

Review

***Strongyloides stercoralis* infection in Ethiopia: systematic review and meta-analysis on prevalence and diagnostic methods**

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Summary

Strongyloides stercoralis is a helminthic intestinal parasite that causes the disease strongyloidiasis. Its prevalence is high in tropics and sub-tropics due to poor sanitation and hygiene. However, its true prevalence is not well known in Ethiopia as most health institutions use low sensitive diagnostic methods. This review aimed to determine the pooled prevalence of *S. stercoralis* at country, and regional state levels. Papers published on *S. stercoralis* in Ethiopia from 2010 to 2020 were collected from PubMed, Google Scholar and Science direct databases and Addis Ababa repository. Identification, screening, checking the eligibility, and inclusion of the relevant literatures were done. Articles with *S. stercoralis* positive results from Ethiopian populations were included. Articles which focused on *Strongyloides* infection in foreigners, and other than stool samples were excluded. The pooled prevalence of *S. stercoralis* and heterogeneity between studies and across regions were computed. From the 43 articles, the overall prevalence of *S. stercoralis* in Ethiopia was 1.82 %. Across regions, relatively high prevalence of *S. stercoralis* (8.78 %) was recorded in Addis Ababa city. High prevalence of *S. stercoralis* was found to be 44.02 % with a combination of formol ether concentration, Baermann concentration, and molecular methods. Low prevalence of 0.26 %, 0.31 %, and 1.20 % was evidenced respectively with Kato-Katz, direct saline microscopy, and formol ether concentration methods. Using random effect analysis, the pooled prevalence of *S. stercoralis* in Ethiopia, across regions and across diagnostic methods was 2.1 % (95 %CI: 1.20 – 3.60), 2.6 % (95 %CI: 0.80 – 8.20) and 3.7 % (95 %CI: 1.10 – 11.70), respectively. The heterogeneity was high ($P < 0.001$). This review revealed that *Strongyloides* infection is probably underreported and its prevalence could be higher than the reported in Ethiopia. Therefore, a revision of the best combination of diagnostic methods could be advisable as it gives better diagnostic results in routine diagnosis of *Strongyloides* infection in Ethiopia.

Keywords: *Strongyloides* infection; prevalence; diagnostic methods; Ethiopia

Introduction

The genus *Strongyloides* is one of the soil-transmitted helminths that infect humans worldwide (Olsen *et al.*, 2009). *Strongyloides stercoralis* and *S. fuelleborni* are the only two species that infect

humans. *Strongyloides stercoralis* infection is prevalent across many areas of tropics and subtropics (Schar *et al.*, 2013), whereas most *S. fuelleborni* human infections are prevalent in Africa (Schad *et al.*, 1989). *Strongyloides* infection is a common problem in communities with poor personal hygiene, poor environmental sanitation.

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tion and open defecation practicing areas (Abrescia *et al.*, 2009). The detection of larvae in stool is the major identification stage of the parasite (Siddiqui *et al.*, 2001). The direct saline microscopy (DSM) is a very simple and rapid diagnostic method (Nielsen *et al.*, 1987); however, it has poor sensitivity in *S. stercoralis* detection (Requena-Méndez *et al.*, 2013). This is due to the fact that low parasite load and irregular larval excretion (Montes *et al.*, 2010), and chronic low-intensity *S. stercoralis* infection (Schar *et al.*, 2013) limit the sensitivity of traditional methods. As a result, misdiagnosis and underreporting of *S. stercoralis* infection by DSM is a common phenomenon.

Although better detection rate of *S. stercoralis* is obtained using one of the following: Baermann concentration technique (BCT), stool culture, Polymerase Chain Reaction (PCR), or a combination of these methods (Campo-Polanco *et al.*, 2018), their limitations to apply as a routine diagnostic method in Ethiopia is a big challenge. This situation forced the health institutions to employ DSM method

for the diagnosis of *Strongyloides* infection. As a result, under diagnosis and underreporting of the true prevalence of *S. stercoralis* infection in Ethiopia is a major problem (Terefe *et al.*, 2019). Thus, the aim of this systematic review and meta-analysis was to provide an overview of the prevalence of *Strongyloides* infection by country and regional label and by diagnostic methods used in Ethiopia.

Materials and Methods

The PubMed, Google Scholar, and Science direct databases and Addis Ababa University repository were searched for articles written in English during the year 2010 to 2020 containing the keywords: “Strongyloidiasis” AND “Ethiopia” OR “*Strongyloides* AND “Ethiopia” OR “*Strongyloides stercoralis*” AND “Ethiopia” OR “Soil-transmitted helminths” AND “Ethiopia”. The electronic data search of studies was conducted from January to 30 June 2020. Identification, screening, checking the eligibility and the inclusion

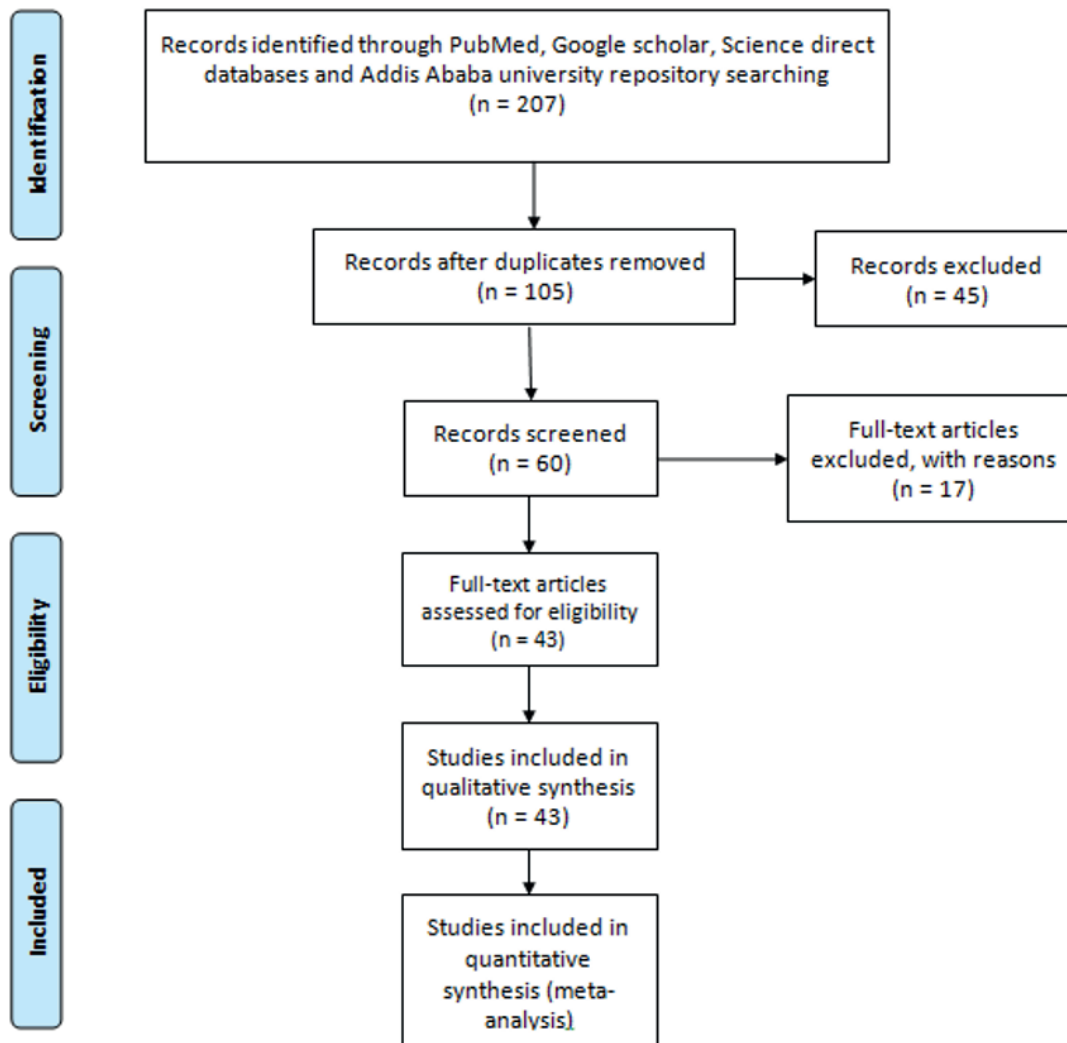


Fig. 1. Overview of search methods of the articles with inclusion and exclusion criteria.

of the relevant literatures were done following the preferred reporting items for systematic reviews and meta-analyses (PRISMA) (Fig 1). Articles were first screened to remove duplication. And then the articles were also screened by reading titles and abstracts and initially excluded if they did not specifically refer to *S. stercoralis* or if they were review articles. Finally, the articles were further screened by reading the full articles and excluded if they did not investigate the prevalence of *Strongyloides* infection.

Inclusion criteria: All studies conducted in Ethiopian populations checking stool samples and diagnosed with DSM, Kato-Katz (KK), formol ether concentration techniques (FECT), BCT, culture, PCR or a combination these diagnostic techniques and got positive result for at least one individual among the study participants were included. Inclusion of literatures only from PubMed, Google Scholar, Science direct databases and Addis Ababa repository was the limitation. To minimize the risk of bias, publication bias assessment was done across studies.

Exclusion criteria: All articles dealing with *Strongyloides* infection in animals, soil, foreigners as study subjects in Ethiopia, non-stool samples, duplications, review articles, case studies, cohort studies and articles conducted before the year 2010 were excluded.

The data was extracted independently from each study and the pooled prevalence of *S. stercoralis* in Ethiopia, and across regions and by average prevalence by diagnostic method were also computed.

The meta-analysis was also performed using comprehensive meta-analysis 2.2 software (Biostat Inc., Englewood, NJ, USA). The pooled prevalence rate of *S. stercoralis* at country was calculated using a random-effect model at 95 % confidence interval (CI). In the subgroup analysis, the pooled prevalence and forest plot of *S. stercoralis* in the regions and diagnostic methods was also calculated. Additionally, separate meta-analyses were performed to compare the effect of diagnostic methods in the detection of *S. stercoralis*. Heterogeneity between studies in region and across diagnostic methods was assessed using Cochran (Q)-value, *P*-value and I^2 and visual inspection of the funnel plot. The level of statistical significance for all tests was set at $P < 0.05$. Publication bias was checked by funnel plot.

Results

A total of 207 studies identified from PubMed, Google scholar, Science direct databases and Addis Ababa University repository. Forty three studies were screened and recorded after duplications removed. Finally, 43 studies were eligible after full text assessment and included in qualitative analysis (Fig 1).

Prevalence of *Strongyloides stercoralis*

A total of 43 studies having *S. stercoralis* reports which full-filled the inclusion criteria and a total of 78,959 study participants were

involved. The overall prevalence of *S. stercoralis* among study participants was 1.82 % [1437/78959] (Table 1).

A relatively high prevalence (55.68 %) of *S. stercoralis* infection was recorded among participants age greater than five years (Aramendia *et al.*, 2020) followed by (20.71 %) in schoolchildren of rural highlands of Amhara Regional State (Amor *et al.*, 2016), (20.0 %) in SNNPR schoolchildren (Eriso F, 2014), (15.05 %) of schoolchildren in the Amhara Regional State (Hailu *et al.*, 2020), and (12.25 %) in patients of health institution of Addis Ababa City (Hailegebriel *et al.*, 2017) among studies conducted in Ethiopia (Table 1).

A very low prevalence of *S. stercoralis*; (0.21 %) in a community children (King *et al.*, 2013), and 0.24 % in patients of Amhara Regional State (Abate *et al.*, 2013), 0.26 % in schoolchildren of Tigray Regional State (Legese *et al.*, 2010), and (0.26 %) in HIV cases in Oromia Regional State (Admasu H, 2013), and 0.29 % in patients (Ramose *et al.*, 2014) was obtained from studies conducted in the country (Table 1).

In this review, the lowest prevalence of *Strongyloides* infection reported from a single study was 0.21 % by FECT (King *et al.*, 2013), followed by 0.24 % by combination of DSM and FECT (Abate *et al.*, 2013), 0.26 % by KK (Leegese *et al.*, 2010) and by combining DSM and FECT (Adamu *et al.*, 2013), and 0.27 % by DSM and FECT combination (Mengist *et al.*, 2017) (Table 1).

Regarding regional reports relatively high prevalence of *S. stercoralis* 55.68 % (Aramendia *et al.*, 2020) and 20.21 % (Amor *et al.*, 2016), was reported using a combination of diagnostic methods in Amhara Regional State followed by 20.0 % among Schoolchildren in SNNPR (Eriso H, 2014), and 12.25 % among patients in Addis Ababa (Hailegebriel *et al.*, 2017) (Table 1).

Among studies used single diagnostic methods, high prevalence (20.0 %) of *S. stercoralis* was recorded by BCT among schoolchildren in SNNPR (Eriso F, 2014) followed by 3.59 % *S. stercoralis* prevalence by FECT in HIV cases in the Amhara Regional State (Eshetu T, 2017) and 3.13 % prevalence by DSM among patients in Amhara Regional State (Huruy *et al.*, 2011).

Using random effect analysis, the pooled prevalence of *S. stercoralis* in Ethiopia was 2.1 % (95 %CI: 1.20 – 3.60). The heterogeneity was high ($Q = 4264.8$, $I^2 = 99.0$ %, $P < 0.001$) (Fig 2).

The studies were distributed symmetrically about the combined effect size that showed the absence of publication bias (Fig 3).

From 43 studies, 16 (37.21 %) were conducted in Amhara regional state followed by 15 (34.88 %) in SNNPR. The number of participants was high 58,917 (74.62 %) and 9,076 (11.49 %) in the SNNPR and the Tigray Regional State, respectively. The pooled prevalence of *S. stercoralis* was relatively high in the Addis Ababa City (8.78 %) followed by (8.54 %) in the Amhara Regional State among regions. Low prevalence *S. stercoralis* infection among regions was recorded in Tigray Regional State (0.67 %) followed by (0.93 %) in SNNPR (Table 2).

Using random effect analysis, the pooled prevalence of *S. stercoralis* across the regions was 2.6 % (95 %CI: 0.80 – 8.20). The

No	First Authors	Year of Pub	Region	Participant history	Sample size	No SS cases	Prevalence (95%CI)	Diagnostic method
1	Hailu T	2020	Amhara	Sch	844	127	15.05 [12.74-17.68]	FECT,STST,BCT,APC
2	Aramendia AA	2020	Amhara	>5 years	792	441	55.68 [52.14-59.17]	FECT,BCT,PCR
3	Getaneh F	2020	Amhara	Patient	67	2	3.0 [0.82-10.25]	DSM, KK
4	Kuti KA	2020	Oromia	FH	198	8	4.04 [2.06-7.77]	DSM, FECT
5	Tsegay B	2020	SNNPR	Children	622	12	1.93 [1.11-3.34]	DSM,FECT
6	Menjetta T	2019	SNNPR	UN/student	13,679	41	0.30 [0.22-0.41]	DSM
7	Gemech A	2019	SNNPR	Prisoner	320	18	5.63 [3.59-8.72]	DSM, FECT
8	Alemu G	2019	SNNPR	Sch	351	7	1.99 [0.97-0.41]	DSM, FECT
9	Alemu G	2018	SNNPR	HIV	220	4	1.82 [0.71-4.58]	DSM, FECT
10	Gebretsadik D	2018	Amhara	HIV	223	1	0.45 [0.02-2.86]	DSM, FECT
11	Hailegebriel T	2018	Amhara	Sch	382	5	1.31 [0.48-3.21]	FECT
12	Teklmariam D	2018	Oromia	Sch	280	4	1.43 [0.46-3.87]	FECT, KK
13	Mengist HM	2017	Oromia	Pregnant	372	1	0.27 [0.01-1.73]	DSM,FECT
14	Eshetu T	2017	Amhara	HIV	223	8	3.59 [1.68-7.21]	FECT
15	Feleke DG	2017	Tigray	Patient	7,663	47	0.61 [0.45-0.82]	DSM,FECT
16	Alemu M	2017	Tigray	Patient	427	8	1.87 [0.87-3.80]	DSM, KK
17	Hailegebriel T	2017	AA	Patient	351	43	12.25 [9.22-16.09]	DSM,FECT, BCT Culture
18	Abdi M	2017	Amhara	Sch	408	3	0.74 [0.25-2.15]	FECT
19	Derso A	2016	Amhara	Pregnant	348	6	1.72 [0.79-3.70]	FECT
20	Amor A	2016	Amhara	Sch	396	82	20.71 [17.01-24.97]	FECT,BCT, PCR
21	Shimlis T	2016	SNNPR	HIV	491	22	4.48 [2.90-6.81]	DSM,FECT
22	Shiferaw MB	2015	Amhara	Patient	464	5	1.08 [0.40-2.65]	DSM,FECT
23	Aleka Y	2015	Amhara	Patient	277	1	0.36 [0.06-2.01]	DSM,FECT
24	Gedle D	2015	SNNPR	HIV	305	5	1.64 [0.70-3.78]	DSM, FECT
25	Ramos JM	2014	SNNPR	Patient	32,191	92	0.29 [0.24-0.35]	DSM
26	Mekonnen B	2014	AA	St/dweller	355	19	5.35 [3.45-8.20]	DSM, FECT, KK
27	Mamo H	2014	Amhara	Prisoner	236	6	2.54 [1.10-5.71]	DSM,FECT
28	Eriso F	2014	SNNPR	Sch	710	142	20.0 [17.16-23.17]	BCT
29	Mahmud MA	2013	Tigray	Sch	600	5	0.83 [0.31-2.05]	DSM,FECT, KK
30	Adamu H	2013	Oromia	HIV	378	1	0.26 [0.01-1.69]	DSM,FECT
31	Bayessa C	2013	SNNPR	Patient	6,342	73	1.15 [0.92-1.44]	DSM, FECT
32	Abera B	2013	Amhara	Sch	778	27	3.47 [2.40-5.00]	FECT, KK
33	Zeynudin A	2013	Oromia	HIV	91	6	6.59 [3.05-13.64]	DSM,FECT
34	Abate A	2013	Amhara	Patient	410	1	0.24 [0.04-1.36]	DSM, FECT
35	King JD	2013	Amhara	Children	2,338	5	0.21 [0.09-0.49]	FECT
36	Fekadu S	2013	SNNPR	HIV	343	12	3.50 [2.01-6.02]	DSM, FECT
37	Teklemariam Z	2013	Harari	HIV	371	15	4.04 [2.46-6.56]	DSM,FECT
38	Wogayehu T	2013	SNNPR	All age	858	51	5.94 [4.55-7.73]	DSM,FECT

39	Huruy K	2011	Amhara	Patient	384	12	3.13 [1.80-5.39]	DSM
40	Legese L	2010	Tigray	Sch	386	1	0.26 [0.05-1.45]	KK
41	Nyantekyi LA	2010	SNNPR	Children	288	2	0.69 [0.19-2.49]	FECT, KK
42	Getaneh A	2010	SNNPR	HIV	384	27	7.03 [4.88-10.04]	DSM, FECT, BCT
43	Belyhun Y	2010	SNNPR	Kid+ Mother	1,813	39	2.15 [1.58-2.93]	FECT
Total					78,959	1,437	1.82 [1.73-1.92]	

*AA = Addis Ababa, SNNPR = Southern Nations, Nationalities Peoples' Region, Sch = School children, FH = Food handler, HIV = Human Immunodeficiency Virus, St = Street, SS = *Strongyloides stercoralis*, Ng = Number, Pub = Publication, UN = University

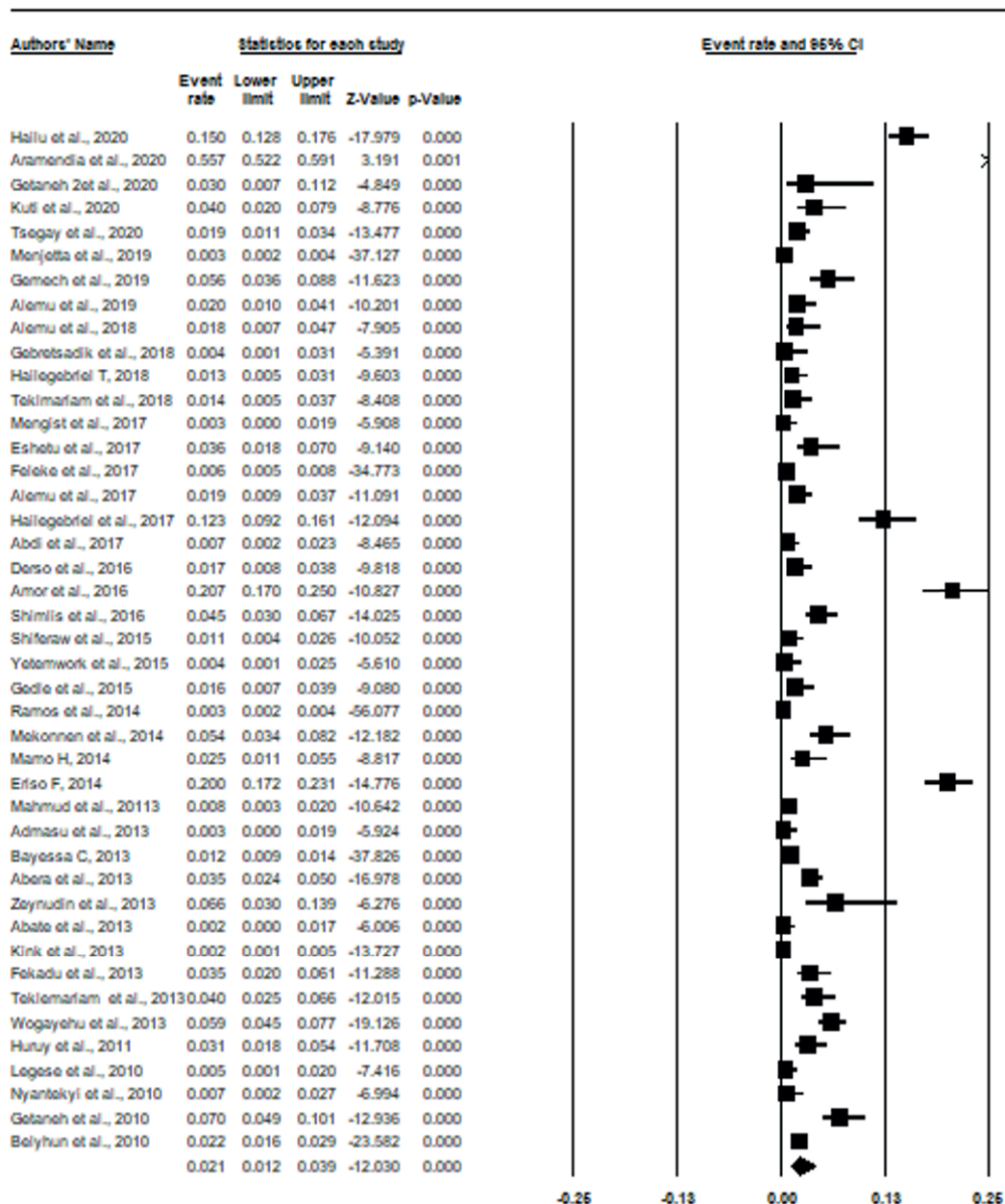


Fig. 2. Forest plot of the prevalence of *S. stercoralis* in Ethiopia using random effect model.

Table 2. The prevalence of *S. stercoralis* in different regions of Ethiopia between 2010 – 2020.

Name of the region	Number of studies [N]	Total examined [N]	SS Positive [N]	Pooled prevalence (95%CI)
Addis Ababa City	2	706	62	8.78 [6.85 – 11.17]
Amhara	16	8,570	732	8.54 [7.96 – 9.16]
Harari	1	371	15	4.04 [2.36 – 6.72]
Oromia	5	1319	20	1.52 [0.96 – 2.38]
SNNPR	15	58,917	547	0.93 [0.85 – 1.01]
Tigray	4	9,076	61	0.67 [0.52 – 0.86]
Total	43	78,959	1,437	1.82 [1.73 – 1.92]

*SS = *Strongyloides stercoralis*

heterogeneity was high ($Q = 1808.2$, $I^2 = 99.7\%$, $P < 0.001$) (Fig 4). In this review, 37 (86.05 %) of the studies were conducted by DSM, KK, FECT or a combination these methods. High prevalence 44.02 % rate of *S. stercoralis* infection was recorded with a combination of FECT, BCT and PCR and followed by 20 % with only BCT and 15.05 % *S. stercoralis* prevalence with a combining FECT, STST, BCT, and culture diagnostic methods (Table 3). A low prevalence of *S. stercoralis* was traced 0.26 %, 0.31 %, and 1.20 % by the respective KK, DSM and FECTs (Table 3).

The pooled prevalence of *S. stercoralis* across different diagnostic methods was 3.7 % (95 %CI: 1.10 – 11.70) using random effect analysis. The heterogeneity was high ($Q = 4376.6$, $I^2 = 99.8\%$, $P < 0.001$) (Fig 5).

Discussion

The true prevalence estimation of *Strongyloides* infection in Ethiopia is generally difficult due to application of very low sensitive diagnostic techniques and the presence of a few studies conducted with high sensitive diagnostic approaches so far in the country. The most widely used methods for the diagnosis of helminthic infections include DSM, FECT and KK. These methods are less sensitive for the detection of *Strongyloides* infection (Siddiqui *et al.*, 2001; Buonfrate *et al.*, 2015). Similarly, in this review, the authors on *Strongyloides* infection have clearly demonstrated that surveys conducted with these three methods mentioned above might provide untrustworthy prevalence reports among the peoples of Ethiopia.

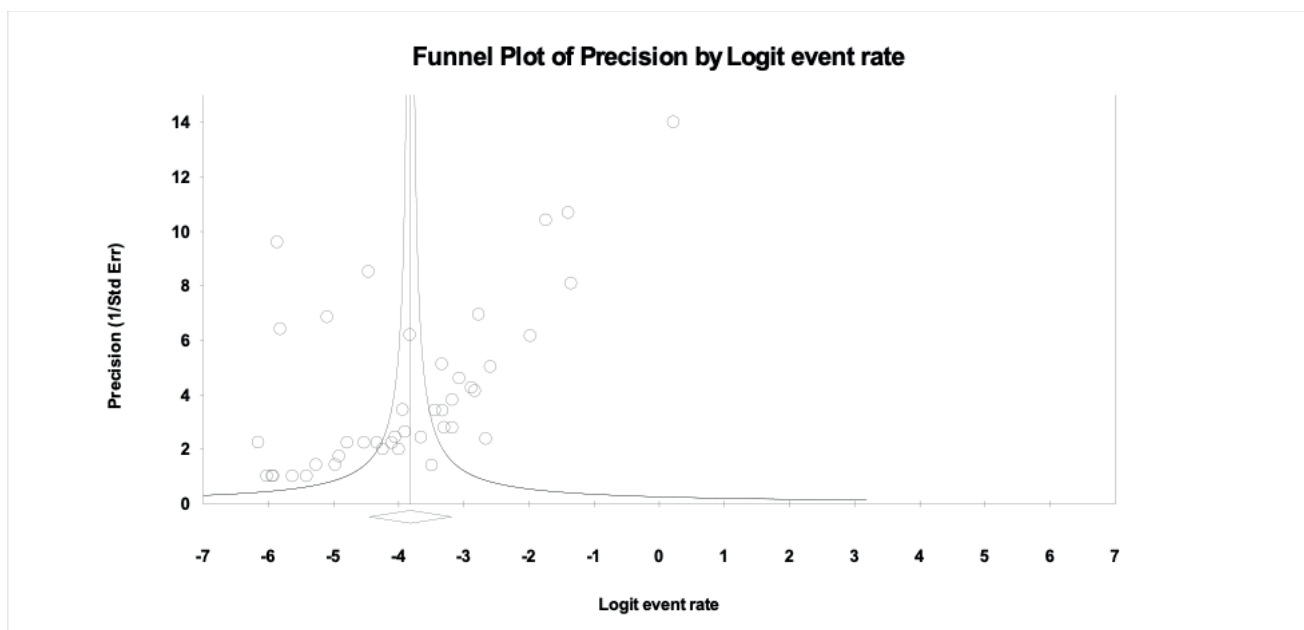


Fig. 3. Detection of the bias of the studies conducted using publication bias model.

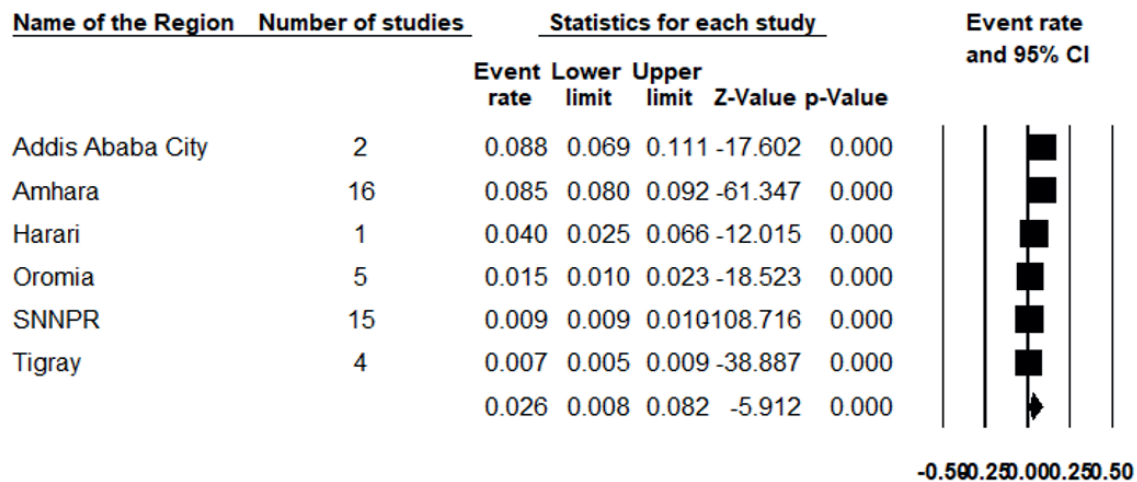


Fig 4. Frost plot of the prevalence of *S. stercoralis* across regions using random effect model.

The low distribution of *Strongyloides* infection in the current review might be explained by the fact that low sensitive diagnostic methods and small quantity (about 2 mg) of stool samples that have been used in DSM. For instance, single stool examined by DSM can give 70 % *S. stercoralis* false negativity (Siddiqui *et al.*, 2001; Mirdha *et al.*, 2009). The intermittent excretion nature (Burke *et al.*, 1978) and low-intensity chronic infection of *S. stercoralis* (Schar *et al.*, 2013) might also affect the true prevalence. In Ethiopia, highly sensitive diagnostic methods are not employed for *Strongyloides* infection and this might be due to their high cost and lack of aware-

ness. As a result, almost all health institutions are still using low sensitive diagnostic methods for the clinical diagnosis of *Strongyloides* infection. This leads to under diagnosis and under-report of *S. stercoralis* infection throughout the country.

On the other hand, spontaneous tube sedimentation technique (STST) (Tello *et al.*, 2012), BCT, stool culture and molecular (e.g. PCR) methods are more sensitive than DSM and FECT for the diagnosis of *Strongyloides* infection (Schar *et al.*, 2013; Buonfrate *et al.*, 2015). A combination of these methods in a single stool sample examination provides a higher detection rate of *S. stercoralis*

Table 3. The prevalence of *S. stercoralis* using different diagnostic methods in Ethiopia between 2010 – 2020.

Diagnostic methods	No of studies [N]	Total examined [N]	<i>S. stercoralis</i> Positive [N]	Pooled prevalence (95%CI)
DSM	3	46,254	145	0.31 [0.26 – 0.36]
KK	1	386	1	0.26 [0.05 – 1.45]
FECT	6	5,512	66	1.20 [0.94 – 1.53]
BCT	1	710	142	20.0 [17.16 – 23.17]
DSM+KK	2	494	10	2.02 [1.10 – 3.68]
DSM+FECT	20	20,535	296	1.44 [1.28 – 1.61]
FECT+KK	3	1,346	33	2.45 [1.72 – 3.46]
DSM+FECT+KK	2	955	24	2.51 [1.65 – 3.77]
DSM+FECT+BCT	1	384	27	7.03 [4.88 – 10.04]
FECT+BCT+PCR	2	1,188	523	44.02 [41.18 – 46.90]
DSM+FECT+BCT+CULTURE	1	351	43	12.25 [9.22 – 16.09]
FECT+STST+BCT+CULTURE	1	844	127	15.05 [12.74 – 17.68]
TOTAL	43	78,959	1,437	

*DSM = Direct saline microscopy, FECT = Formol ether concentration technique, KK = Kato-Katz, STST = Spontaneous tube sedimentation technique, BCT = Baermann concentration technique, PCR = Polymerase chain reaction

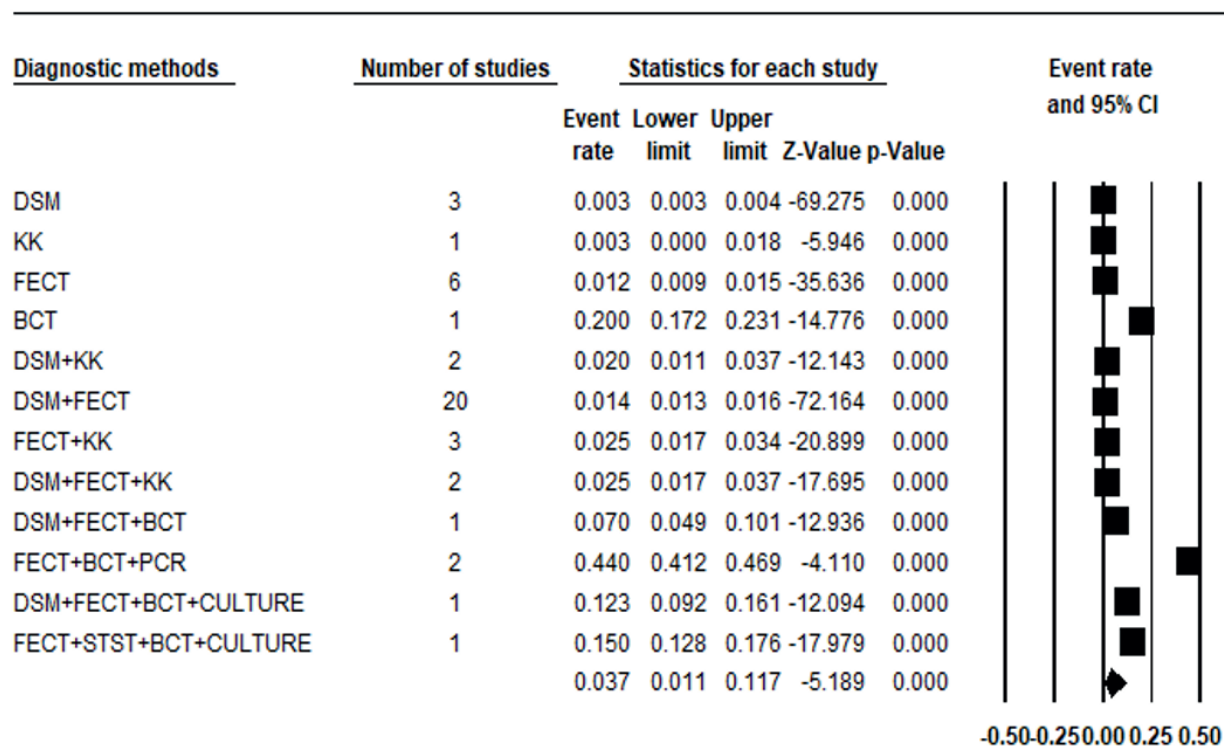


Fig 5. Frost plot of *S. stercoralis* prevalence across different diagnostic methods using random effect model.

infection (Aranzazu *et al.*, 2016; Albonico *et al.*, 2016; Hailu *et al.*, 2020). Reports in this review showed that those studies conducted using a combination of more than one method provided a better *Strongyloides* infection detection rate in Ethiopia (Abera *et al.*, 2013; Aranzazu *et al.*, 2016; Tamirat *et al.*, 2017; Hailu *et al.*, 2020). However, the sensitivity of these tests is not perfect since they were performed on a single faecal specimen which might underestimate the true prevalence. Therefore, there is a need to define a standard protocol in diagnostic methods being used to detect *S. stercoralis* in Ethiopia, especially in health institutions. Such priority recommendations might be important for elaboration of mapping of *S. stercoralis* infection in the country.

In the current review, the overall prevalence of human *S. stercoralis* infection in Ethiopia was low (1.82 %). This result is lower than from previous reports 5.1 % among human immune-viruses (HIV) infected cases reported previously globally (Ahmadpour *et al.*, 2019), and 20 % obtained from a large heterogeneity population and diagnostic methods in Latin America (Buonfrate *et al.*, 2015). The high prevalence in the previous studies might be justified as both reviews include studies conducted by serological tests which are much more sensitive tests (Bisoffi *et al.*, 2013). The study participants in the former study were also among HIV cases only. In addition, the variation in the ambient environment could favor the high prevalence of *Strongyloides* infection.

The prevalence of *S. stercoralis* infection was varied across re-

gions of Ethiopia and relatively high prevalence of recorded in Addis Ababa City and Amhara Regional State. This difference might be due to the difference in the diagnostic methods used, sample size and the health status of study participants. For instance, all the participants in the Addis Ababa City were street dwellers and HIV cases who are highly vulnerable to *S. stercoralis* infection.

Generally, the low prevalence of *S. stercoralis* in Ethiopia is due to absence of better sensitive diagnostic methods and the low attention given to *S. stercoralis* infection, unlike other soil-transmitted helminthes by policy makers. Based on this review, we encourage scholars to further work on the standardization of *S. stercoralis* test protocols and to advise policy makers for the inclusion of *S. stercoralis* in soil-transmitted helminthes prevention and control package.

Limitation of this review: We used only PubMed, Google Scholar and Science direct databases and Addis Ababa University databases as a source of articles which might be the limitation of the current review.

Conclusions: This review confirmed that the prevalence of *S. stercoralis* is under-reported in Ethiopia due to the use of low sensitive diagnostic methods. Diagnostic methods including culture, BCT or PCR or a combination these methods give better detection rate of *S. stercoralis* infection. Therefore, there is a need to revise the current diagnostic methods of *Strongyloides* infection to

have better sensitive diagnostic methods in the country. Further research is also desirable to break the transmission cycle and reduce the impacts of *Strongyloides* infection in Ethiopia.

Conflicts of Interest

The authors declare that we have no conflict interests.

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