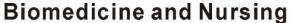
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#### SEROPREVALENCE OF SMALL RUMINANT BRUCELLOSIS IN ETHIOPIA: SYSTEMATIC REVIEW AND META-ANALYSIS

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**ABSTRACT: Objectives:** The purpose of this research is to perform a meta-analysis and systematic review on seroprevalence of small ruminant brucellosis in Ethiopia. **Methods:** The data searching journal like PubMed, Science Direct, Scopus, Embase and Google Scholar was used to search the articles. All articles are screened, which was reported seroprevalence of small ruminant brucellosis in Ethiopia to be included in the study. This systematic review and meta-analysis included 19 papers. Meta-analysis using random-effects models were made to calculate the pooled seroprevalence of brucellosis. **Results:** The study determined that the estimated pooled seroprevalence of small ruminant brucellosis was 3.0% (95% CI: 0.02, 0.03). According to the subgroup analysis, a statistically significant difference was found between the disease and the study region, publication year, laboratory technique used and studies years. Subgroup analysis by study regions the highest prevalence was observed in the Oromia region, with a prevalence of 3%, whereas the lowest prevalence was reported in the Amhara region, with a prevalence of small ruminant brucellosis in Ethiopia (Egger's test, p = 0.001). Conclusions: This analysis demonstrates the high seroprevalence of small ruminant brucellosis in Ethiopia and the necessity of suitable intervention strategies, such as increased public awareness creations and vaccination campaigns, as well as ongoing surveillance to manage and prevent brucellosis in cattle husbandry methods.

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Keywords: Brucellosis, Ethiopia, Meta-analysis, Seroprevalence, Small ruminant

#### **1. INTRODUCTION**

The World Health Organization (WHO) has classified brucellosis as a neglected zoonotic bacterial disease and determined that it has the largest public health burden among all community segments [18]. This is due to lack of effective control and proper disease surveillance [33, 21]. Animal and public health issues related to brucellosis persist in many poor nations, such as Ethiopia, where the disease is still endemic [6]. The currently recognized species includes Brucella abortus, B. Melitensis, B. Suis, B. Ovis, B. Canis, B. Ceti, B. Pinnipedialis, B. Neotomae, B. Microti and B. Inopinata [27]. The two major Brucella species known to infect sheep and goats are B. melitensis and B. ovis; however, B. abortus has also been observed to periodically increase in sheep and goat populations [29, 5]. In human, Brucellosis is always caused by B. melitensis (cause Undulant or Malta fever) followed by B. suis, B. abortus and B. canis [15].

The disease is transmitted to humans primarily from eating raw or undercooked animal products or through direct contact with infected animals. It causes a systemic infection with clinical manifestations such as fever, sweats, fatigue and joint pain [22]. The prevalence of brucellosis is affected by several risk factors such as production system, host and environmental factors [29]. In sheep and goats that are sexually mature, brucellosis is limited to the reproductive tract and typically causes placentitis and abortion in pregnant. *Brucella melitensis* and *B. abortus* are zoonotic pathogens that cause disease in humans [28, 29].

Brucellosis causes significant financial losses, such as a trade barrier for animals and animal products and restricts to free animal movements [37]. In addition, it causes in losses from fetus abortion, breeding failure (culling), and decreased milk production in the affected animal population.

The disease is often prevalent in traditional pastoral communities both in animals and humans but, due to lack of awareness the disease is not diagnosed and treated [2].

Generally, poor hygiene, prevalence of the disease in animals that expose humans from infected animals or their products influence the occurrence of the disease in humans. Cattle producers, veterinarians, animal health professionals, workers in abattoirs, laboratory personnel, and members of the general public who consume animal products are among the occupational categories most at risk of infection [3]. The conventional way of living, prevailing attitudes and inadequate understanding of the illness provide conducive circumstances for the dissemination and exchange of Brucellosis. The dearth of readily available alternatives and straightforward, reasonably priced remedies makes it challenging to control the hazards connected to these behaviors. Costeffectiveness in brucellosis control is likely to exist. To illustrate the advantages of intervention, accurate quantitative data on brucellosis in humans and livestock is crucial [35].

The prevention and control of brucellosis in small ruminants will contribute to reduce human brucellosis incidence, especially in the endemic regions of Ethiopia. Therefore, adequate knowledge of the epidemiology of Brucellosis is of great public health and economic importance, particularly amongst cattle owners, animal and animal product consumers, as this will greatly assist in controlling its infections. This study aimed to determine the pooled seroprevalence of small ruminant brucellosis by a systematic review and meta-analysis in Ethiopia.

# 2. METHODS

The systematic review and Meta-analysis were performed

according to the Preferred Reporting Items for Syste matic review and Meta-Analysis (PRISMA) flow chart guideline [24]. The STROBE checklist was used to ensure the inclusion of relevant information from the selected articles in the analysis. The outcome of interest was the proportion for small ruminant brucellosis.

# 2.1 Literature Search Strategy and Eligibility Criteria

The purpose of this meta-analysis and comprehensive review was to calculate the weighted seroprevalence of small ruminant brucellosis. Literature was searched in Pub Med, Science Direct, Scopus, African Journal Online and Google Scholar databases until July 18, 2022 to September 27, 2022. During an online article search, a Boolean operator and/or was utilized by combination of keywords related to the issue.

The following were the main search terms: "brucellosis" or

"Brucella"; "seroprevalence" or "prevalence" or "Sero epidemiology"; "risk factors" or "potential factors"; and "sheep and goat" or "ovine and Caprine" or "Ethiopia" AND "Small Ruminants"

We find studies with any of the keywords in their titles, abstracts, and complete texts using the Boolean operators "OR" and "AND." Moreover, unpublished thesis manuscripts were also accessed from University of Gondar library and College of Veterinary Medicine and Animal Sciences.

# 2.2 Inclusion and Exclusion Criteria

To ensure that the papers found during the search were eligible, we employed the subsequent inclusion criteria: 1) unique, peer-reviewed research papers and theses from Ethiopia; 2) cross-sectional studies that provided the seroprevalence of brucellosis in small ruminants; 3) articles with full-text studies; 4) research that included small ruminants in any type of management system as part of the targeted study population (intense or extensive). In this case, extensively managed small ruminants are kept on the grazing pasture and obtain their feed by grazing without supplementation; intensively managed small ruminants are those that are kept indoors the entire day or leave the house for leisure only a few hours each day; Studies reported the overall sample size and the outcome of interest (number of positive samples); 5) studies were conducted utilizing serological diagnostic tests such as, RBPT for screening and CFT or ELISA for confirmation; 6) studies provided the total sample size and the outcome of interest (number of positive samples); 7) studies published only in English language; and 8) studies published online between 2011 up to 2022. Papers which did not meet the abovementioned criteria were excluded. Besides, the references of the selected papers will be check manually to find relevant papers that were not retrieved in the database search [36].

# 2.3 Study selection and Data Extraction Procedure

Records identified from various electronic databases, indexing services and directories would be exported to Endnote software version X7. We found, noted, and deleted duplicate records. Two independent researchers were extract full text data and evaluate the eligibility of them for final inclusion. In each case, the rest authors play a critical role in solving discrepancies arose between two authors to come up to consensus.

Similarly, data extraction format were prepared based on first author, publication year, study year, geographical location (region), study design, sampling method, sample size, diagnostic test, setting and number of positive samples among the study groups. Seroprevalence of small ruminant brucellosis would calculate by dividing the number of positive cases by the total number of individuals used for the study in a given population at a given period. The study effect size and their corresponding confidence intervals would be calculated from the extracted data. Microsoft Excel datasheet was used to code and manage all extracted information from all relevant studies.

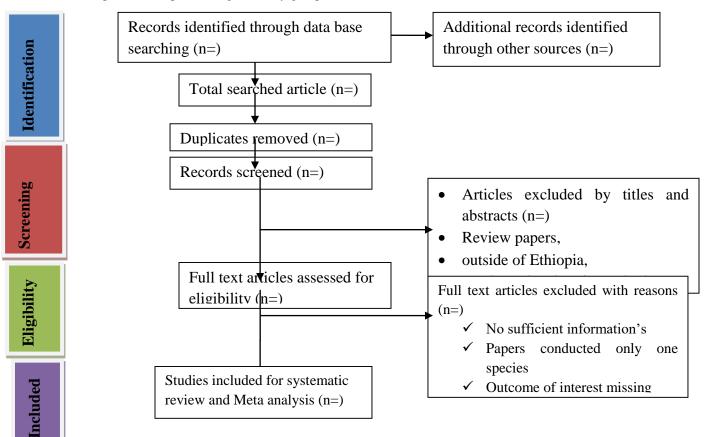


Figure 1: PRISMA guide line flow chart format describing the article selection procedure.

# 2.4 Study Quality Assessment

Two independent researchers were evaluated the quality of the included papers using a quality assessment checklist (standard strengthening the Reporting of Observational Studies in Epidemiology checklist (STROBE) which includes 22 items to make up the quality assessment checklist, which covers the title, abstract, introduction, methodology, results, and discussion of the articles.

The checklist comprised items evaluating the objectives, includes various material and methods

(e.g., sample size, study population, bias, statistical methods), outcomes and constraints of the research. The checklist included items assessing objectives, different components of the methods (eg, study design, sample size, study population, bias, statistical methods), results, limitations, and funding of the studies. The article quality scores were ranged from 0 to 44. Following the checklist (STROBE), searched papers were classified into 3 groups: low quality score (<15.50), moderate quality score (15.50-29.50) and high quality score (30.0-44.0) [17].

Table 1: STROBE Checklist for quality assessment of included studies STROBE Statement Checklist of items that should be included in reports of cross-sectional studies.

	Item No	
		Recommendation
Title and abstract	1	( <i>a</i> ) Indicate the study's design with a commonly used term in the title or the abstract
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any pre specified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	( <i>a</i> ) Give the eligibility criteria, and the sources and methods of selection of participants
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	( <i>a</i> ) Describe all statistical methods, including those used to control for confounding
		(b) Describe any methods used to examine subgroups and interactions
		(c) Explain how missing data were addressed
		( <i>d</i> ) If applicable, describe analytical methods taking account of sampling strategy

strategy

 $(\underline{e})$  Describe any sensitivity analyses

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
Outcome data	15*	Report numbers of outcome events or summary measures
Main results	16	( <i>a</i> ) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(b) Report category boundaries when continuous variables were categorized
		( <i>c</i> ) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done eg analyses of subgroups and interactions, and sensitivity analyses
Key results	18	Summarize key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

#### 2.5 Meta-Analysis

Data on the seroprevalence and corresponding 95% confidence intervals (CIs) of the disease were calculated for each study. The pooled prevalence estimates would be compute using the formula given by [9]. Forest plot diagram was employed to present the heterogeneity among studies, outcomes of meta-

analysis that display estimates of the seroprevalence, and their corresponding CIs of all included studies together with the pooled effect size. Similarly, subgroup analyses for the primary outcome (seroprevalence of brucellosis) would be done by study region, publication year, laboratory technique employed (CFT or ELISA) and sample size category. Cochran's Q-statistics and inverse variance index ( $I^2$ ) would be computed to determine the heterogeneity and inconsistency (true variation) among studies, respectively. Similarly, we considered the  $I^2$  values of 25%, 50% and 75% as low, medium and high heterogeneity respectively [19]. The tau statistics ( $\tau^2$ ) was used to assess the variance of the effect size estimates across the population of the study.

Based on the heterogeneity assessment result, we used DerSimonian and Laird's random-effects method (if the p-value of the Q test is 5%) or Mantel-Haenszel's fixed-effects method to pool the estimations [39]. Small study effects and publication bias presence were then visualized using funnel plot diagrams and, Egger's and Begg's asymmetry tests [11]. A funnel plot was computed using effect size and its corresponding standard error of the effect size. STATA software version 17 is used to do the metaanalysis.

# 3. RESULTS 3.1 Descriptive literature search results

A total of 187 potentially relevant studies were identified from several sources including PubMed,

Science Direct, Scopus and Google scholar. From these, 27 duplicated articles were removed with the help of Endnote 7. The remaining 160 records were screened using their titles and abstracts and 134 of them were excluded. Full texts of 26 records were then evaluated for eligibility. From these, 7 articles were excluded due to the outcome of interest was found missing, insufficient and/or ambiguous.

A total of 19 articles were eligible for the final systematic review and Meta-analysis from all screened studies. All of the eligible studies have been used RPBT and ELISA or CFT for antibody detection. These selected eligible articles were conducted namely; Oromia, Tigray, Amhara, Somali and Oromia and Somali. From 19 published articles a total of 10,067 samples of small ruminant (both sheep and goats) were subjected to disease detection. The sample size of

shoat ranges from 226 to 985 in each study area of Et hiopia. The seroprevalence of the disease in the 19 ar ticles was ranges from 1.40% to 9.1%. The mean sam ple size from overall report was 528.94. Finally, a tot al of 19 articles fulfilled the eligibility criteria and qu ality assessment and thus included for systematic revi ew and meta-analysis.

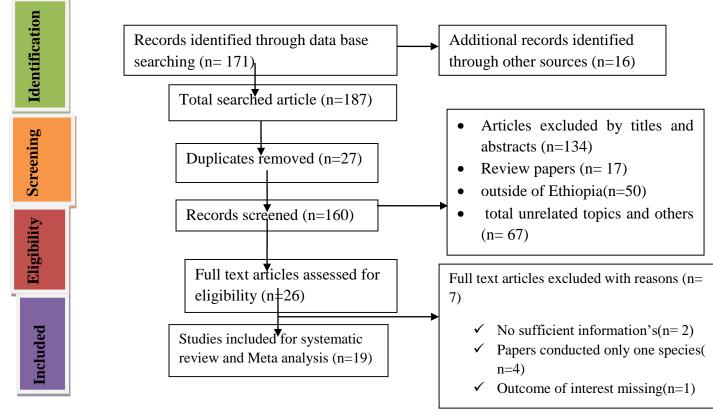


Figure 2: PRISMA guide line flow chart describing the article selection process.

# **3.2 Descriptive Study Characteristics**

The final 19 eligible studies which were considered for determining the seroprevalence of brucellosis in small

ruminants are summarized for systematic review and Meta-analysis. The studies were published in the year between 2011 and 2022. All the selected studies were cross-sectional study design in nature.

Author	Publication Year	Study area	Laboratory	Total	Diseased	Prevalence	Quality	Sco
			Techniques	Sample			re	
[35]	2018	Oromia	CFT	424	11	0.026	34	
[16]	2012	Oromia	CFT	384	35	0.091	38	
[41]	2018	Oromia	ELISA	283	23	0.081	37	
[25]	2021	Oromia	CFT	470	14	0.030	32	
[1]	2015	Oromia	ELISA	840	39	0.046	36	
[20]	2014	Oromia	RBPT	384	6	0.016	28.5	
[26]	2017	Tigray	CFT	558	10	0.018	29	
[39]	2014	Oromia and	CFT	420	15	0.036	30.5	
		Somali						
[12]	2013	Oromia	CFT	384	9	0.023	31	
[27]	2019	Oromia	CFT	762	11	0.014	27.5	
[10]	2011	Somali	CFT	730	11	0.015	28	
[22]	2017	Somali	CFT	291	4	0.014	27.5	
[36]	2015	Amhara	CFT	714	5	0.007	27	
[4]	2021	Somali	CFT	226	4	0.018	30	
[32]	2013	Tigray	CFT	985	15	0.015	29	
[31]	2015	Somali	CFT	285	6	0.021	30	
[38]	2015	Oromia	CFT	853	15	0.018	29.5	
[42]	2022	Oromia	CFT	384	6	0.016	31	
[14]	2022	Oromia	CFT	690	23	0.033	35	

Table 2: Characteristics of selected studies describing the seroprevalence of small ruminant brucellosis	1. E41.1
I apple 7.1 paracteristics of selected stilling descripting the seconcevalence of small filminant princellosis	in Ethiopia
1 doie 2. Characteristics of science according the science of small running fractions	m Lunopia.

#### 3.3 Meta-analysis

#### 3.3.1 Pooled prevalence estimate

Due to the expected variation between studies, randomeffects meta-analyses were employed using the total sample size and number of positives (effect size and standard error of the effect size). An overall pooled prevalence of the disease was estimated to be 3% (0.02 to 0.03 of 95% CI).

#### 3.4 Summary of Meta-analysis

Random-effects meta-analyses were employed using the prevalence and standard error of prevalence for effect size and standard error of the effect size and using author and publication year for the study label of the Metaanalysis.

Author with Publication year	Effect size	(95% conf. interval)	% Weight	
[35]	0.026	0.011 - 0.041	5.17	
[16]	0.091	0.062 - 0.120	3.27	
[41]	0.081	0.049 - 0.113	2.94	
[25]	0.030	0.014 - 0.045	5.13	
[1]	0.046	0.032 - 0.061	5.30	
[20]	0.016	0.003 - 0.028	5.57	
[26]	0.018	0.007 - 0.029	5.77	
[39]	0.036	0.018 - 0.053	4.77	
[12]	0.023	0.008 - 0.039	5.17	
[27]	0.014	0.006 - 0.023	6.09	
[10]	0.015	0.006 - 0.024	6.05	
[22]	0.014	0.000- 0.027	5.43	

[36]	0.007	0.001 - 0.013	6.34	
[4]	0.018	0.001 - 0.035	4.85	
[32]	0.015	0.008 - 0.023	6.19	
[31]	0.021	0.004 - 0.038	4.93	
[38]	0.018	0.009 - 0.026	6.05	
[42]	0.016	0.003 - 0.028	5.57	
[14]	0.033	0.020 - 0.047	5.43	
Theta		0.025	0.018- 0.032	

#### **3.5 Forest Plot**

Due to the expected variation between studies, random effects meta-analyses were carried out using the prevalence and standard error of prevalence (effect size and standard error of the effect size). ( $\chi^2 = 0.00$ ; I<sup>2</sup> = 85.65%, DF = 18, H<sup>2</sup>=6.96, Q - test = 82.72 and P -

value 0.00). Individual study prevalence estimates ranged from 1.40% to 9.1% with the overall random pooled prevalence of 3% (95% CI: 0.02, 0.03). Studies weighted approximately equal with weights on individual studies ranging from 2.94% to 6.19% due to high heterogeneity between studies.

Study						with 95%		Weight (%)
Teshome et al.,2018	-					0.03 [ 0.01,	0.04]	5.17
Efa et al.,2012			-	 		0.09 [ 0.06,	0.12]	3.27
Wubishet et al.,2018				 		0.08 [ 0.05,	0.11]	2.94
Muhidin et al.,2021						0.03 [ 0.01,	0.05]	5.13
Abiot et al.,2015		-	-			0.05 [ 0.03,	0.06]	5.30
Lemu et al.,2014						0.02 [ 0.00,	0.03]	5.57
Mulalem et al.,2017	_	-				0.02 [ 0.01,	0.03]	5.77
Tsehay et al.,2014						0.04 [ 0.02,	0.05]	4.77
Dabassa et al.,2013	-		-			0.02 [ 0.01,	0.04]	5.17
Mustefa et al.,2019	-	-				0.01 [ 0.01,	0.02]	6.09
Bekele et al.,2011	-	-				0.02 [ 0.01,	0.02]	6.05
mohammed et al.,2017						0.01 [ 0.00,	0.03]	5.43
Tewdros and Dawit,2015	-	ŀ				0.01 [ 0.00,	0.01]	6.34
Ahad,2021						0.02 [ 0.00,	0.03]	4.85
Teklue et al.,2013	-	-				0.02 [ 0.01,	0.02]	6.19
Sintayehu et al.,2015	-		-			0.02 [ 0.00,	0.04]	4.93
Tsegay et al.,2015	-	-				0.02 [ 0.01,	0.03]	6.05
Yune et al.,2022						0.02 [ 0.00,	0.03]	5.57
Dosa et al.,2022			-			0.03 [ 0.02,	0.05]	5.43
Overall		$\blacklozenge$				0.03 [ 0.02,	0.03]	
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = 85.63\%$ , $H^2 = 6.96$								
Test of $\theta_i = \theta_j$ : Q(18) = 82.72, p = 0.00								
Test of $\theta$ = 0: z = 6.73, p = 0.00								
	Ó		.05	.1	.1	5		
Pandom offacts PEMI model								

## Random-effects REML model

Figure 3: Forest Plot depicting the seroprevalence of small ruminant brucellosis in Ethiopia.

## 3.6 Subgroup Meta-Analysis

3.6.1 Subgroup Analysis by study Regions

Subgroup analyses were done for study Regions (Oromia, Somali Oromia and Somali, Amhara and

Tigray regions of Ethiopia). Thus, high seroprevalence was observed in Oromia region 3% (95% CI: 0.02 - 0.05), whereas the same prevalence was observed in both Somali and Tigray region 2% (95% CI: 0.01– 0.02) and the lowest prevalence was observed in Amhara region 1% (95% CI: 0.00– 0.01).

Amhara Amhara Heterogeneity: $\tau^2 = 0.00$ , $I^2 = .\%$ , $H^2 = .$ Test of $\theta_i = \theta_j$ : Q(0) = 0.00, p = .	•				_
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = .\%$ , $H^2 = .$	•				
	•			0.01 [ 0.00, 0.01]	6.34
Test of $\theta_i = \theta_j$ : Q(0) = 0.00, p = .				0.01 [ 0.00, 0.01]	
Oromia					
Oromia				0.03 [ 0.01, 0.04]	5.17
Oromia		_		 0.09 [ 0.06, 0.12]	3.27
Oromia				 0.08 [ 0.05, 0.11]	2.94
Oromia				0.03 [ 0.01, 0.05]	5.13
Oromia				0.05 [ 0.03, 0.06]	5.30
Oromia		-		0.02 [ 0.00, 0.03]	5.57
Oromia		<b>I</b> —		0.02 [ 0.01, 0.04]	5.17
Oromia	-			0.01 [ 0.01, 0.02]	6.09
Oromia	-			0.02 [ 0.01, 0.03]	6.05
Oromia		-		0.02 [ 0.00, 0.03]	5.57
Oromia				0.03 [ 0.02, 0.05]	5.43
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = 90.39\%$ , $H^2 = 10.41$				0.03 [ 0.02, 0.05]	
Test of $\theta_i = \theta_j$ : Q(10) = 55.79, p = 0.00					
Oromia and Somali					
Oromia and Somali				0.04 [ 0.02, 0.05]	4.77
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = .\%$ , $H^2 = .$	<			0.04 [ 0.02, 0.05]	
Test of $\theta_i = \theta_j$ : Q(0) = 0.00, p = .					
Somali					
Somali	-			0.02 [ 0.01, 0.02]	6.05
Somali				0.01 [ 0.00, 0.03]	5.43
Somali				0.02 [ 0.00, 0.03]	4.85
Somali				0.02 [ 0.00, 0.04]	4.93
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = 0.00\%$ , $H^2 = 1.00$	•			0.02 [ 0.01, 0.02]	
Test of $\theta_i = \theta_j$ : Q(3) = 0.54, p = 0.91	•				
Tigray					
Tigray		-		0.02 [ 0.01, 0.03]	5.77
Tigray				0.02 [ 0.01, 0.02]	6.19
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = 0.17\%$ , $H^2 = 1.00$	•			0.02 [ 0.01, 0.02]	
Test of $\theta_i = \theta_j$ : Q(1) = 0.16, p = 0.69	Ť				
Overall	•			0.03 [ 0.02, 0.03]	
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = 85.63\%$ , $H^2 = 6.96$	-				
Test of $\theta_i = \theta_j$ : Q(18) = 82.72, p = 0.00					
Test of group differences: $Q_b(4) = 19.06$ , p = 0.00					
	ó	.05	.1	15	
Random-effects REML model					
igure 4: Subgroup analysis by study regions					

3.6.2 Subgroup Analysis by publication year category

Subgroup analyses were done by articles publication year category. Thus, the same seroprevalence was

observed the publication year category from 2011 - 2014 and 2015 - 2018 with the prevalence 3 %( 95% CI: 0.00 - 0.06 and 0.01 - 0.04) and the publication

# year category from 2019 - 2022 with prevalence of 2% (95% CI: 0.01 - 0.03) respectively.

Study		Weight
Study 1	with 95% Cl	(%)
Efa et al.,2012	0.09 [ 0.06, 0.12]	3.27
Lemu et al.,2014		5.57
Tsehay et al.,2014		4.77
Dabassa et al.,2013		5.17
Bekele et al.,2011		6.05
Teklue et al.,2013		6.19
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = 93.87\%$ , $H^2 = 16.32$	0.03 [ 0.01, 0.05]	0.10
Test of $\theta_i = \theta_j$ : Q(5) = 29.80, p = 0.00		
2		
Teshome et al.,2018		5.17
Wubishet et al.,2018	0.08 [ 0.05, 0.11]	2.94
Abiot et al.,2015		5.30
Mulalem et al.,2017		5.77
mohammed et al.,2017		5.43
Tewdros and Dawit,2015	0.01 [ 0.00, 0.01]	6.34
Sintayehu et al.,2015	0.02 [ 0.00, 0.04]	4.93
Tsegay et al.,2015		6.05
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = 89.45\%$ , $H^2 = 9.48$	0.03 [ 0.01, 0.04]	
Test of $\theta_i = \theta_j$ : Q(7) = 44.19, p = 0.00		
3		
Muhidin et al.,2021		5.13
Mustefa et al.,2019		6.09
Ahad,2021	0.02 [ 0.00, 0.03]	4.85
Yune et al.,2022		5.57
Dosa et al.,2022		5.43
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = 47.93\%$ , $H^2 = 1.92$ Test of $\theta_i = \theta_j$ : Q(4) = 7.57, p = 0.11	<ul> <li>0.02 [ 0.01, 0.03]</li> </ul>	
Overall	• 0.03 [ 0.02, 0.03]	
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = 85.63\%$ , $H^2 = 6.96$	► 0.03 [ 0.02, 0.03]	
Test of $\theta_i = \theta_j$ : Q(18) = 82.72, p = 0.00		
Test of group differences: $Q_b(2) = 0.81$ , p = 0.67		
Random-effects REML model	0 .05 .1 .15	

**Note:** - 1=2011 - 2014, 2=2015 - 2018, 3=2019 - 2022 Figure 5: Subgroup analysis by publication year category

3.6.3 Subgroup Analysis by Laboratory techniques

Subgroup analyses were done for laboratory techniques (RBPT, CFT and ELISA). Thus, high

seroprevalence was observed in ELISA6% (95% CI: 0.03 - 0.09) followed by CFT and RBPT with both the same seroprevalence of 2% (95% CI: 0.00 - 0.02 and 0.00 - 0.03) respectively.

Study				with 95% CI	Weight (%)
1					
Lemu et al.,2014		-		0.02 [ 0.00, 0.03]	5.57
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = .\%$ , $H^2 = .$				0.02 [ 0.00, 0.03]	
Test of $\theta_i = \theta_j$ : Q(0) = 0.00, p = .					
2					
Wubishet et al.,2018				0.08 [ 0.05, 0.11]	2.94
Abiot et al.,2015				0.05 [ 0.03, 0.06]	5.30
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = 73.93\%$ , $H^2 = 3.84$				0.06 [ 0.03, 0.09]	
Test of $\theta_i = \theta_j$ : Q(1) = 3.84, p = 0.05					
3					
Teshome et al.,2018		<b>—</b>		0.03 [ 0.01, 0.04]	5.17
Efa et al.,2012				0.09 [ 0.06, 0.12]	3.27
Muhidin et al.,2021				0.03 [ 0.01, 0.05]	5.13
Mulalem et al.,2017		-		0.02 [ 0.01, 0.03]	5.77
Tsehay et al.,2014				0.04 [ 0.02, 0.05]	4.77
Dabassa et al.,2013		<b>—</b>		0.02 [ 0.01, 0.04]	5.17
Mustefa et al.,2019	-			0.01 [ 0.01, 0.02]	6.09
Bekele et al.,2011	-			0.02 [ 0.01, 0.02]	6.05
mohammed et al.,2017				0.01 [ 0.00, 0.03]	5.43
Tewdros and Dawit,2015	·			0.01 [ 0.00, 0.01]	6.34
Ahad,2021				0.02 [ 0.00, 0.03]	4.85
Teklue et al.,2013	-			0.02 [ 0.01, 0.02]	6.19
Sintayehu et al.,2015				0.02 [ 0.00, 0.04]	4.93
Tsegay et al.,2015	-			0.02 [ 0.01, 0.03]	6.05
Yune et al.,2022		-		0.02 [ 0.00, 0.03]	5.57
Dosa et al.,2022				0.03 [ 0.02, 0.05]	5.43
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = 72.83\%$ , $H^2 = 3.68$	•			0.02 [ 0.02, 0.03]	
Test of $\theta_i = \theta_j$ : Q(15) = 51.72, p = 0.00					
Overall	•			0.03 [ 0.02, 0.03]	
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = 85.63\%$ , $H^2 = 6.96$					
Test of $\theta_i = \theta_j$ : Q(18) = 82.72, p = 0.00					
Test of group differences: $Q_b(2) = 6.11$ , p = 0.05			I		
Random-effects REML model	0	.05	.1	.15	
ote: - 1=RBPT, 2=ELISA, 3=CFT					
$\mathbf{U}_{\mathbf{C}} = \mathbf{I} - \mathbf{N} \mathbf{D} \mathbf{\Gamma} \mathbf{I}, 2 - \mathbf{L} \mathbf{L} \mathbf{I} \mathbf{S} \mathbf{A}, 3 - \mathbf{C} \mathbf{\Gamma} \mathbf{I}$					

Figure 6: Subgroup analysis by Laboratory techniques.

#### 3.6.4 Subgroup analysis by sample size

Subgroup analyses were done for sample size which has been categorized into three parts like <300, 300 - 600 and >600. Thus, high seroprevalence was

observed in both sample size category of <300 and 300 - 600 with the seroprevalence of 3% (95% CI: 0.00 - 0.06 and 0.01 - 0.05), whereas the least prevalence was observed in sample size category of >600 with 2% (95% CI: 0.01– 0.03) respectively.

Study					with §	95% CI	Weigl (%)
1							
Wubishet et al.,2018			_		0.08[0.	05, 0.11]	2.94
mohammed et al.,2017					0.01[0.	00, 0.03]	5.43
Ahad,2021		_			0.02[0.	00, 0.03]	4.85
Sintayehu et al.,2015					0.02[0.	00, 0.04]	4.93
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = 89.37\%$ , $H^2 = 9.41$					0.03[0.	00, 0.06]	
Test of $\theta_i = \theta_j$ : Q(3) = 15.02, p = 0.00							
2							
Teshome et al.,2018		<b>—</b>			0.03[0.	01, 0.04]	5.17
Efa et al.,2012		-			0.09 [ 0.	06, 0.12]	3.27
Muhidin et al.,2021					0.03[0.	01, 0.05]	5.13
Lemu et al.,2014		-			0.02 [ 0.	00, 0.03]	5.57
Mulalem et al.,2017		-			0.02 [ 0.	01, 0.03]	5.77
Tsehay et al.,2014					0.04 [ 0.	02, 0.05]	4.77
Dabassa et al.,2013		<b>—</b>			0.02 [ 0.	01, 0.04]	5.17
Yune et al.,2022		-			0.02 [ 0.	00, 0.03]	5.57
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = 84.97\%$ , $H^2 = 6.65$ Test of $\theta_i = \theta_j$ : Q(7) = 27.85, p = 0.00					0.03 [ 0.	.02, 0.04]	
3							
Abiot et al.,2015					0.05 [ 0.	.03, 0.06]	5.30
Mustefa et al.,2019	-				0.01[0.	01, 0.02]	6.09
Bekele et al.,2011	-				0.02[0.	01, 0.02]	6.05
Tewdros and Dawit,2015	-				0.01[0.	00, 0.01]	6.34
Teklue et al.,2013	-				0.02[0.	01, 0.02]	6.19
Tsegay et al.,2015					0.02[0.	01, 0.03]	6.05
Dosa et al.,2022					0.03[0.	02, 0.05]	5.43
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = 86.72\%$ , $H^2 = 7.53$	•	•			0.02[0.	01, 0.03]	
Test of $\theta_i = \theta_j$ : Q(6) = 32.63, p = 0.00							
Overall	•				0.03 [ 0.	02, 0.03]	
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = 85.63\%$ , $H^2 = 6.96$							
Test of $\theta_i = \theta_j$ : Q(18) = 82.72, p = 0.00							
Test of group differences: $Q_b(2) = 1.45$ , p = 0.48	·						
	0	.05		.1	.15		

Figure 7: Subgroup analysis by Sample size.

# **3.7 Publication Bias**

3.7.1 Funnel plot for visualizing publication bias

We assessed publication bias and small study effects by funnel plot observation and Egger's test for small study effects. The funnel plot that visually observed there were asymmetry in which the result of effect estimates against its standard error showed that there was some evidence of publication bias and small study effect on studies reporting the seroprevalence of brucellosis in small ruminant in Ethiopia.

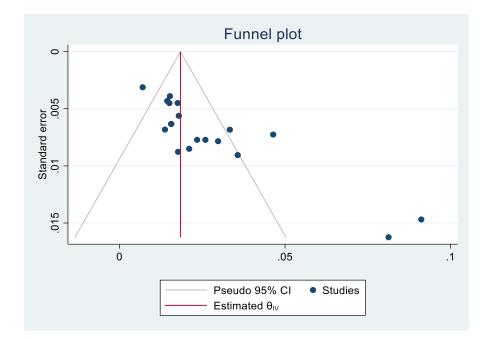


Figure 8: Funnel plot that assesses publication bias.

3.7.2 Egger test detecting publication bias

From Egger's test statistics result there was publication bias and small study effect since the estimated bias coefficient 4.729 with standard error 0.666 and p - value 0.001.

Table 4: Egger test that assesses publication bias.

# 3.8 Meta-Regression

Meta-regression analysis was done for each variable included in the study separately. The variables coded as categorical variables and those variables included were study regions, publication year, study year, laboratory techniques and sample size were employed. Those variables with p-values <0.05 were used in the multivariable Meta regression analysis. Only laboratory techniques had significant value and retained in the final multivariable Meta regression analysis.

Table5:Summary of final multivariable Meta-regression analysis.

# 4. DISCUSSION

Brucellosis induces considerable human suffering and huge economic losses in animals [8, 34]. It has a significant public health implication for a pastoral

Std.Ef f	Coefficien t	Std. err	p- valu e	95% conf . interval
Slope	-0.0072	0.	0.07	-0.015 -
		004	2	0.0006
Bias	4.729	0.66	0.00	3.423 -
		6	0	6.035

Variable s		Coeffic ient	Std. errs.	P- value	95%Conf. interval
Laborat ory techniqu es	R ef.				
	2	0.041	0.016	0.009	0.010 - 0 .072
	3	0.006	0.012	0.635	-0.018 - 0.030

community in consequence of lifestyles, feeding habits, close contact with animals, low awareness, and poor hygienic conditions which favors infection [7]. Also, it can generally cause significant loss of productivity through abortion, prolonged calving, kidding, or lambing interval, low herd fertility, and comparatively low milk production in farm animals.

The disease impairs socio-economic development for livestock owners, which represents a vulnerable sector in rural populations in general and pastoral communities in particular. Even though, most reports have made either limited geographic coverage or are relatively confined to a single agro ecology, these stated evidences strongly suggest that brucellosis might be a widespread problem in Ethiopia [33](Terefe *et al.*, 2017).

But the seroprevalence of the disease is affected by different factors like, environmental factors, the number of samples, type of strains, stage of infection and type of diagnostic techniques used. The approaches of Meta-analysis allow identifying the role of such factors, by combining results of different reports, with different designs, agro ecology and locations. Good meta-analysis outputs are relevant for the management and control of an infectious disease like Brucellosis that could not be identified by individual studies alone [13] . This is the first quantitative meta- analysis on the sero-prevalence of small ruminant brucellosis in Ethiopia to the best of our knowledge for evidence based decision.

We have used 19 cross sectional studies with 10067 serum samples that have been undertaken between years from 2011 to 2022 in Ethiopia were included in this study; the pooled seroprevalence of small ruminant brucellosis was 3.0%. This result is higher than the meta-analysis report of [30] from sheep and goat in China where the pooled prevalence was 2%. Similarly, the current finding was higher than the reports of [38] who reported prevalence of 1.80% from small ruminant selected in different area in Oromia region in Ethiopia. The current finding is in line with the report of [14,25] from small ruminant brucellosis in Oromia region in Ethiopia where the pooled prevalence was 2.97 and 3.30% respectively.

Mean while, the current finding was lower than the reports of [1, 16, 41] from small ruminant brucellosis in different districts of Oromia region in Ethiopia where the pooled seroprevalence was 4.64%.8.13% and 9.1% respectively. The difference in the seroprevalence of small ruminant brucellosis in the different studies could be due to differences in the geographical location and animal husbandary practice between the different study areas. Therefore, information on the actual seroprevalence of the small ruminant brucellosis in the country helps the policymakers to develop appropriate strategies regarding prevention and control protocols. In the

present study, the subgroup analysis showed that there was a statistically significant association between the disease and study regions, publication year, laboratory technique employed and study years. Also, there was evidence of publication bias and small study effects (Egger's test, p = 0.001) on studies reporting the seroprevalence of small ruminant brucellosis in Ethiopia.

# **5. LIMITATIONS**

The potential limitation of this systematic review and the heterogeneity. meta-analysis was The heterogeneity of the included studies could be due to various factors such as differences in study design, diagnostic criteria, and study populations, which can affect the generalisability of the findings. All studies included in this systematic review and meta-analysis had a cross-sectional design. The cross-sectional design of these studies may limit their ability to establish causal relationships or capture seasonal variations in the incidence of small ruminant brucellosis. Another potential limitation is the language restriction of the English-language articles, which may have excluded relevant studies published in other languages.

# 6. CONCLUSION AND RECOMMENDATIONS

We conduct a systematic review and meta-analysis to assess the seroprevalence of brucellosis in small ruminant in Ethiopia. The seroprevalence of brucellosis in small ruminant is different in different parts of Ethiopia. There is a limited knowledge and studies about the systematic review and Meta-analysis in many regions of the country and the findings are heterogeneous. The result of this meta-analysis shows that the pooled prevalence estimate of the disease in the country is 3.0%. Therefore, the pooled seroprevalence of small ruminant brucellosis is used for evidence-based disease control in Ethiopia.

Based on the above conclusions the following recommendations are forwarded;

- The overall data demands intervention measures, including vaccination and enhanced public awareness, and further surveillance for the control and prevention of brucellosis in livestock husbandry practices.
- Further studies were needed to understand the epidemiology of brucellosis in Ethiopia, including the risk factors, transmission dynamics, and genetic diversity of the causative agent. This should provide valuable information for the development of effective prevention and control strategies.

• To consider the significance of small ruminant brucellosis in the national economy, strategies to reduce the prevalence and burden of brucellosis the government and other stakeholders prioritized and offered adequate funding to carry out necessary activities, such as screening, diagnosis, treatment, and surveillance.

#### **Data Sharing Statement**

All data generated during this study are included.

#### **Author Contributions**

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

#### Disclosure

The authors declare that they have no competing interest.

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