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Prevalence of human brucellosis in Ethiopia: systematic review and meta-analysis

Fikir Asrie[1*], Mastewal Birhan[2], Mulat Dagnew[3] and Nega Berhane[2]

Abstract

Brucellosis is a significant public health challenge in Ethiopia, which is characterized by a high prevalence among humans. The disease is primarily transmitted through the consumption of unpasteurized dairy products, direct contact with infected animals, or inhalation of contaminated aerosols. In addition to its impact on human health, brucellosis imposes substantial economic burdens. However, existing epidemiological studies provide inconsistent prevalence estimates, underscoring the need for a more comprehensive and systematic analysis of the disease's burden and associated risk factors in Ethiopia. This systematic review and meta-analysis aimed to generate representative data on the prevalence of human brucellosis in Ethiopia. We searched databases like PubMed and Science Direct for articles published between 2007 and 2022. The analysis included 26 studies covering 5,718 human serum samples. The Complement Fixation Test served as the confirmatory diagnostic test. The results suggest a relatively high seroprevalence of human brucellosis in Ethiopia, with an overall pooled prevalence of 14.0% (95% CI: 10.23, 18.12). Prevalence varied significantly across regions, with the highest observed in Afar (24.21%) and the lowest in Oromia (7.75%). Substantial heterogeneity was observed (I^2 = 97.64%), suggesting significant variations in prevalence across regions and over time. Additionally, the analysis suggests a possible increasing trend in prevalence over the years. Human brucellosis is a significant health concern in Ethiopia, and further research is crucial for effective prevention and control. The higher prevalence than previously reported in meta-analyses underscores the urgent need for intervention strategies from policymakers, such as the Ministry of Health. Identifying risk factors associated with human brucellosis is essential for implementing effective control measures. Prioritizing brucellosis prevention and control is vital for ensuring public health and well-being. Prospero registration number: CRD42022350237.

Keywords Brucellosis, Ethiopia, Human, Meta-analysis, Prevalence, Systematic review

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Introduction

Background

Brucellosis is a zoonotic infectious disease caused by bacteria of the genus Brucella [1]. The disease is commonly transmitted from animals to humans through various routes, including ingestion of contaminated food products, direct contact with infected animal tissues or discharge, such as saliva, urine, or feces, and inhalation of aerosols containing the bacteria. Contact with placentas, aborted fetuses, or other reproductive materials from infected animals is another significant route of transmission [2].

Brucellosis manifests as an acute or persistent febrile illness with diverse clinical presentations [3]. Historically, it has been referred to by various names including Mediterranean fever, Malta fever, gastric remittent fever, and undulant fever. Although humans are accidental hosts for Brucella, the disease remains a significant global public health concern due to its potential to cause severe illness and its prevalence as a zoonotic infection [4]. Symptoms can range from mild flu-like conditions to severe, prolonged illnesses lasting weeks or months. Common symptoms include fever, sweating, fatigue, weight loss, headache, and joint pain. In severe cases, complications such as neurological disorders, endocarditis, and abscess formation in the bones or testes may occur.

Brucellosis also poses a major economic challenge, as it affects patient productivity and animal production [5]. Brucella are small, gram-negative, aerobic coccobacilli capable of surviving inside host cells. They preferentially localize in the reproductive organs of animals, causing abortions, stillbirths, and infertility. The bacteria are shed in large numbers in animal urine, milk, placental fluid, and other bodily fluids, contaminating the environment and posing a risk to other animals and human [6].

People who work closely with animals are at an increased risk of exposure to *Brucella*. High-risk groups include farmers, butchers, hunters, veterinarians, slaughterhouse workers, and laboratory personnel [7]. Pastoralists, who depend on livestock for their livelihood, face particularly high risks due to their regular contact with animals and the consumption of raw dairy products [8]. In sub-Saharan Africa, where pastoralism is common, brucellosis is a significant public health issue, particularly in areas with limited healthcare access [8].

Several studies have investigated the prevalence of brucellosis among Ethiopian pastoralist communities, but their findings are inconsistent, with reports varying from high to low prevalence [9]. Among pastoralists in Ethiopia, the incidence of human brucellosis is estimated at 160 per 100,000 person-years, compared to 28 per 100,000 person-years in sedentary populations [10].

Ethiopia, located in the Horn of Africa, has the largest livestock population and the second-largest human population in Africa [11]. Livestock production is a key income source, particularly in rural areas where agriculture is the main economic activity. The close relationship between humans and animals in Ethiopia, where animals are often considered family members, also increases the risk of zoonotic disease transmission, including brucellosis.

Although studies have explored the prevalence and incidence of brucellosis in Ethiopia, extensive nationwide research remains lacking [12]. Understanding the current disease burden, incidence, and variations is crucial. Therefore, the objective of this study is to assess the pooled prevalence of human brucellosis in Ethiopia through a systematic review and meta-analysis.

Materials and methods

Protocol and registration

The review protocol was registered with the National Institute for Health Research the International Prospective Register of Systematic Reviews (PROSPERO) under registration number CRD42022350237 and it is accessible at https://www.crd.york.ac.uk/Prospero.

Study design and search strategy

A systematic review and meta-analysis of published and unpublished studies were conducted to determine the pooled prevalence of human brucellosis in Ethiopia. The review included eligible studies identified through a combination of electronic database searches and manual retrieval from reference lists of relevant articles. Additional articles were indicated using the "related articles" feature in PubMed, and an open search of the Ethiopian Ministry of Health websites and national surveys was conducted to uncover prevalence data not published in scientific journals.

The search was focused on English-language articles, limited to human studies, and covered the period from September 2007 to August 2022. The following electronic databases were searched: PubMed, Science Direct, African Journals Online (AJOL), Embase, and Google Scholar. Medical Subject Heading (MeSH) terms such as "Brucellosis," "Brucella," "Seroprevalence," "Prevalence," "Sero-epidemiology," "Human," and "Ethiopia" were used. Boolean operators "OR" and "AND" were applied to identify studies containing relevant keywords in titles, abstracts, or full texts.

The inclusion process was followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A PRISMA checklist was used to ensure that all relevant information was included in the systematic review and meta-analysis [13] (Table 1). Additionally, EndNote X9 reference management software was utilized to organize and manage the retrieved literature throughout the study.

Table 1 Characteristics of studies included in the systematic review and Meta-analysis on the prevalence of human brucellosis in Ethiopia (2007–2022)

Authors	Year of publication	Regions of Ethiopia	Sample size	Seropositive	Prevalence	Reference
Wagi FG. et al.	2021	Afar	120	12	10.0	[8]
Mehari S. et al.	2021	Afar	444	140	31.5	[14]
Lakew A. et al.	2019	Somali	211	5	2.4	[15]
Ibrahim M. et al.	2021	Somali	190	5	2.6	[16]
Tschopp R. et al.	2021	Afar	594	266	44.8	[17]
Tschopp R. et al.	2021	Somali	215	67	31.2	[17]
Workalemahu B. et al.	2017	Southern	243	26	10.7	[18]
Genene R. et al.	2009	Oromia	88	30	34.1	[19]
Genene R. et al.	2009	Southern	17	5	29.4	[19]
Genene R. et al.	2009	Amhara	100	3	3.0	[19]
Tsegaye A. et al.	2017	Oromia	149	7	4.7	[20]
Mohammed A. et al.	2019	Afar	172	82	47.7	[21]
Zewold SW. et al.	2012	Afar	200	30	15.0	[22]
Tibesso G. et al.	2014	Oromia	93	2	2.2	[23]
Haileselassie M. et al.	2011	Amhara	246	3	1.2	[24]
Getahun TK. et al.	2021	Oromia	166	7	4.2	[25]
Tadele T. et al.	2007	Oromia	56	2	3.6	[26]
Mekonen K	2016	Oromia	250	15	6.0	[27]
Zewdie W	2020	Oromia	86	35	40.7	[28]
Edao BM. et al.	2020	Oromia	341	9	2.6	[29]
G/Michael D. et al.	2016	Oromia	48	1	2.1	[30]
Teshome YB. et al.	2021	Amhara	499	167	33.5	[31]
Hilemelkot M	2007	Amhara	238	9	3.8	[32]
Jaffar M. et al.	2018	Oromia	231	11	4.8	[33]
Zerfu B. et al.	2018	Afar	630	28	4.4	[34]
Ahmed EY. et al.	2008	Afar	91	15	16.5	[35]

Three independent authors (FA, NB, MB) was conducted the search process. The eligibility criteria were defined based on the following key terms: [1] population (Patients diagnosed with brucellosis); [2] outcome (Results from serological testing for *Brucella*); [3] study design (Prevalence studies, cross-sectional studies, epidemiological studies, observational studies, and longitudinal studies.); and [4] study site (Regions of Ethiopia).

Inclusion and exclusion criteria

To identify eligible studies for the analysis, a systematic selection process was implemented based on predefined inclusion and exclusion criteria. Studies were included if they were published in English, available as full-text articles, conducted between September 2007 and August 2022, and focused on the prevalence of human brucellosis. Additionally, eligible studies utilized cross-sectional or cohort designs and employed confirmatory diagnostic tests, such as the Complement Fixation Test (CFT). Conversely, studies were excluded if their titles or abstracts were unrelated to the outcomes of interest, if they were review articles, case reports, or duplicates, or if they relied solely on the Rose Bengal Plate Test (RBPT) as the diagnostic method. Studies conducted before September 2007 or lacking full-text availability were also excluded.

Data extraction

Important data from each selected study were extracted using a data extraction format prepared and summarized in Microsoft Excel by two authors independently (FA and MB). Disagreements were resolved by consensus and discussion with a third author (NB and MD). Whenever further information was required, the author was contacted via email. The data extraction format for the primary outcome included the first author, region (according to Ethiopian political administration), publication year, study design, sample size, and the number of Brucella-infected and suspected patients.

Outcome

This review aimed to investigate studies on the prevalence of human brucellosis among patients suspected of having the disease in Ethiopia. Seroprevalence was calculated the as the ratio of Brucella-infected patients to the total number of patients suspected of having human brucellosis. Seroprevalence was defined as the presence of IgG antibodies in the serum/plasma of suspected patients using the complement fixation test (CFT) method.

Quality assessment

Quality assessment was conducted based on the Joanna Briggs Institute (JBI) Critical Appraisal Checklist adapted for prevalence studies using 9 criteria [36] The checklist consists of nine items that evaluate various aspects of prevalence studies, such as the appropriate sample frame, adequate sample size, detailed description of study subjects and settings, valid methods for identifying the condition, standard and reliable measurement of the condition, appropriate statistical analysis, and adequate response rate. Scores were assigned to each item, with the total quality score ranging from 0 to 9. Studies were classified as low-, medium-, or high-quality based on their total score, with high- and medium-quality articles included in the final analysis of the review [37].

Data analysis

Data were analyzed using Stata version 14 software package (Stata Corporation, College Station, TX, USA). A random effects model was used to determine pooled prevalence and the 95% confidence interval (CI) by employing the approach of DerSimonian and Laird [38]. In addition, the Freeman Turkey arcsine methodology was used to address the stabilizing variances [39]. Heterogeneity of the study results was assessed using the I^2 test. Significant heterogeneity was considered for $P < 0.10$ and $I^2 > 50\%$ [40, 41]. Possible sources of variation were explored using sensitivity and subgroup analyses by stratifying studies according to predetermined variables, study region, and year of publication. Publication bias was measured using the Begg's funnel plot and Egger's regression [42]. A P-value < 0.05 on the Egger test was considered indicative of statistically significant publication bias. The forest plot with 95% CI pooled the overall prevalence of human brucellosis infection was summarized by using figure. This systematic review and meta-analysis were based on (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement [43].

Ethical statement and dissemination

As this systematic review was based on published data, ethical approval was not required. The final report will be disseminated through publication in a peer-reviewed scientific journal and will be presented at local, regional, national, and international conferences.

Results

Design, study selection and searching process

This systematic review and meta-analysis was conducted according to the PRISMA guideline [44]. After the search process was completed and duplicates were removed, 491 studies were retrieved through manual and electronic search. An electronic search was performed using PubMed, Google Scholar, Science Direct, EMBASE, Cochrane Library, and reference lists of previous related studies to retrieve more related articles. Because of duplications in the records, from the total records 160 of them were removed from the retrievals due to duplication of records. The number of records rejected by reading only the title was 202. Of the remaining129 studies, 69 were excluded after reading their abstracts because they were not relevant to this review in terms of the outcome study is interested. The full-text copies of the remaining 62 studies that met or potentially met the inclusion criteria were assessed. After further screening and removing irrelevant articles, 26 papers were retained for inclusion in the final analysis (Fig. 1).

Key characteristics of studies included

Of the 26 included articles, 10 were conducted in Oromia, seven in Afar, four in Amhara, and five in other regions of Ethiopia (three in Somali and two in Southern). According to the study design, all the studies were cross-sectional. The relevant features of each study, including study population, sample size, region, study design, and year of publication, were summarized in (Table 1).

Qualitative systematic review of human brucellosis in Ethiopia

The prevalence of human brucellosis was significantly high [14, 17, 19, 28]. In one study, the prevalence of human brucellosis was 47.7% [21]. This systematic review and meta-analysis included 26 articles to estimate the pooled prevalence of human brucellosis in Ethiopia. Using a fixed effects model, the overall magnitude of brucellosis in humans was 14% (AOR, 95% CI = 10.23–18.12) (Fig. 2).

Subgroup analysis

To explore the source of heterogeneity, subgroup analysis was performed in the study site regions. Based on the study area, the pooled prevalence of human brucellosis was found to be 14.18% (95% CI = 10.23–18.12). The maximum and minimum prevalence rates of human brucellosis in subgroup analysis were 24% in Afar and 7.75% in Oromia region of Ethiopia, respectively (Fig. 3).

Sensitivity analysis and publication bias

To assess the stability of the results, a sensitivity test was performed by omitting each study at a time. There was no significant change in the pooled prevalence of human brucellosis after excluding one of the included studies at 95% CI, 10.23–18.12. This indicates that no individual study significantly influenced the pooled prevalence of human brucellosis. The funnel plot did not show any evidence of publication bias. The sensitivity analysis results showed that all findings were within 95% CI (between

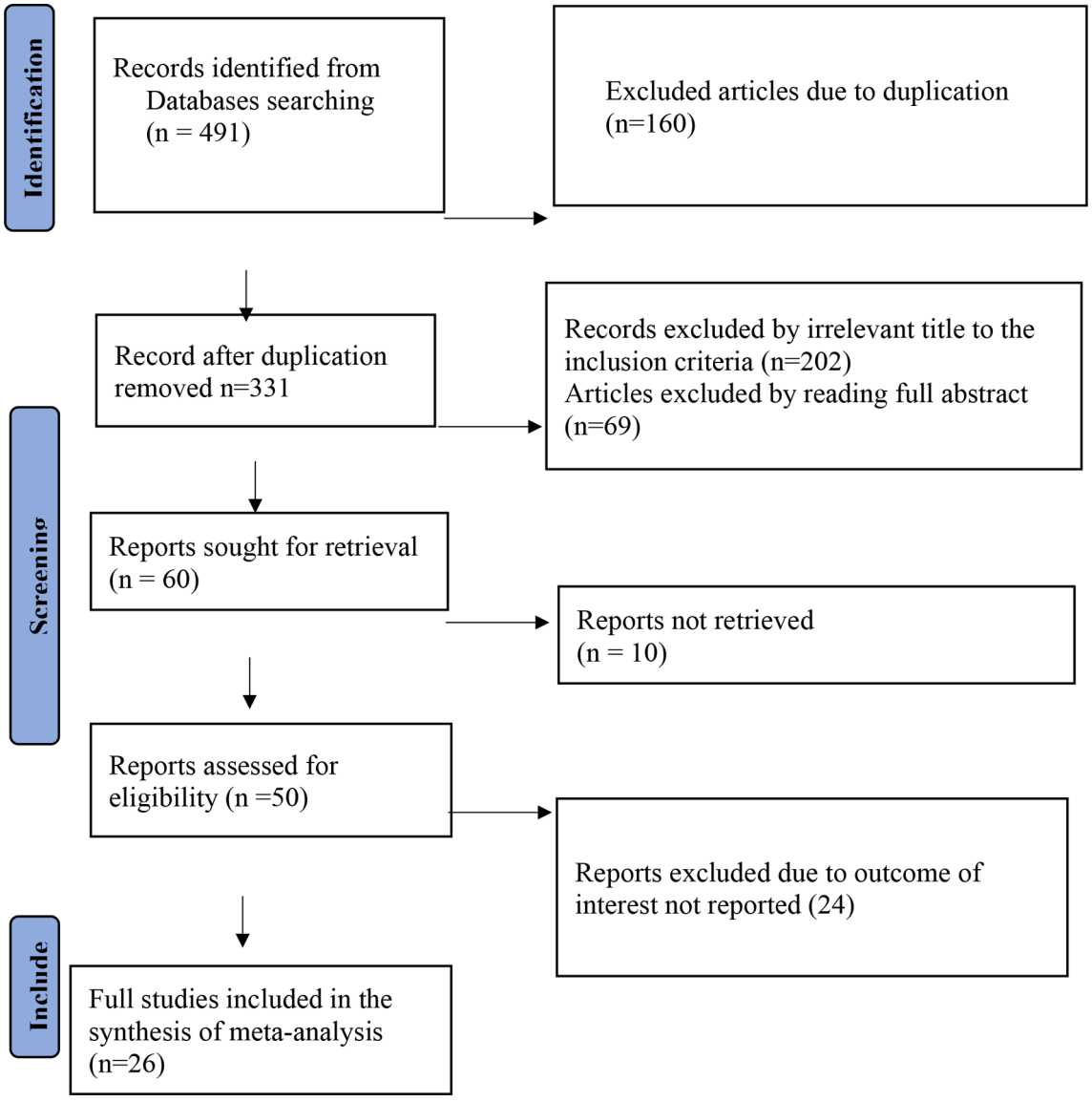

Fig. 1 Flow chart diagram and PRISMA checklist illustrating the selection of studies for the systematic review and meta-analysis of the prevalence of human brucellosis among patients suspected of having brucellosis in Ethiopia, 2022 (including identified, screened, eligible, and included studies). Articles may have been excluded for multiple reasons

lower confidence interval and upper confidence intervals) (Fig. 4).

Meta regression

There was a gradual increase in human brucellosis in Ethiopia from 2007 to 2022 (Fig. 5); however, there was no significant association between publication year and prevalence of human brucellosis.

Publication bias

A visual funnel plot and Egger's regression test were used to assess publication bias. The funnel plot was asymmetrical, indicating evidence of publication bias (Fig. 6). Egger's regression test further confirmed significant publication bias ($p = 0.000$). Additionally, Egger's test identified publication bias ($p = 0.000$) but showed no evidence of a small study effect (Fig. 7).

Figure 7: Publication Bias (Egger's Test for Small Study Effect).

Following a trim-and-fill analysis, nine additional studies were included, bringing the total to 35 studies. Using a fixed-effect model, the pooled prevalence estimate was 3.5% (95% CI: 2.95–4.05). In contrast, the random-effect model yielded a pooled prevalence estimate of 4.2% (95% CI: -0.495–8.890).

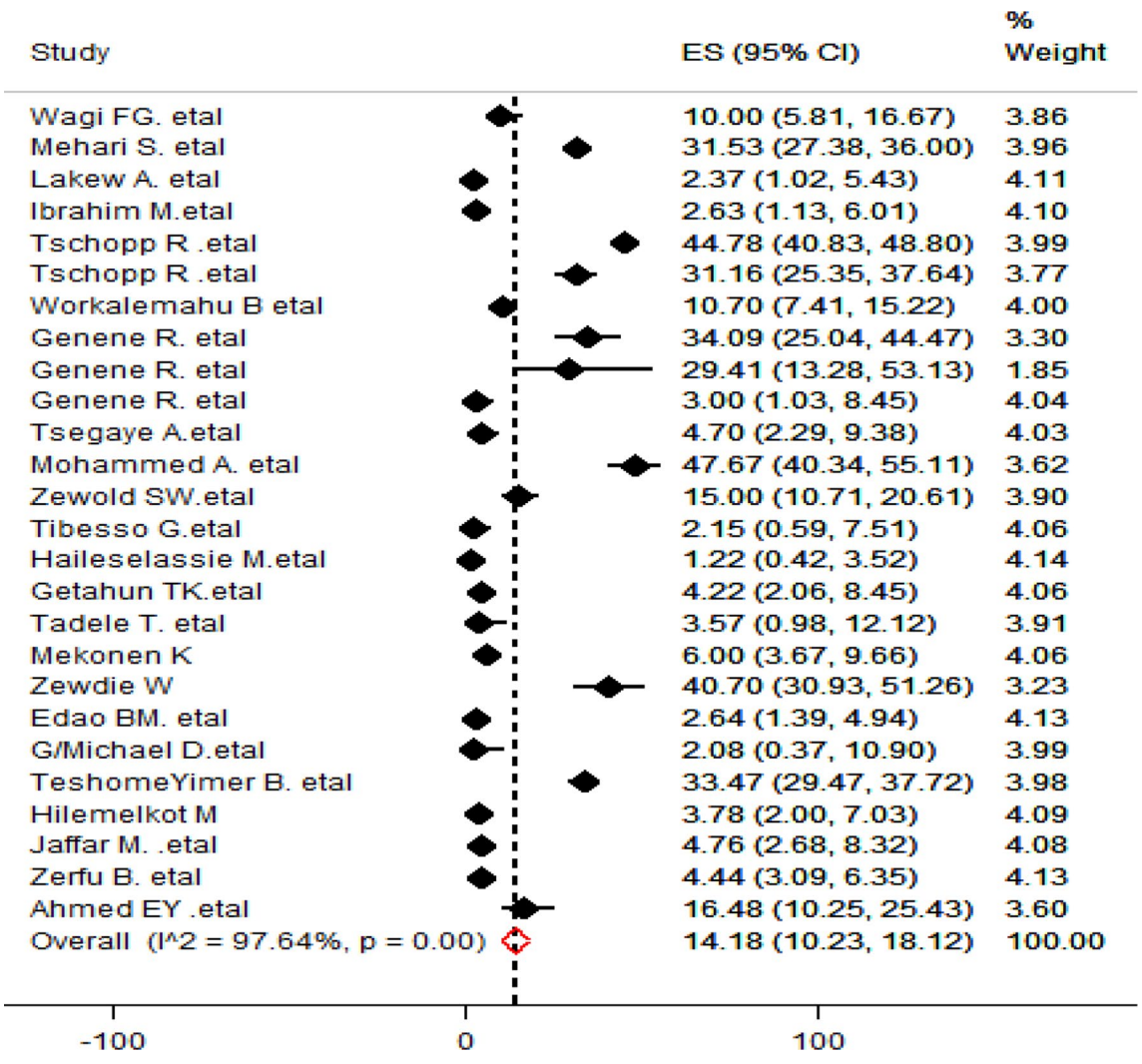

Fig. 2 Forest plot of the pooled prevalence of human brucellosis in Ethiopia from 2007 to 2022

Discussion

Human brucellosis remains a global public health challenge, particularly in developing countries, where it has significant consequences for human health, social stability, and economic development [45, 46]. This systematic review and meta-analysis analyzed 26 original studies encompassing a total of 5,718 suspected human brucellosis cases. Serum samples collected in these primary studies estimated a pooled prevalence of 14%.

This pooled prevalence aligns closely with previous studies conducted in Nigeria 17.6% [47], Uganda 17.0% [48]. However, it is higher than findings from Kenya's National Survey (3%) [49], Sudan 1% [50], Tanzania 7.7% [51], Ethiopia 6.7% [10], and Somalia 0.6% [52]. Possible explanations for these discrepancies include a lack of awareness about brucellosis, unhealthy food habits (such as consuming unpasteurized dairy products or undercooked meat), traditional animal husbandry practices, and insufficient surveillance and vaccination programs.

Conversely, the pooled prevalence in this study was lower than the findings from Tanzania 22.7% [53], America from 1968 to 2006 50% [54], Egypt (23.6% and 24.3% [55, 56]), Kenya 44% [48], Nigeria 30.8% [57]. Differences in prevalence across studies could stem from variations in geographic location, diagnostic methods, health policies, farming systems, and socio-economic conditions.

Subgroup analysis

The prevalence of human brucellosis varied significantly across Ethiopian regions. The highest prevalence was observed in the Afar region 24% (95% CI: 10–39), followed by other regions such as Somali and Southern Ethiopia (13%; 95% CI: 5–21), Oromia (10%; 95% CI: 0–21), and Amhara (8%; 95% CI: 4–11). These differences could be attributed to geographic and cultural factors, including dietary habits, levels of awareness, and traditional farming practices.

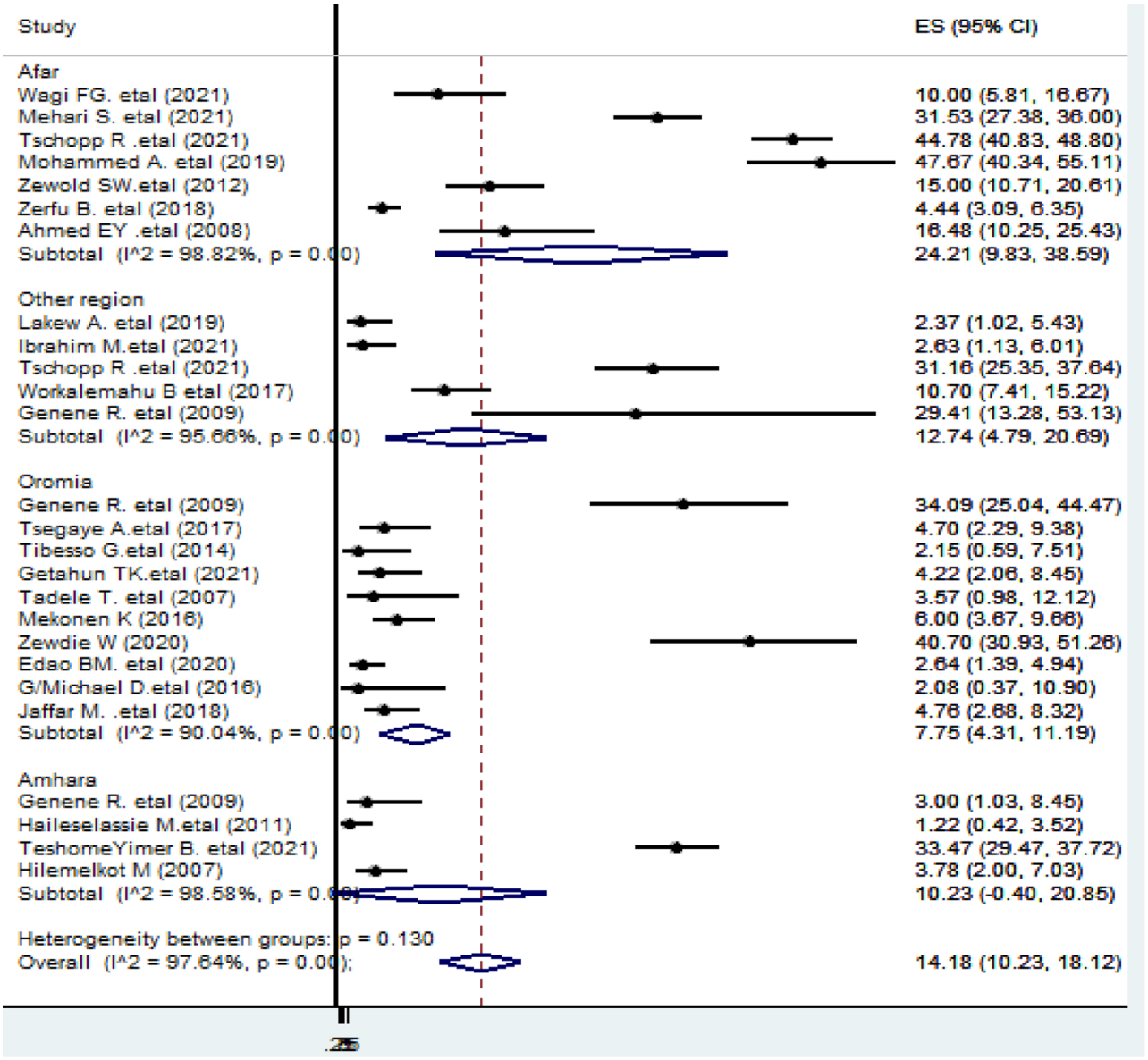

Fig. 3 Subgroup analysis by study area (Region) human brucellosis in Ethiopia from 2007 to 2022

In the Afar region of Ethiopia, more than 80% of the population depends on pastoral activities, spending extensive time with their livestock. Their primary food sources are animal-based products, particularly milk, which is often consumed unboiled. The consumption of unpasteurized or undercooked animal products plays a crucial role in the transmission of brucellosis.

The prevalence of human brucellosis in Afar region of Ethiopia 24% (95% CI: 10–39), was comparable to studies from Egypt 23.6% and 24.3% [55, 56] and Tanzania 22.7% [53]. However, it was higher than findings from Nigeria17.6% [47], Uganda 17% [48], Kenya 3% [49],Sudan 1% [50],Tanzania 7.7% [51],Ethiopia 6.7% [10] and Somalia 0.6% [52]. Conversely, it was lower than reports from Kenya 44% [48] and Nigeria 30.8% [57]. The possible reason for discrepancy may be due to the difference in the sample size, difference in the lifestyle of the society, type of diagnostic protocol employed and socioeconomic status of the study population.

Accurate data on the prevalence of human brucellosis in Ethiopia is crucial for informing policymakers and public health officials. This information can guide the development of targeted prevention and control strategies, including public awareness campaigns, improvement of diagnostic capacity, implementation of effective vaccination programs for livestock, and promotion of safe food-handling practices.

Efforts to reduce human brucellosis should prioritize regions like Afar, where pastoral livelihoods and traditional dietary practices increase the risk of transmission.

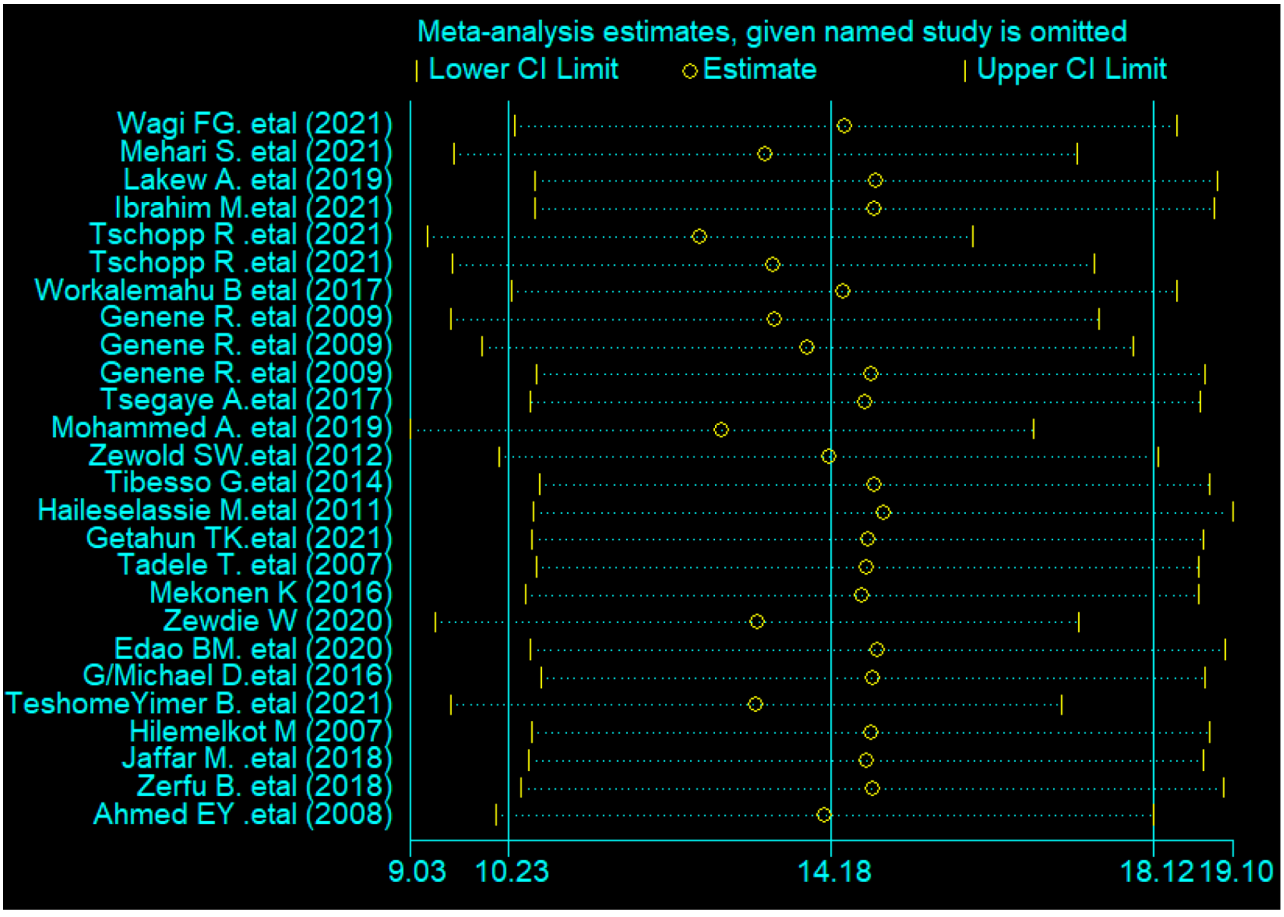

Fig. 4 Sensitivity analysis prevalence of human brucellosis in Ethiopia from 2007 to 2022

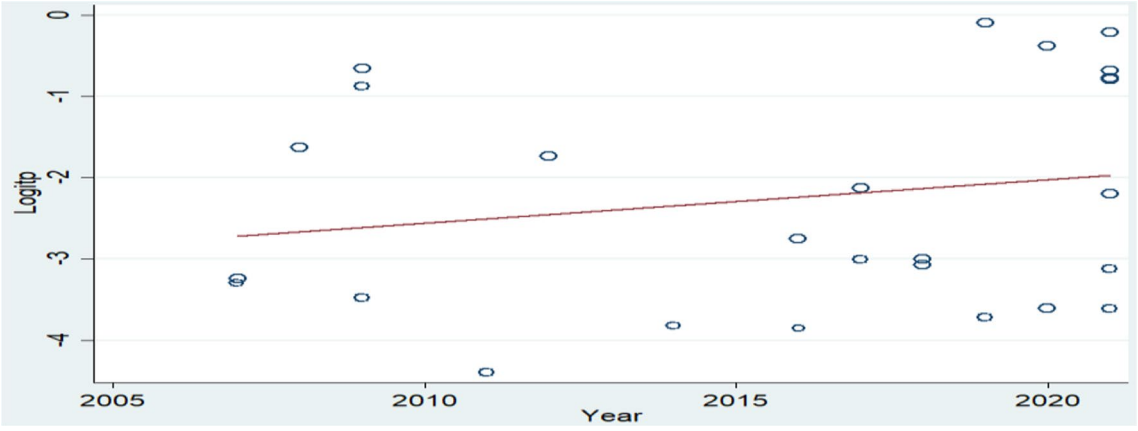

Fig. 5 Meta regression prevalence of human brucellosis in Ethiopia from 2007 to 2022

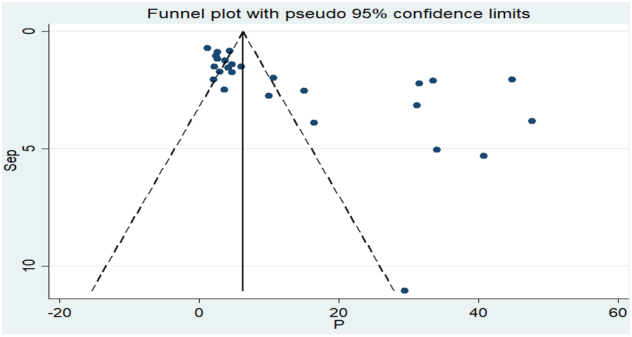

Fig. 6 Funnel plot to assess publication bias of included studies on the prevalence of human brucellosis in Ethiopia from 2007 to 2022

Tailored interventions addressing local socio-economic and cultural factors are essential to mitigate the burden of brucellosis and its socio-economic consequences.

Strength and limitation of this review

Strengths

This study represents the first published systematic review and meta-analysis to provide a comprehensive estimate of the burden of human brucellosis in Ethiopia. By contributing to the existing knowledge on the epidemiology of the disease, the study offers valuable insights for policymakers, public health officials, and healthcare providers, addressing critical gaps in understanding the disease's impact. Additionally, the involvement of experts in health science, medical biotechnology, and clinical veterinary medicine throughout key stages, including search, screening, appraisal, and data extraction, ensures the evidence generated is both comprehensive and accurate. This multidisciplinary approach significantly enhances the study's credibility and reliability. Furthermore, data reporting adheres to the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol (PRISMA-P 2015 Statement), ensuring transparent and accurate reporting. This adherence not only bolsters the quality of the study but also facilitates the replication and comparison of findings with those of other studies, contributing to broader research endeavors.

Limitations

The potential limitations of this systematic review and meta-analysis primarily stem from the heterogeneity of the included studies. This heterogeneity may arise from various factors, such as differences in study design, diagnostic criteria, and patient populations, potentially affecting the generalizability of the findings. Additionally, all studies included in the review employed a cross-sectional design, which limits the ability to establish causal relationships or account for seasonal variations in the incidence of human brucellosis. Another notable limitation is the restriction to English-language articles, which may have excluded relevant studies published in other languages, thereby introducing a potential language bias.

Conclusion and recommendations

Based on the findings of this systematic review and meta-analysis, it is clear that human brucellosis is a significant public health issue in Ethiopia, with a pooled prevalence estimate of 14%. Reducing the prevalence and burden of brucellosis requires a multidisciplinary approach involving the government, healthcare workers, researchers, and the community. Therefore, it is recommended that

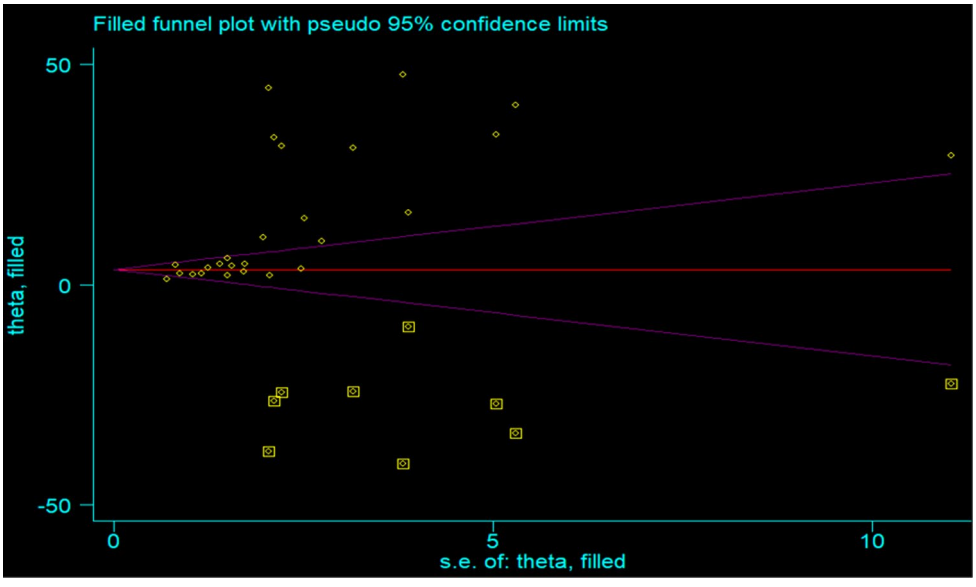

Fig. 7 Trim and fill analysis prevalence of human brucellosis in Ethiopia from 2007 to 2022

the Ethiopian government and other stakeholders take necessary actions to address the high prevalence and burden of brucellosis. Key measures include increasing public awareness about the disease, its modes of transmission, and prevention methods through public health campaigns, community outreach programs, and educational initiatives in schools and universities. Brucellosis screening should be integrated into routine assessments of febrile illnesses at healthcare facilities, and healthcare workers should be trained to effectively recognize and manage cases. This can be supported by providing rapid diagnostic tests and ensuring the availability of appropriate treatment options. Additionally, the Ethiopian government should strengthen its brucellosis surveillance system to facilitate the early detection of outbreaks and prompt responses to prevent further spread of the disease. Further research is needed to better understand the epidemiology of brucellosis in Ethiopia, including risk factors, transmission dynamics, and the genetic diversity of the causative agent. This research will provide critical information for developing more effective prevention and control strategies. Finally, adequate funding should be allocated to support the implementation of brucellosis control programs, enabling the government and other stakeholders to carry out essential activities such as screening, diagnosis, treatment, and surveillance.

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Author contributions
All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by all the authors. The first draft of the manuscript was written by {FA and NB} and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability
All available data and materials are included in the manuscript.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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