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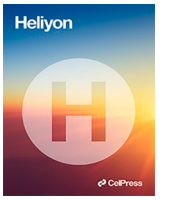

Research article

Bacterial etiology of community-acquired pneumonia among adult patients in Ethiopia: A systematic review and meta-analysis

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ABSTRACT

Background and objective: According to the Global Burden of Diseases, Injuries, and Risk Factors, lower respiratory infections cause more than 2.3 million deaths globally, with a majority occurring in sub-Saharan Africa, including Ethiopia.

Community-acquired pneumonia (CAP) is a major contributor to global mortality and morbidity. Understanding the prevalence and common bacterial causes of CAP is crucial for clinicians to accurately diagnose and improve patient satisfaction. The purpose of this systematic review was to report the pooled prevalence and common bacterial etiologies of CAP among adult patients in Ethiopia.

Methods: This review was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. A comprehensive search of the published articles between January 2000 and October 2022 was performed using open access electronic databases such as PUBMED, Science Direct, CINAHL, HINARI, Google Scholar, and local university repositories. Cochrane Q and I^2 values were used to assess heterogeneity among the studies. Publication bias was assessed using funnel plots and Egger's test. The random-effects model was used to estimate the pooled prevalence.

Results and conclusions: Of all the publications that were thoroughly searched, 9 studies with 2496 participants met the criteria for analysis. All of the studies were cross-sectionally designed and most of the studies used convenient sampling techniques. The included studies consisted of two conducted among adult patients diagnosed with CAP and living with HIV/AIDS, while the remaining seven studies were conducted among adult patients diagnosed with CAP without HIV/AIDS. The combined prevalence of bacterial causes of community-acquired pneumonia (CAP) among adult patients was found to be 39.18% (CI 36.34–42.02), with an I^2 of 52.6 and a P value of 0.032. The primary bacterial cause was *Klebsiella pneumoniae* (9.1%), followed by *Streptococcus pneumoniae* (8.11%), and *Staphylococcus aureus* (6.8%). Therefore, it is advisable to introduce a diagnostic tool for identifying specific causative agents and drug resistance, which could lead to improved treatment and better patient outcomes by reducing the need for empirical treatments.

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1. Introduction

1.1. Background

Lower respiratory infections are a significant cause of both morbidity and mortality, particularly in low-income countries like Ethiopia [1,2]. Community-acquired pneumonia (CAP) is an acute illness that results from an infection of the lung parenchyma outside of a hospital setting. Pneumonia can manifest in various ways, ranging from mild cases marked by fever and cough to severe cases resulting in sepsis and respiratory failure [3].

To diagnose CAP, 2011 European Respiratory Society guidelines suggest looking for acute illness with cough and at least one new focal chest sign, fever lasting more than four days, dyspnea or tachypnea, and new lung shadowing on a chest radiograph. Risk factors for developing CAP include a history of pneumonia, chronic respiratory disease, comorbidities, and lifestyle factors such as smoking, alcohol abuse, and overcrowding [3,4]. The leading bacterial cause of CAP is *Streptococcus pneumoniae*, followed by *Staphylococcus aureus*, gram-negative Enterobacteriaceae, and *Pseudomonas aerogenosa* [5–7]. Viruses and fungi can also cause CAP [5,8].

1.2. The burden of community-acquired pneumonia in the world

The annual incidence of CAP in European adults varies between 1.07 and 1.7 per 1000 population, increasing with age [9]. In six Latin American countries, hospitalizations due to pneumonia among adults aged >65 years range from 27,000 in Colombia to 200,000 in Brazil [10]. In the Asia-Pacific region, incidence rates vary, with the highest rate of 30,000 in Southeast Asia [11]. Lower respiratory tract infections, which account for 6.1% of fatalities worldwide, are the leading infectious cause of death, according to data from the World Health Organization (WHO) [12]. According to the Global Burden of Disease 2016 Study, from 2006 to 2016, the overall death rate from low respiratory tract infections fell to 8.2% (95% UI, −12.4, −3.9), and the age-standardized rate to 22.4% (95% UI, −25.3, -18.9) [13]. The mortality rate for CAP in the United States is high, with almost one in three hospitalized patients dying within a year of diagnosis [14].

1.3. The burden of community-acquired pneumonia in Africa

Every year, approximately 4 million cases of pneumonia and 200,000 deaths are reported in sub-Saharan Africa [15]. Research conducted across Africa has revealed that adults with community-acquired pneumonia have varying death rates, such as 19% in Senegal, 18% in Uganda, and 16% in the Central African Republic, with an in-hospital death rate ranging from 6% to 15% [16]. In 2015, CAP was the second leading cause of death in Ethiopia, where pneumonia accounted for the highest morbidity and the second leading cause of mortality among all age groups [2].

Numerous primary studies on bacterial etiology have been conducted across different regions of Ethiopia [17–20], and one systematic review has been conducted on the prevalence of community-acquired pneumonia among children under five years of age [21]. There is no nationally representative data on this aspect. In primary studies bacterial etiologies of community-acquired pneumonia from adult patients, *Streptococcus pneumoniae*, *Klebsiella* species, *S. aureus, H. influenzae*, *Pseudomonas* species and *Acinetobacter* species are frequently isolated with different levels of resistance for different antibiotics [17–20,22,23].

Understanding the prevalence of the bacterial etiology of CAP is very important for researchers, policymakers, and others to allocate resources for the proper management and prevention of this disease. In addition, knowing the specific bacterial etiologies and their distribution in specific localities allows the clinician to make a definitive diagnosis, which, in turn, reduces the emergence of multiple drug-resistant pathogens by decreasing empiric treatment strategies and increasing patient satisfaction. There is no nationally representative data on the prevalence of bacterial etiology of CAP and common bacterial isolates. This systematic review aimed to report common bacterial causes of CAP among adult patients in Ethiopia.

2. Methods

2.1. Study protocol and registration

The methodology, study selection, data extraction, and result reporting for the present review adhered to the Preferred Reporting Items for Systematic Reviews & Meta-Analysis (PRISMA) guidelines 2020 [24] (supporting file 1). The research question was developed based on conditions, context, and population (**COCOPO**) criteria [25]. Endnote (version X8) reference management software was used to download, organize, review, and cite the related articles. The protocol for this review was registered in PROSPERO and the corresponding ID was CRD42022357896 (https://www.crd.york.ac.uk/prospero/).

2.2. Condition

This review focuses on studies that report the pooled prevalence of bacterial etiology in community-acquired pneumonia (CAP) and its common causes as the primary outcome. The initial diagnosis of bacterial CAP is established based on an acute illness characterized by cough and at least one of the following: new focal chest signs, fever lasting more than 4 days, or dyspnea/tachypnea, without any other obvious causes, and is supported by chest radiograph findings showing new lung shadowing. In elderly patients, chest radiograph shadowing is observed alongside an acute clinical illness (unspecified) without any other apparent causes.

2.3. Context

This review includes all primary research articles done in the Ethiopia setting.

2.4. Population

This review included all primary articles that reported the bacterial etiology of CAP among adult patients.

2.5. Search strategy

A comprehensive search of published literature was conducted using electronic databases such as PUBMED, Science Direct, CINAHL, HINARI, and Google Scholar. The search terms were combined using Boolean operators. For example, in PUBMED, the following search terms were used, with some modifications for other databases as presented in the manuscript **(**Supporting **file 2: Table S1)**. (All Fields] OR "Bacteria" [All Fields] [23]1 OR "bacteriology" [All Fields] OR "bacterial profile" [All Fields] OR "bacterial etiology" [All Fields] OR "bacterial isolates" [All Fields] OR "bacterial pathogen" [All Fields] OR ("Bacteria" [MeSH Terms] OR "Microbiology" [MeSH Terms])) AND ("Pneumonia" [MeSH Terms] OR ("bacterial pneumonia" [All Fields] OR "lower respiratory tract infection" [All Fields] OR "acute lower respiratory tract infections" [All Fields] OR "community-acquired" [All Fields] OR "Pneumonia" [All Fields] OR "LRTI" [All Fields] OR "CAP" [All Fields])) AND ("Ethiopia" [All Fields] OR "Ethiopia" [MeSH Terms]). Then, for unpublished works, the institutional repositories of Addis Ababa University, the University of Gondar, and Jimma University were searched. Between January 2000 and October 2022, all English-language studies were deemed eligible for review. On October 16, 2022, the databases were searched. We did not, however, look for any publications in any of the restricted databases (Scopus, Web of Science, and Cochrane Library).

2.6. Eligibility criteria

All primary articles published between 2000 and October 2022 in English in peer-reviewed journals or grey literature among adult Ethiopian patients ($\geq$18 years) suspected to have symptomatic bacterial CAP. We excluded studies if they were not fully accessible.

3. Data extraction and quality assessment

3.1. Data extraction

The data searched in the listed electronic databases were extracted using AMS and AM. The extracted data included the author's last name, year of publication, study design, study area (geographic location), study population, and sample size. Any disagreement between the two authors during the extraction procedure was resolved through exhaustive discussion.

3.2. Risk of bias (quality) assessment

The eligibility of studies for this review was assessed using the JBI quality appraisal checklist for cross-sectional studies to evaluate their quality [26]. The checklist comprises approximately nine items, including the identification of the target population, adequacy of recruitment, sample size, descriptions of subjects and settings, coverage of the identified sample, standardized condition measurement, reliable condition measurement, adequacy of statistical analysis, and response rate adequacy. According to the JBI checklist, studies with a quality score of 50% or higher were considered high-quality and included in the analysis. (Supporting file 3: Table S2).

3.3. Data analysis

For all statistical analyses, the extracted data were imported into Microsoft Excel version 13 and then exported to Stata version 16 (Stata Corporation, College Station, TX, USA). Heterogeneity between trials was evaluated using I^2 statistics and the Cochrane Q test. I2 values of 25%, 50%, and 75% were considered to denote low, medium, and high levels of heterogeneity, respectively. Publication bias was assessed using a funnel plot and Egger's test. A random-effects model (DerSimonian-Laird approach) was used for the study due to evidence of statistical heterogeneity. Additionally, a sensitivity analysis was conducted to determine the impact of a single study on the overall estimate.

3.4. Analysis of subgroups or subsets

Subgroup analysis and meta-regression were utilized to investigate potential sources of variation (such as geographical location, study design, publication year, and sample size) among the studies.

4. Result

4.1. Study selection

A total of 1616 articles were obtained by searching the following databases: PUBMED (n = 91), Embase (n = 169), CINAHL (n = 7), HINARI (n = 216), Science Direct (n = 1093), Google Scholar (the first 38 articles sorted by relevance), and the local university repository (n = 2). After removing duplicates, 1440 articles were screened based on title and abstract, and only 52 met the eligibility criteria for full-text review. Finally, only nine articles were included in the quantitative meta-analysis (Fig. 1).

4.2. Study characteristics

This systematic review includes nine studies with 2496 study participants, with individual sample sizes ranging from 163 to 414. Among these studies, four were conducted in the Amhara region (Dessie [20], Gondar [18], Bahir Dar [17,27]), two in SNNP (Arbaminch [23] and Hawassa [19]), and the remaining three were independently reported from the Addis Ababa [28], Oromia [29] and Tigray regional states [30]. All of the studies were cross-sectionally designed and most of the studies used convenient sampling techniques and were published between 2000 and October 2022. Seven of the included studies were performed among adult patients diagnosed with CAP, whereas the remaining two studies were performed among adult patients living with HIV/AIDS and diagnosed with CAP (Table 1 and Supporting file 4: Table S3).

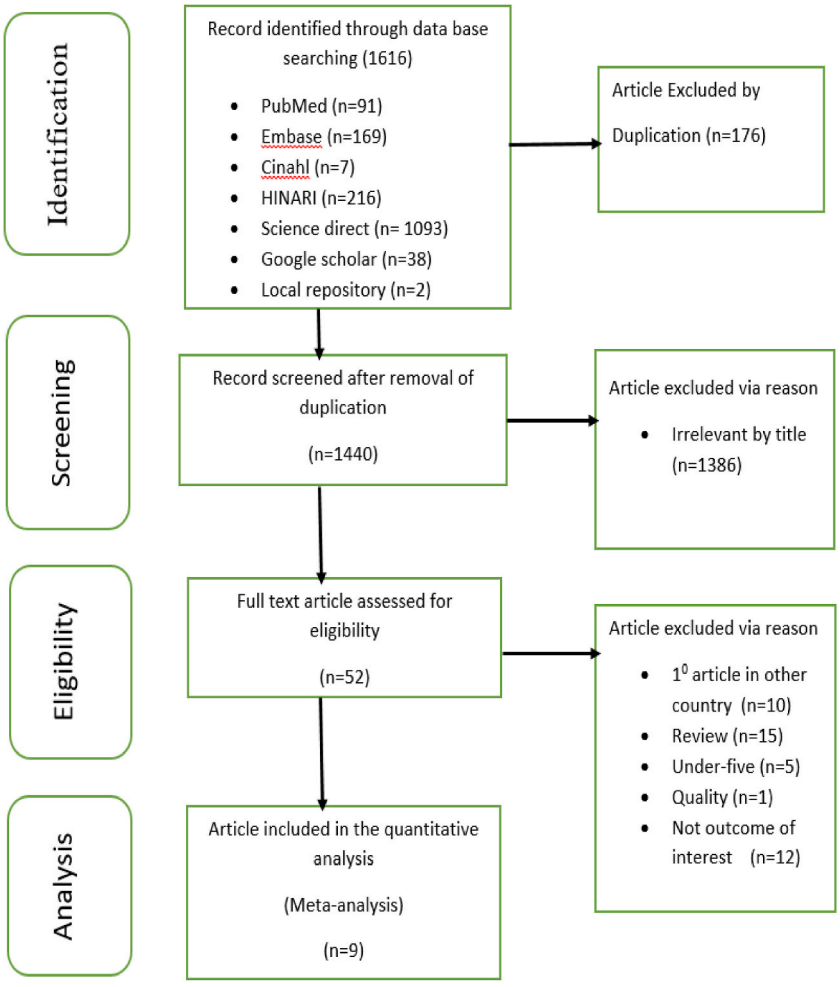

Fig. 1. PRISMA flow diagram of included studies to estimate the prevalence of bacterial etiology of community acquired pneumonia among adult patients in Ethiopia.

Table 1
Characteristics of studies done on bacterial etiology of CAP among adult patients in Ethiopia in the year between 2000 and October 2022.

Authors	Year	Study Region	Study participant	Study design	Sample size	Cases
Nurahmed et al. [22]	2020	Addis Ababa	CAP	cross sectional	240	77
Assefa et al. [18]	2022	Amhara	CAP	cross sectional	312	123
Gebre et al. [19]	2021	SNNP	CAP	cross sectional	406	136
Regasa et al. [29]	2015	Oromia	CAP	cross sectional	133	60
Regasa [23]	2014	SNNP	CAP	cross sectional	170	73
Tewodros Dessie et al. [20]	2021	Amhara	CAP	cross sectional	406	157
Temesgen et al. [17]	2019	Amhara	CAP	cross sectional	414	167
Gebre Adhanom et al. [30]	2019	Tigray	CAP among HIV patients	cross sectional	252	110
Derbew and yohanns [27]	2020	Amhara	CAP among HIV patients	cross sectional	163	68

4.3. The prevalence of bacterial etiology of CAP among adult patients in Ethiopia

The prevalence of bacterial etiology of community-acquired pneumonia (CAP) among the adult patients included in this systematic review varied from 32.1% to 45.1%. The combined prevalence of nine studies on bacterial etiology of CAP, using a random-effects model, was 39.18% with a 95% confidence interval (CI) of 36.34–42.02, as depicted in the forest plot below (Fig. 2). We observed significant heterogeneity across studies ($I^2 = 52.6\%$, $P = 0.032$). Considering the common bacterial causes, *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, and *Staphylococcus aureus* had a combined prevalence of 9.1% (7.9–10.2), 8.11% (4.9–11.3), and 6.8% (4.4–9.3), respectively (Table 2).

4.4. Subgroup analysis

To identify the source of heterogeneity across studies, subgroup analysis was performed using different characteristics. Based on region the pooled prevalence in the Amhara region was 39.8%: 95% (37.1–42.4) and SNNP 37.7%: 95% (28.5–46.9) (Table 3). Subgroup analysis based on sample size was done by taking the mean sample size of all included studies as a cutoff, and the pooled prevalence of those less than 277 was 40.8%: 95% (35.7–45.8) whereas studies with sample size of more than 277 indicated 37.9%: 95% (34.8–41.0) of bacterial CAP among studies. Furthermore, the pooled prevalence was 38.25%: 95% (35.2–41.3) according to the year of publication of research published after 2017. Additionally, with relation to the study population, the pooled prevalence of those without HIV infection was 38.32 (35.14–41.49) (Table 3).

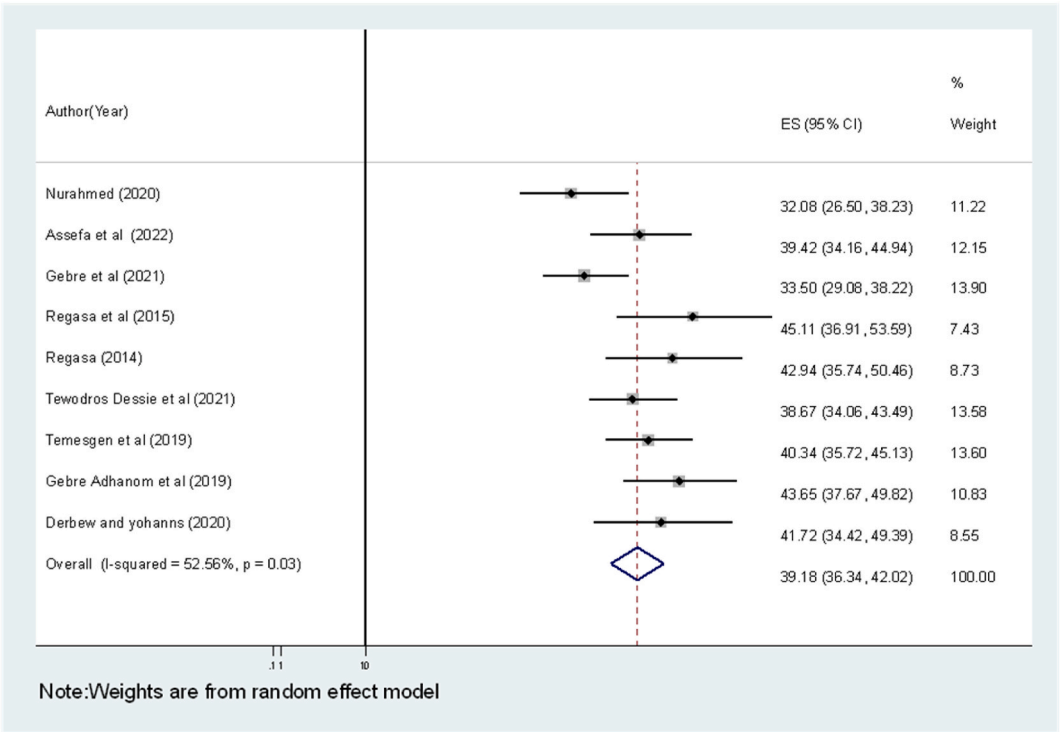

Fig. 2. Forest plot showing the pooled prevalence of bacterial etiology of CAP among adult patients in Ethiopia.

Table 2
The pooled prevalence of common bacterial etiology of CAP among adult patients in Ethiopia.

Types of bacterial isolate	No of studies	total No of positive	Pooled prevalence 95% CI	I^2 % & p value
Streptococcus pneumoniae	9	212/2496	8.11 (4.9–11.3)	92.0 (0.000)
Staphylococcus aureus	9	171/2496	6.8 (4.4–9.3)	86.3 (0.000)
Klebsiella pneumoniae	9	240/2496	9.1 (7.9–10.2)	48.6 (0.049)
Escherichia coli	9	102/2496	3.96 (2.7–5.2)	61.3 (0.008)
Pseudomonas aeruginosa	9	111/2496	3.98 (2.6–5.4)	71.8 (0.000)
Hemophilus influenzae	7	44/1850	2.04 (1.2–2.8)	34.0 (0.168)

Table 3
Subgroup analysis to identify the source of heterogeneity across the studies done on bacterial etiology of CAP among adults patients in Ethiopia.

Subgroup		No of studies	Pooled prevalence (CI)	I^2 (%)	P-value
Region	Amhara	4	39.8 (37.1–42.4)	0	0.89
	SNNP	2	37.7 (28.5–46.9)	77.7	0.03
	Oromia	1	45.1 (36.7–53.6)	0	0.00
	Mekele	1	43.7 (37.5–49.8)	0	0.00
	AA	1	32.1 (26.2–37.9)	0	0.00
Sample size	<277	4	40.8 (35.7–4 5.8)	61.7	0.03
	≥277	4	37.9 (34.8–41.0)	39.5	0.18
Year of publication	2000–2017	2	43.9 (38.3–49.5)	0	0.71
	2018–2022	7	38.25 (35.2–41.3)	53.9	0.04
Study population	CAP without HIV/AIDS	7	38.32 (35.14–41.49)	54.69	0.04
	CAP among HIV/AIDS patients	2	42.89 (38.13–47.65)	0	0.00

4.5. Meta-regression

In addition to subgroup analysis, the source of heterogeneity was checked using meta-regression by considering the continuous variable sample size and year of publication. The results show that none of these variables affected the pooled estimates, as indicated in Table 4.

4.6. Publication bias

The presence of bias across studies was checked using the graphical funnel plot test and its objective analog, Egger's test. In our results, there was no publication bias as indicated by the symmetric funnel plot and non-significant Egger's test ($p = 0.156$), as shown in Table 5 and Fig. 3, respectively.

4.7. Sensitivity analysis

Sensitivity analysis was performed to identify outlier studies, and the results showed that the estimates of all included studies were within the confidence interval of the pooled estimate, suggesting the robustness of the aggregated estimate (Table 6).

5. Discussion

In our study, we systematically reviewed nine articles on the prevalence of bacterial etiology of CAP among adult patients in Ethiopia. Meta-analysis results showed that the pooled prevalence of bacterial etiology of CAP among adult patients was 39.18% (36.34–42.02). This report was in line with a study conducted in Sudan 42% [32] and lower than that in Ghana, 84.5% [33] Nigeria, 69.6% and 45.2% [34,35], Zambia 59% [36], Egypt 50.4% [37], Saudi Arabia 46.6% [38], Pakistan 75% [39], in a different region of India, 46.3%, 52.83%, 58.8%, 83% [40–43], Bangladesh 61.83% [44]; a multicenter study in China, 74.4% [31]; Asian countries, 44.8% [11] Iran, 44% [45] Spain, 50.7% [46] Vietnam, 61.8% [47] and Ukraine 100% [48]. This variation may be attributed to differences in the study setting, the characteristics of the study population, and sample size. In addition, methodological disparities (such as the use of molecular and serological detection methods for both typical and atypical pneumonia causative agents in some

Table 4
Meta-regression of selected variables to see their effect on the pooled prevalence of bacterial etiology of CAP among adult patients in Ethiopia.

Prevalence	Coef.	Std. Err.	T	P > t	[95% CI]
Sample size	−0.0092	0.01	−0.52	0.62	−0.05–0.03
Year of publication	−4.078	4.99	−0.82	0.44	−16.3–8.13
_cons	45.35	4.50	10.07	0.00	34.3–56.4

Table 5
Publication bias across studies done on bacterial etiology of CAP among adult patients in Ethiopia. Number of studies = 9 Root MSE = 0.0353.

Std_Eff	Coef.	Std. Err	T	P>|t|	[95% Conf. Interval]
Slope	3.388093	0.1692194	20.02	0.000	2.987953–3.788233
Bias	0.0922202	0.0580423	1.59	0.156	−0.045028 0.2294684

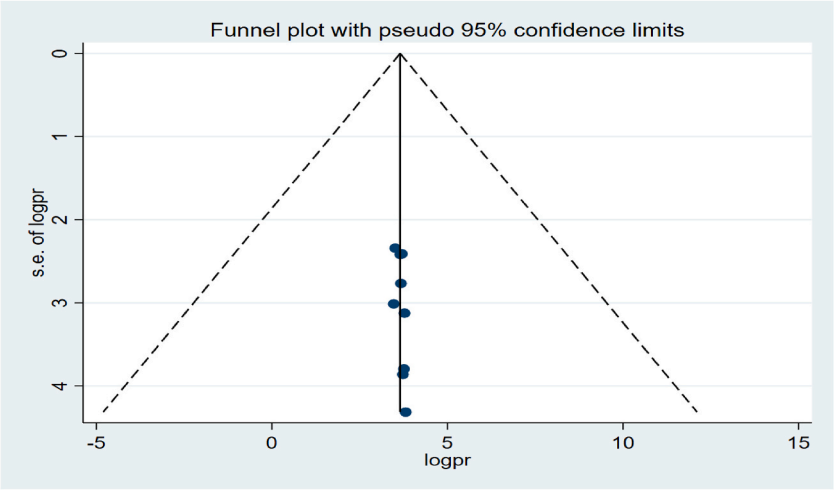

Fig. 3. Funnel plot to see the publication bias across studied done on bacterial etiology of CAP among adult patients in Ethiopia.

Table 6
Sensitivity analysis across studies done on bacterial etiology of CAP among adult patients in Ethiopia.

Study omitted	Estimate	[95% Conf. Interval]
Nurahmed (2020) [22]	39.5	37.5–41.5
Assefa et al. (2022) [18]	39.0	36.6–41.5
Gebre et al. (2021) [19]	39.6	37.6–41.6
Regasa et al. (2015) [29]	38.7	36.5–40.9
Regasa (2014) [31]	38.8	36.5–41.0
Tewodros Dessie et al. (2021) [20]	39.1	36.6–41.6
Temesgen et al. (2019) [17]	38.8	36.4–41.4
Gebre Adhanom et al. (2019) [30]	38.6	36.3–40.80
Derbew and yohanns (2020) [27]	38.9	36.5–41.18
Combined	39.0	36.8–41.2

studies) could also account for this inconsistency.

The pooled prevalence (39.18%: 95% CI of (36.34–42.02) of the bacterial etiology of CAP among adult patients in this study, was higher than that reported by Kishimbo et al. in India (13.9%) [49] and another study in Tanzania (20.8%) [50]. This may be a selective report of only a gram-negative bacterial isolate [49].

In this meta-analysis, the most common cause of CAP among adult patients in Ethiopia is *Klebsiella pneumoniae* followed by *Streptococcus pneumoniae* and *Staphylococcus aureus, Escherichia coli, Haemophilus influenzae,* and other bacteria. This finding is similar to those reported in Sudan [32], Nigeria [51], Tanzania [50], Egypt [37], and India [43]. The overall predominant isolates identified were *Klebsiella pneumoniae* among HIV infected population suspected with CAP which included in this review. While S. pneumoniae were reported previously as dominant bacterial species [17,50]. These predominance of *Klebsiella pneumoniae* as etiology of CAP in this review might be explained by patient type (two of reviewed articles participants had HIV infected) and shift in trend of bacterial causes of CAP [27,30,50]. According to this review and other studies, various bacterial etiologies in CAP have significant role [52]. With the use of advanced diagnostic techniques, specific etiology of CAP are increasingly being identified for the better management of CAP.

5.1. Limitation of the study

The meta-analysis's included studies only included four regions (Amhara, SNNPR, Tigray and Oromia) and one administrative city (Addis Ababa) nationwide; additionally, the review excluded factors related to bacterial causes of CAP and the antibiotic susceptibility profiles of individual bacterial species. Consequently, additional country-based studies are advised to evaluate confounding factors.

6. Conclusions

The meta-analysis revealed that the overall prevalence of bacterial causes in community-acquired pneumonia (CAP) is 39.8%. The most common causative agents of CAP are *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, and *Staphylococcus aureus*. Therefore, enhancing the precise diagnosis and treatment of bacterial CAP could be achieved by integrating standard microbiological, serological, and molecular diagnostic methods, thus mitigating the risk of treatment failure linked to empirical approaches.

Ethics declarations

This systematic review and meta-analysis was adhered to the Preferred Reporting Items for Systematic Reviews & Meta-Analysis (PRISMA) guidelines (supporting file 1).

Funding

No funding was used in this review.

Availability of data and materials

All the data used in this study are included in this manuscript and it's supporting information files.

CRediT authorship contribution statement

Abdurezak Mohammed Seid: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Wondwossen Tadesse:** Writing – review & editing, Writing – original draft, Validation, Supervision, Data curation. **Mesfin Menza:** Writing – review & editing, Validation, Supervision, Formal analysis, Data curation. **Ritbano Ahmed Abdo:** Writing – review & editing, Visualization, Validation, Supervision, Formal analysis, Data curation. **Abdulhakim Mussema:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e28008.

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