiology and antimicrobial resistance of *Escherichia coli* in broiler chickens, farmworkers, and farm sewage in Bangladesh. Veterinary Medicine and Science. 2022;8(1):187-99.

25. Mesele F, Leta S, Amenu K, Abunna F. Occurrence of *Escherichia coli* O157: H7 in lactating cows and dairy farm environment and the antimicrobial susceptibility pattern at Adami Tulu Jido Kombolcha District, Ethiopia. BMC Veterinary Research. 2023;19(1):6.
26. Mohamed N, Ghazal A, Ahmed AAH, Zaki A. Prevalence and determinants of antimicrobial resistance of pathogens isolated from cancer patients in an intensive care unit in Alexandria, Egypt. Journal of the Egyptian Public Health Association. 2023;98(1):9.
27. Nabti LZ, Sahli F, Radji N, Mezaghcha W, Semara L, Aberkane S, *et al*. High prevalence of multidrug-resistant *Escherichia coli* in urine samples from inpatients and outpatients at a tertiary care hospital in Setif, Algeria. Microbial Drug Resistance. 2019;25(3):386-93.
28. Ortiz-Díez G, Mengíbar RL, Turrientes M-C, Artigao M-RB, Gallifa RL, Tello AM, *et al.* Prevalence, incidence and risk factors for acquisition and colonization of extended-spectrum beta-lactamase-and carbapenemase-producing *Enterobacteriaceae* from dogs attended at a veterinary hospital in Spain. Comparative Immunology, Microbiology and Infectious Diseases. 2023;92:101922.
29. Patolia S, Abate G, Patel N, Patolia S, Frey S. Risk factors and outcomes for multidrug-resistant Gram-negative bacilli bacteremia. Therapeutic advances in infectious disease. 2018;5(1):11-8.
30. Renk H, Stoll L, Neunhoeffer F, Hölzl F, Kumpf M, Hofbeck M, *et al*. Suspicion of respiratory tract infection with multidrug-resistant *Enterobacteriaceae*: epidemiology and risk factors from a Paediatric Intensive Care Unit. BMC infectious diseases. 2017;17:1-9.
31. Salamonowicz-Bodzioch M, Frączkiewicz J, Czyżewski K, Zając-Spychała O, Gorczyńska E, Wróbel G, *et al*. Analysis of incidence and risk factors of the multidrug resistant gastrointestinal tract infection in children and adolescents undergoing allogeneic and autologous hematopoietic cell transplantation: a nationwide study. Annals of Hematology. 2022;101:191-201.
32. Salgado-Caxito M, Benavides JA, Munita JM, Rivas L, García P, Listoni FJ, *et al*. Risk factors associated with faecal carriage of extended-spectrum cephalosporin-resistant *Escherichia coli* among dogs in Southeast Brazil. Preventive Veterinary Medicine. 2021;190:105316.
33. Šámal V, Paldus V, Fáčková D, Mečl J. Multidrug-resistant bacteria in urine culture among patients with spinal cord injury and disorder: Time to first detection and analysis of risk factors. Spinal Cord. 2022;60(8):733-8.
34. Sarba EJ, Kelbesa KA, Bayu MD, Gebremedhin EZ, Borena BM, Teshale A. Identification and antimicrobial susceptibility profile of *Escherichia coli* isolated from backyard chicken in and around ambo, Central Ethiopia. BMC veterinary research. 2019;15:1-8.
35. Shaikh S, Fatima J, Shakil S, Rizvi SMD, Kamal MA. Risk factors for acquisition of extended spectrum beta lactamase producing *Escherichia coli* and *Klebsiella pneumoniae* in North-Indian hospitals. Saudi Journal of Biological Sciences. 2015;22(1):37-41.
36. Sharif MR, Soltani B, Moravveji A, Erami M, Soltani N. Prevalence and risk factors associated with extended spectrum beta lactamase producing *Escherichia coli* and *Klebsiella pneumoniae* isolates in hospitalized patients in Kashan (Iran). Electronic physician. 2016;8(3):2081.
37. Tola MA, Abera NA, Gebeyehu YM, Dinku SF, Tullu KD. High prevalence of extended-spectrum beta-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae* fecal carriage among children under five years in Addis Ababa, Ethiopia. PloS one. 2021;16(10):e0258117.
38. van Dulm E, Tholen AT, Pettersson A, van Rooijen MS, Willemsen I, Molenaar P, *et al*. High prevalence of multidrug resistant *Enterobacteriaceae* among residents of long term care facilities in Amsterdam, the Netherlands. PLoS One. 2019;14(9):e0222200.

39. Wang X, Li Q, Kang J, Yin D, Li X, Wang S, *et al.* Mortality risk factors and prognostic analysis of patients with multi-drug resistant Enterobacterales infection. Infection and Drug Resistance. 2022:3225-37.
40. Wu P-C, Cheng M-F, Wang J-L. Risk factors and prevalence of mcr-1-positive *Escherichia coli* in fecal carriages among community children in Southern Taiwan. Frontiers in Microbiology. 2021;12:748525.
41. Zeng Y, Deng L, Zhou X, Zhang C, Hu Z, Chen Y, *et al*. Prevalence and risk factors of tet (X4)-positive *Enterobacteriaceae* in human gut microbiota. Journal of Global Antimicrobial Resistance. 2022;31:15-21.
42. Ramatla T, Ramaili T, Lekota KE, Ndou R, Mphuti N, Bezuidenhout C, *et al.* A systematic review and meta-analysis on prevalence and antimicrobial resistance profile of *Escherichia coli* isolated from water in africa (2000–2021). Heliyon. 2023.
43. Hadifar S, Moghoofei M, Nematollahi S, Ramazanzadeh R, Sedighi M, Salehi-Abargouei A, *et al*. Epidemiology of multidrug resistant uropathogenic *Escherichia coli* in Iran: a systematic review and meta-analysis. Japanese journal of infectious diseases. 2017;70(1):19-25.
44. Moradi Y, Eshrati B, Motevalian SA, Majidpour A, Baradaran HR. A systematic review and meta-analysis on the prevalence of *Escherichia coli* and extended-spectrum β-lactamase-producing *Escherichia coli* in pregnant women. Archives of gynecology and obstetrics. 2021;303:363-79.
45. Zelalem A, Sisay M, Vipham JL, Abegaz K, Kebede A, Terefe Y. The prevalence and antimicrobial resistance profiles of bacterial isolates from meat and meat products in Ethiopia: a systematic review and meta-analysis. International Journal of Food Contamination. 2019;6:1-14.
46. Padhi BK, Manna S, Pallepogula DR, Kumar J, Joshi B, Sah R, *et al*. Prevalence of Gram-negative Bacteria in Maternal Cervical Secretions: A Systematic Review and Meta-analysis. Prevalence. 2022;1(4).
47. Assefa A, Bihon A. A systematic review and meta-analysis of prevalence of *Escherichia coli* in foods of animal origin in Ethiopia. Heliyon. 2018;4(8).
48. Chelkeba L, Fanta K, Mulugeta T, Melaku T. Bacterial profile and antimicrobial resistance patterns of common bacteria among pregnant women with bacteriuria in Ethiopia: a systematic review and meta-analysis. Archives of Gynecology and Obstetrics. 2022;306(3):663-86.
49. Minisha F, Mohamed M, Abdulmunem D, El Awad S, Zidan M, Abreo M, *et al*. Bacteriuria in pregnancy varies with the ambiance: a retrospective observational study at a tertiary hospital in Doha, Qatar. Journal of Perinatal Medicine. 2019;48(1):46-52.
50. Chan YQ, Chen K, Chua GT, Wu P, Tung KTS, Tsang HW, *et al*. Risk factors for carriage of antimicrobial-resistant bacteria in community dwelling-children in the Asia-Pacific region: a systematic review and meta-analysis. JAC-Antimicrobial Resistance. 2022;4(2):dlac036.
51. Chamosa LS, Álvarez VE, Nardelli M, Quiroga MP, Cassini MH, Centrón D. Lateral antimicrobial resistance genetic transfer is active in the open environment. Scientific reports. 2017;7(1):513.
52. Leungtongkam U, Thummeepak R, Tasanapak K, Sitthisak S. Acquisition and transfer of antibiotic resistance genes in association with conjugative plasmid or class 1 integrons of Acinetobacter baumannii. PLoS One. 2018;13(12):e0208468.
53. Wójcicki M, Świder O, Daniluk KJ, Średnicka P, Akimowicz M, Roszko MŁ, *et al*. Transcriptional regulation of the multiple resistance mechanisms in *Salmonella*—a review. Pathogens. 2021;10(7):801.
54. Ramatla T, Mileng K, Ndou R, Tawana M, Mofokeng L, Syakalima M, *et al*. Campylobacter jejuni from slaughter age broiler chickens: genetic characterization, virulence, and antimicrobial resistance genes. International Journal of Microbiology. 2022;2022.

55. Soto SM. Role of efflux pumps in the antibiotic resistance of bacteria embedded in a biofilm. Virulence. 2013;4(3):223-9.
56. Połaska M, Sokołowska B. Bacteriophages—a new hope or a huge problem in the food industry. AIMS microbiology. 2019;5(4):324.
57. Dehkordi MK, Halaji M, Nouri S. Prevalence of class 1 integron in *Escherichia coli* isolated from animal sources in Iran: a systematic review and meta-analysis. Tropical Medicine and Health. 2020;48.
58. Galindo-Méndez M. Antimicrobial resistance in *Escherichia coli*. *E Coli* Infections-Importance of Early Diagnosis and Efficient Treatment. 2020:1-20.
59. Struelens MJ. The epidemiology of antimicrobial resistance in hospital acquired infections: problems and possible solutions. Bmj. 1998;317(7159):652-4.

Figures

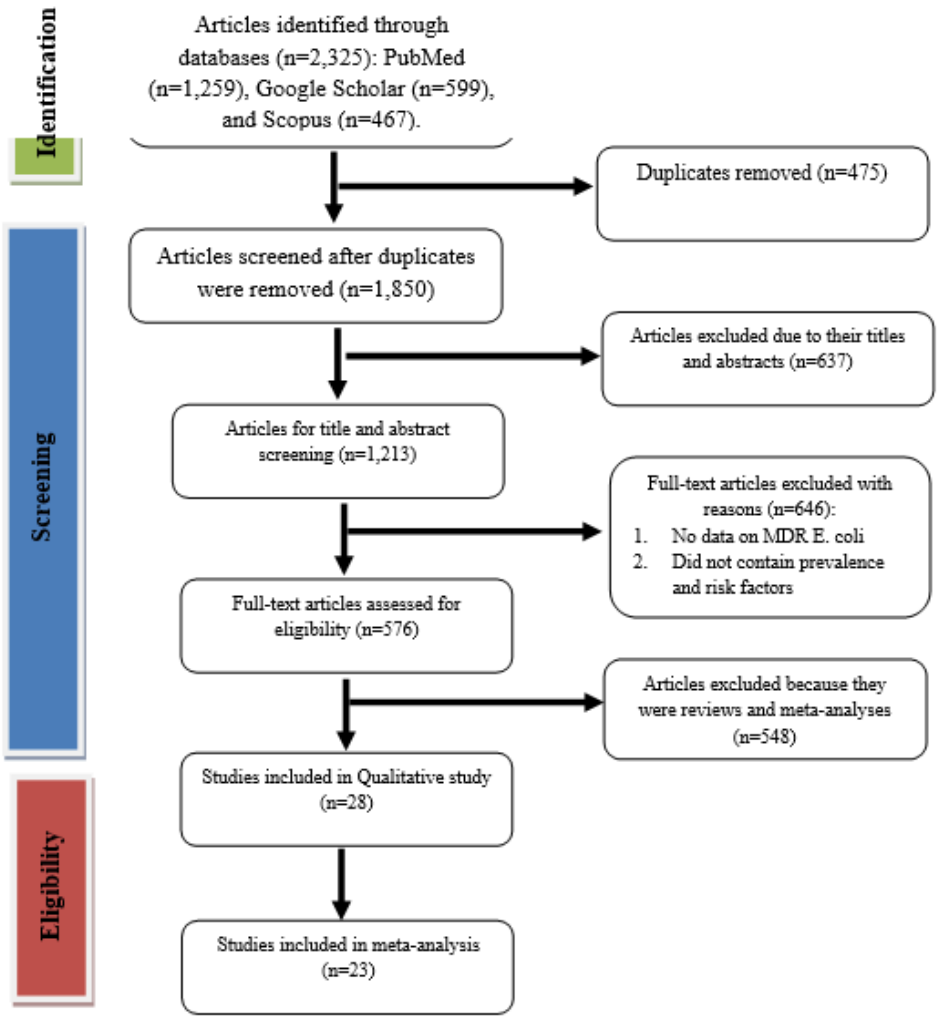

Figure 1

A flow diagram showing the selection of articles for the systematic review and meta-analysis

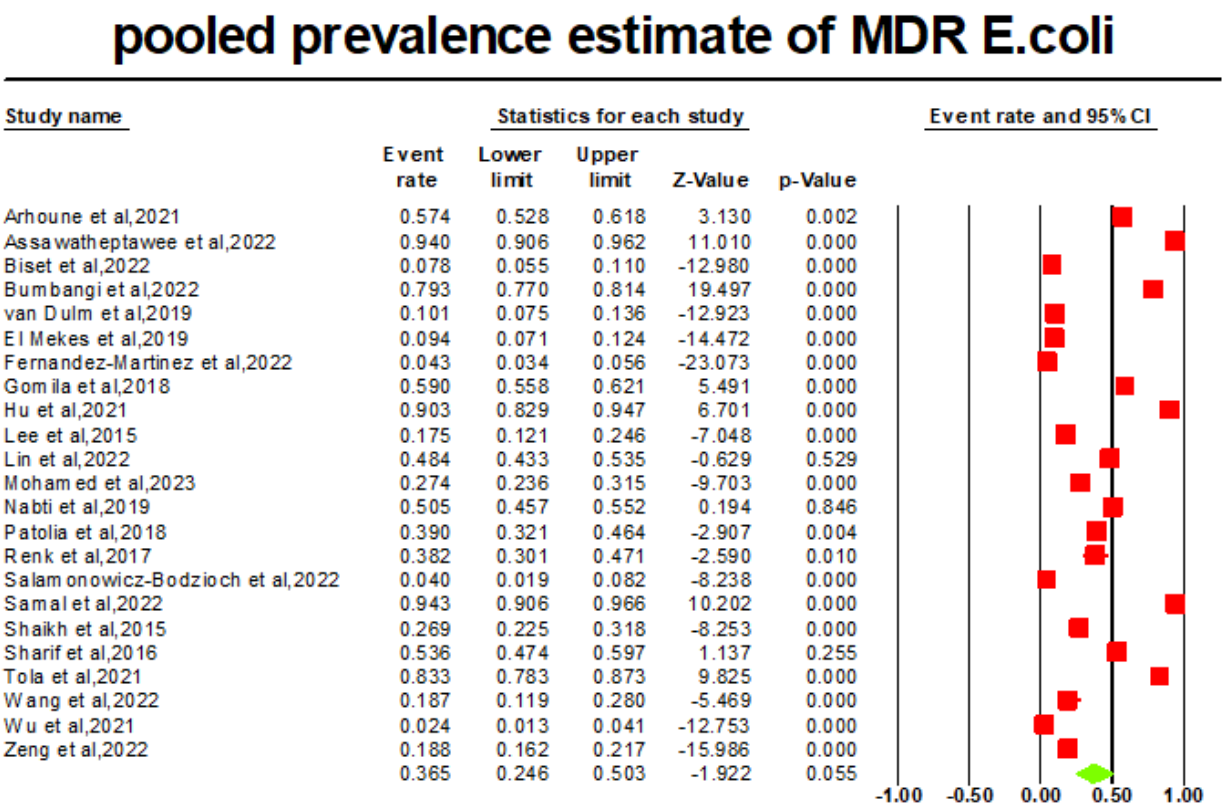

Figure 2

Forest plot showing pooled prevalence of multidrug-resistant *E. coli* globally (2015-2023).

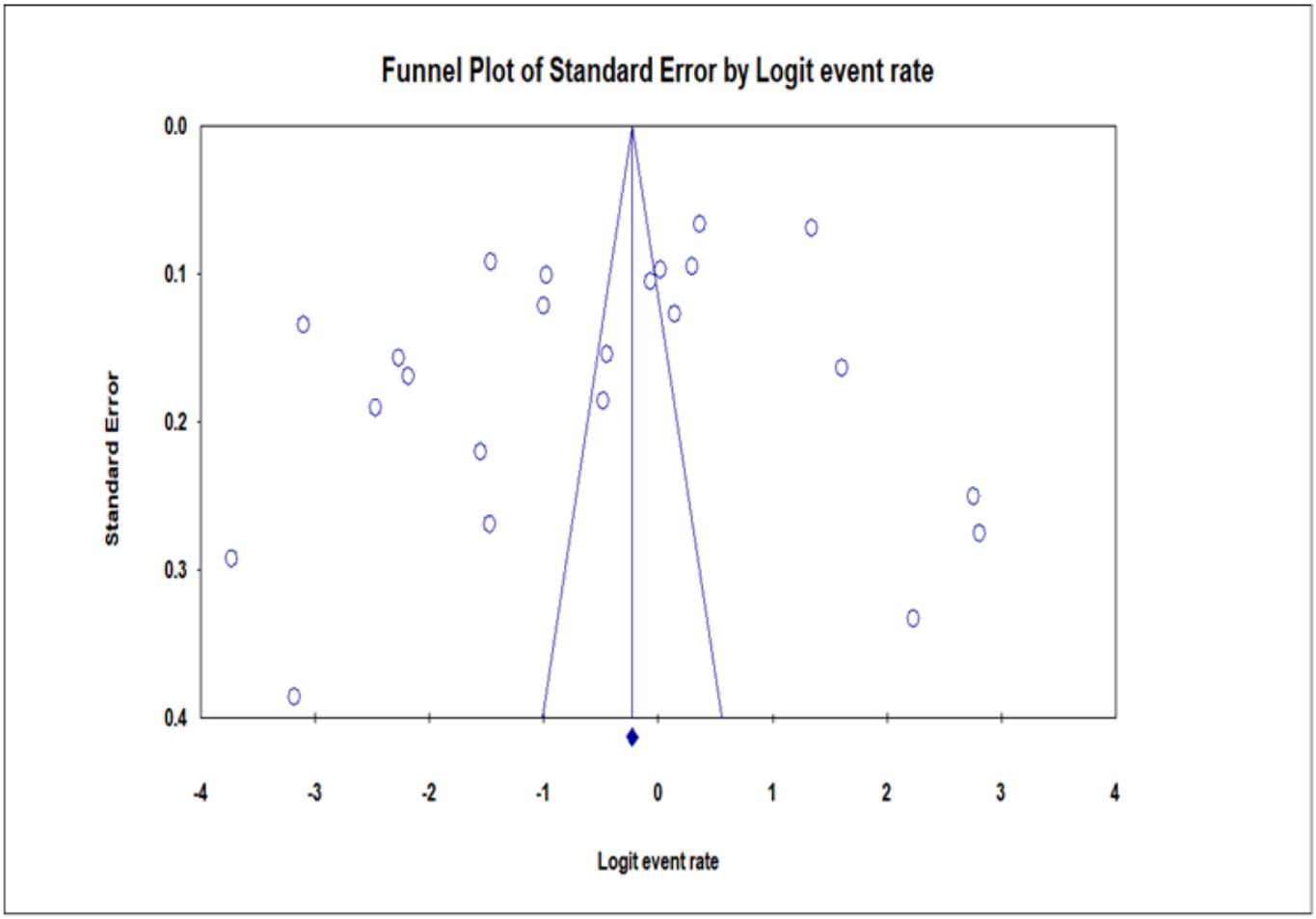

Figure 3

Funnel plot showing the pooled prevalence estimate of the study Subgroup analysis

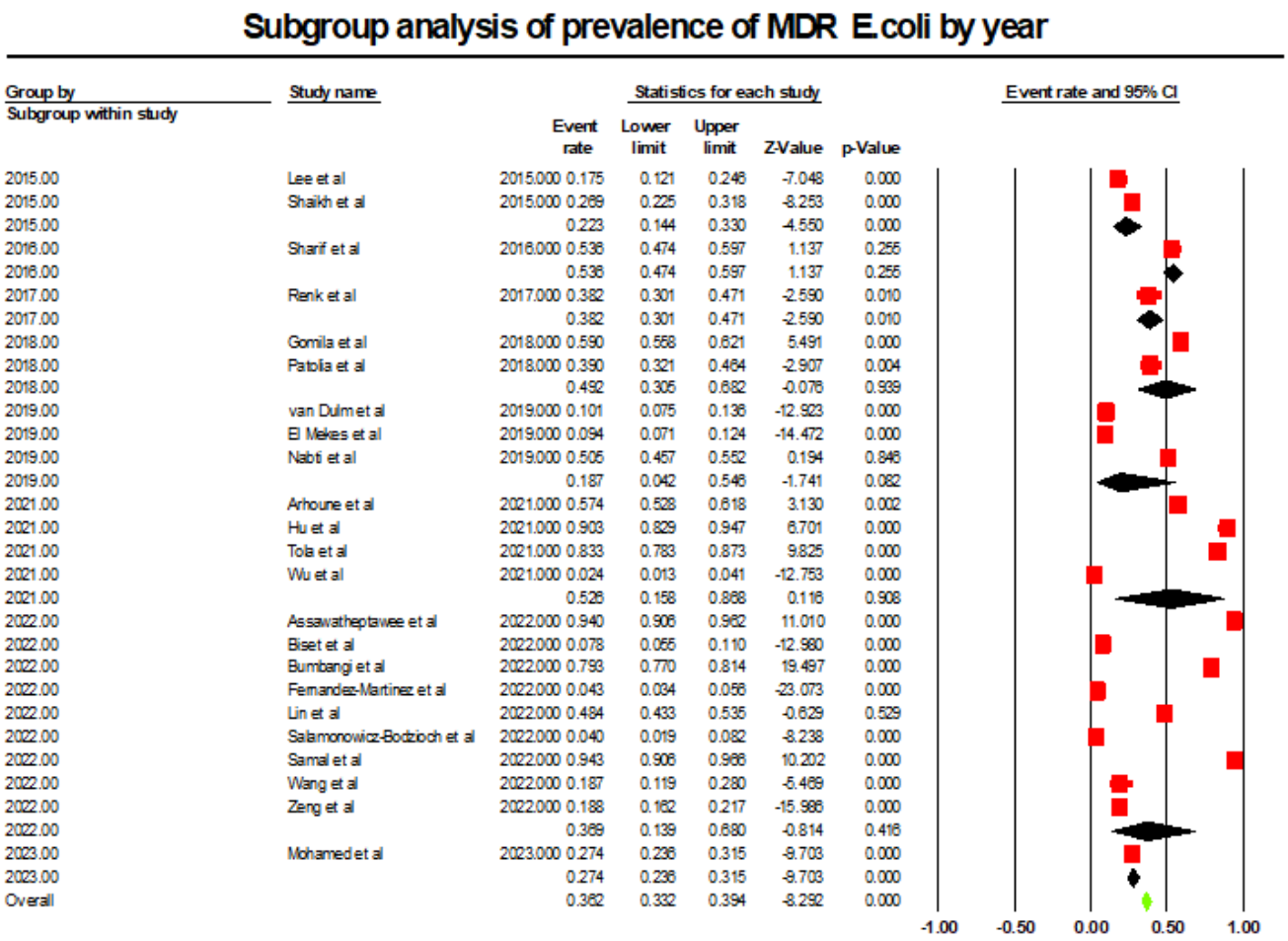

Figure 4

Forest plot showing subgroup analysis of the prevalence of multidrug-resistant *E. coli* by publication year Subgroup analysis by country

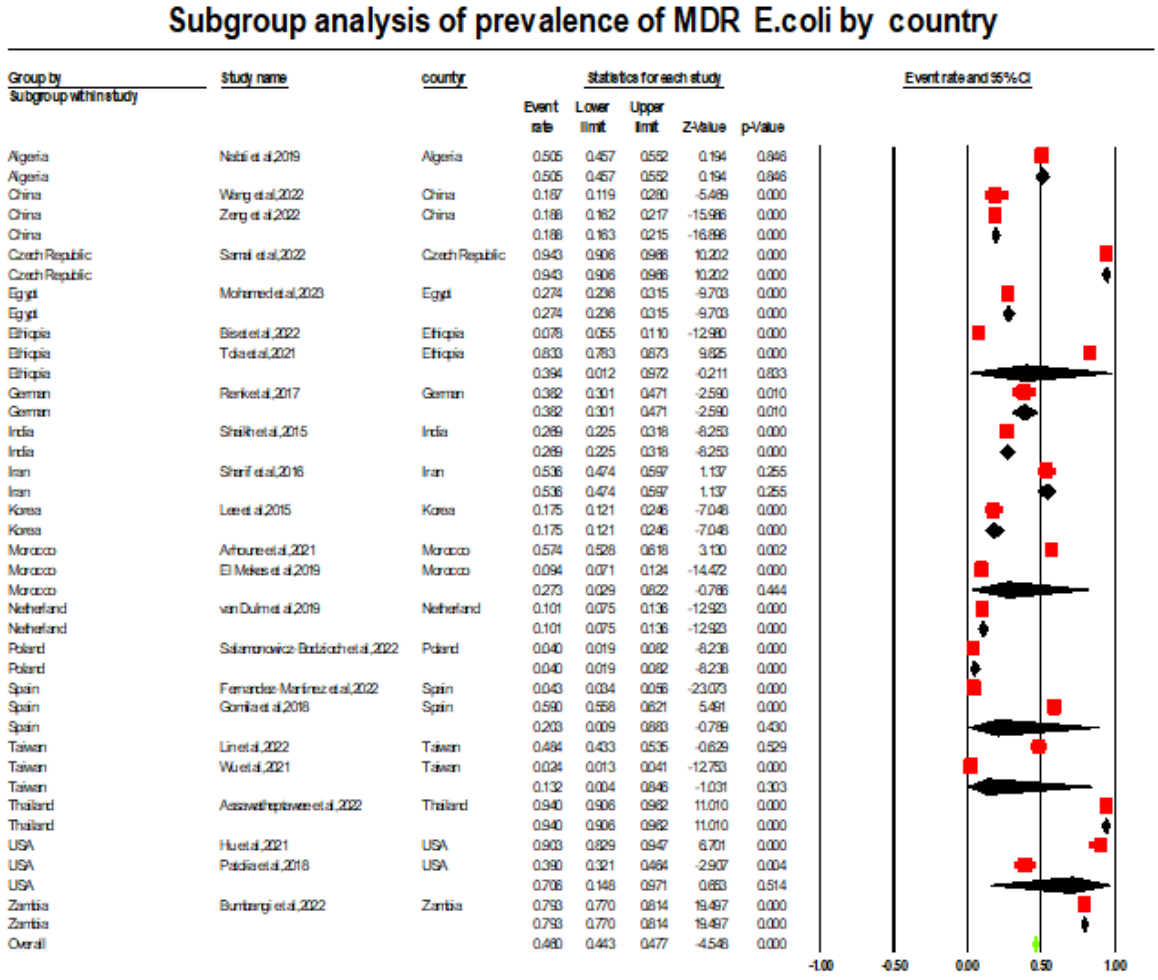

Figure 5

Forest plot showing subgroup analysis of the prevalence of multidrug-resistant *E. coli* by country

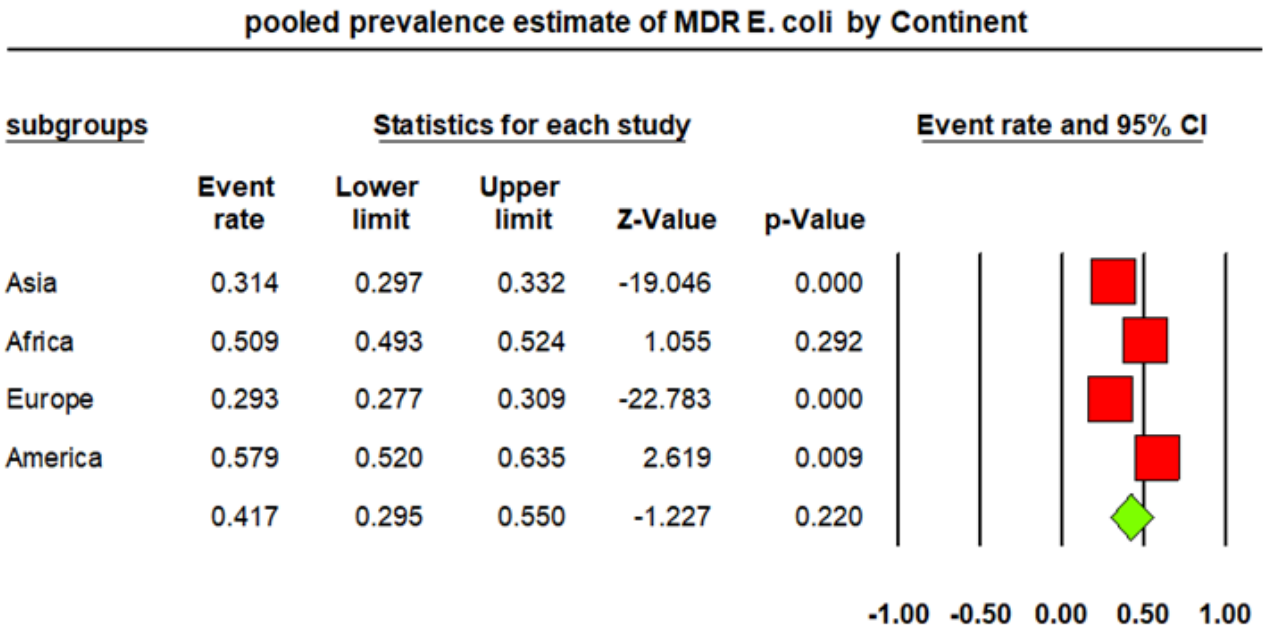

Figure 6

Forest plot showing the pooled prevalence estimate of MDR *E. coli* grouping by continent

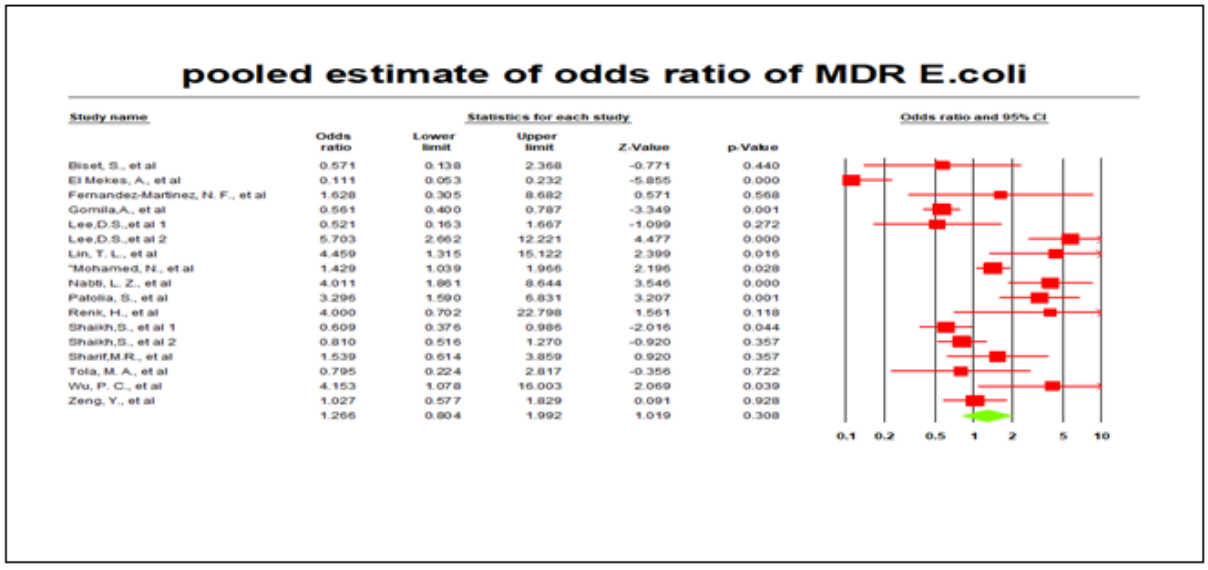

Figure 7

Forest plot showing the pooled odds ratio of risk factors associated with multidrug-resistant *E. coli* globally from 2015 and 2023.

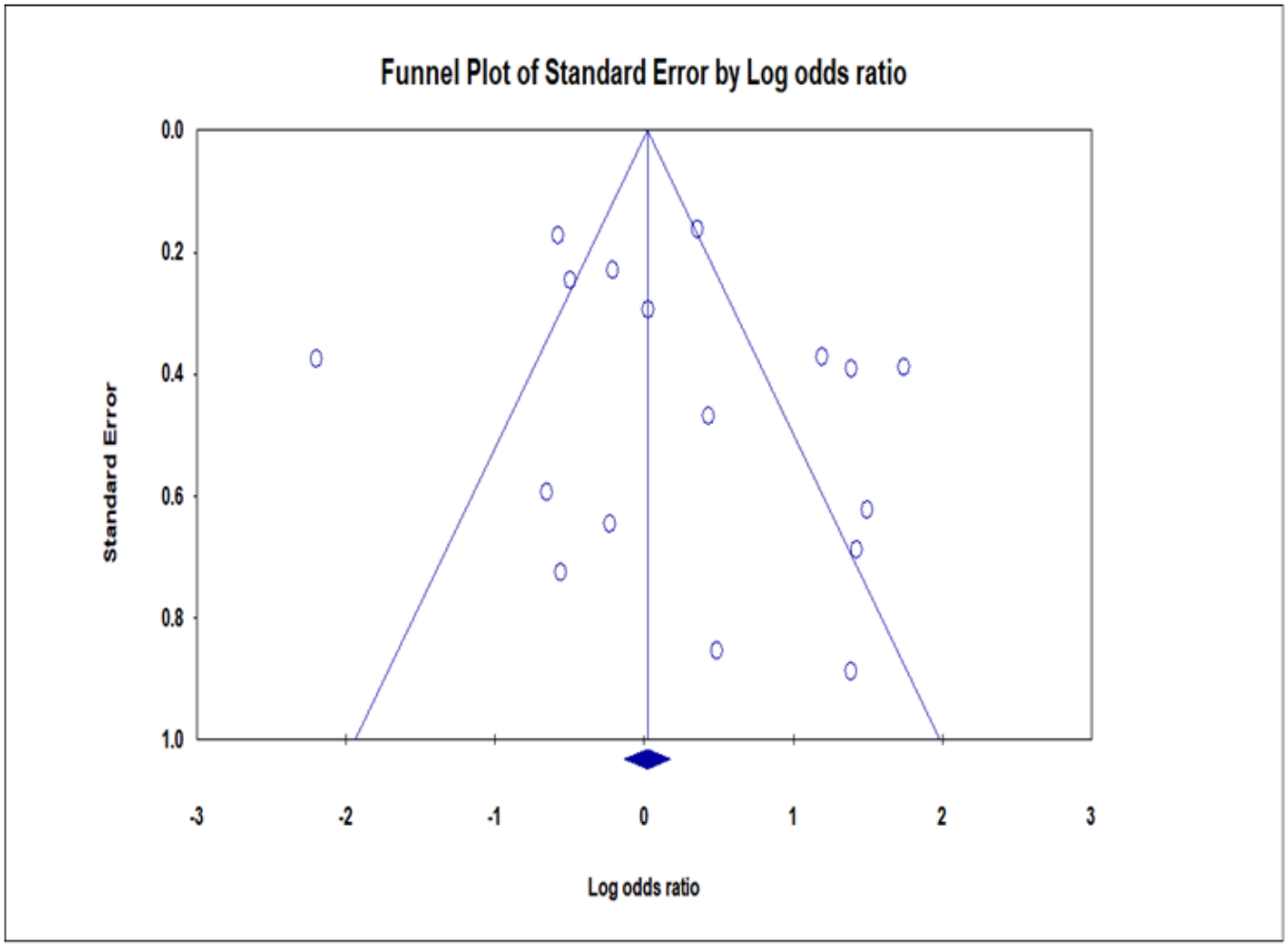

Figure 8

Funnel plot of the pooled odds ratio of the two risk factors in the study (with pseudo-95% confidence intervals)

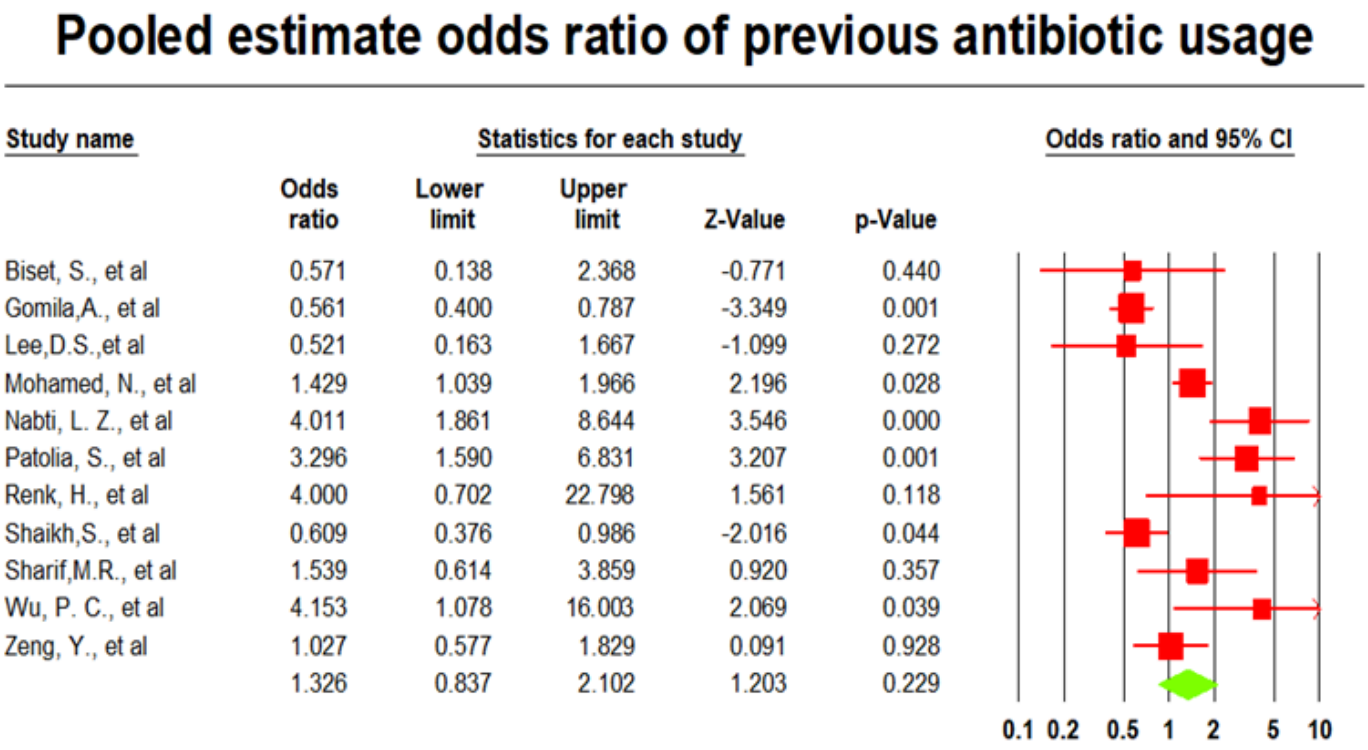

Figure 9

Forest plot showing the pooled odds ratio estimate of the previous antibiotic usage with a 95% confidence interval

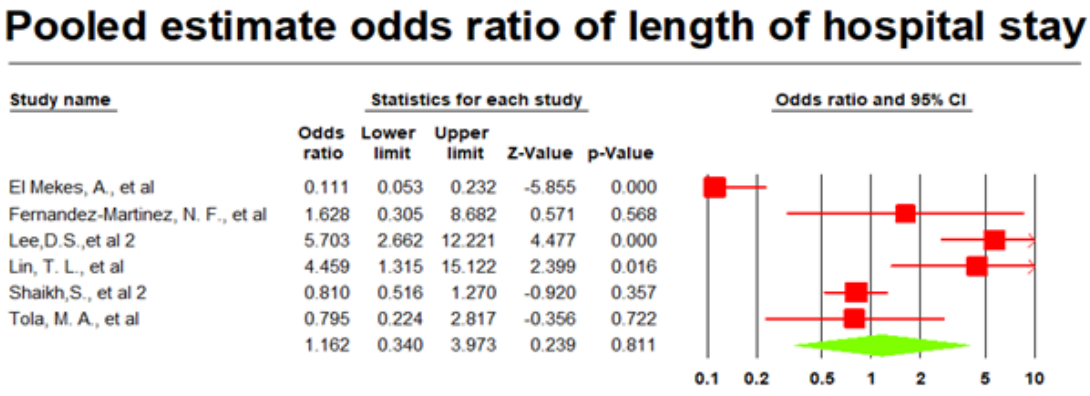

Figure 10

Forest plot showing the pooled estimated odds ratio of the length of hospital stay