National burden of intestinal parasitic infections and its determinants among people living with HIV/AIDS on anti-retroviral therapy in Ethiopia: A systematic review and meta-analysis

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Abstract
Objectives: The aim of this systematic review and meta-analysis is designed to assess the pooled prevalence and determine risk factors of intestinal parasitic infections among people living with HIV/AIDS on anti-retroviral therapy in Ethiopia.

Methods: International databases: PubMed, Web of Science, Cochrane Library, Scopus, PsycINFO, African Journals Online, and Google Scholar were systematically searched. Publication bias was determined using the funnel plot and Egger’s regression tests. Heterogeneity between the studies included in this review was checked by $I^2$ statistic. The DerSimonian and Laird random-effects model was applied to estimate the pooled effect size. Sub-group, meta-regression, and sensitivity analysis were conducted. Overall, meta-analysis was done using Stata version 14 statistical software.

Results: Twenty-seven studies with 8946 individuals were included, the estimated pooled prevalence of intestinal parasitic infections among people living with HIV/AIDS on anti-retroviral therapy was 40.24% (95% confidence interval = 33.8–46.6). Based on sub-group analysis, the highest prevalence was observed in the Tigray region 45.7% (95% confidence interval = 7.9–83.5), followed by Oromia region 42.2% (95% confidence interval = 28.8–55.6). Availability of latrine (odds ratio = 26.6, 95% confidence interval = 2.8–15.8), presence of animals at home (odds ratio = 2.7, 95% confidence interval = 1.2–5.8), and source of drinking water (odds ratio = 3.2, 95% confidence interval = 1.3–7.5) were significantly associated with intestinal parasitic infections.

Conclusion: These findings indicated that the prevalence of intestinal parasites among people living with HIV/AIDS was high in Ethiopia.

Keywords
Intestine, parasite, infections, HIV/AIDS, determinants, meta-analysis, Ethiopia

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Introduction
The HIV is one of the greatest challenges facing mankind. An estimated 33 million adults and children are living with the virus globally. Sub-Saharan Africa was the most affected region.1 People with advanced stages of HIV infection are vulnerable to secondary microbial and parasitic diseases that are generally termed as opportunistic infections. This is due...
to the fact that they take the advantage of offered by a weakened immune system.\(^1\)\(^2\) Opportunistic infections account for about 80% of deaths among HIV/AIDS patients than the virus itself, and of these, more than 47% happen due to intestinal parasitic infections which usually affect the gastrointestinal system and spread to other body parts.\(^3\)

Opportunistic infection typically began to manifest when the cluster for differentiation (CD4) lymphocytes count of an infected person declines below critical level, that is, for adults 800 cells/mm\(^3\) of which the normal value is 1200 cells/mm\(^3\). When the immune system is suppressed, intestinal parasitic infections can be fatal usually resulting to death in less than 2 years unless the patient receives specific therapy for HIV infection which are highly active anti-retroviral treatment (HAART) with anti-parasitic infections.\(^2\)

Intestinal parasites are the major cause of morbidity and mortality in many tropical countries including Ethiopia where HIV/AIDS is endemic.\(^4\) Intestinal parasitic infections are parasites which reside in the gastrointestinal system and can be caused by either protozoan or helminthic parasites. Protozoan infections such as Cryptosporidium parvum, Cyclospora cayetanensis, Isospora belli, Entamoeba histolytica, and Giardia lamblia, and helminthic infections such as Strongyloides stercoralis, Ascaris lumbricoides, and hookworms are some of the most common opportunistic and pathogenic intestinal parasites which are mostly encountered among people with HIV/AIDS.\(^5\)\(^6\) The sign and symptoms include severe chronic watery diarrhea with frequent and explosive bowel movements accompanied by loss of appetite, weight loss, abdominal cramp, nausea, fever, headache, and vomiting.\(^7\) However, the severity of infections depends on parasite factors (parasite species, load, length of infection, and co-infection), host factors (nutritional and immunological status), and socioeconomic factors.\(^8\)

The occurrence of intestinal parasitic infections in HIV/AIDS patients depends upon the endemicity of that particular parasite in the community, lifestyle, and nature of the population. Among intestinal parasitic infections, C. parvum, I. belli, and S. stercoralis have been the most commonly identified organisms in HIV-infected individuals with diarrhea from Ethiopia and other parts of the world.\(^9\)\(^10\) Different primary studies in Ethiopia showed the magnitude of intestinal parasitic infections as a great health, economic, and social impact, that is, in terms of treatment costs. However, inconsistent and wide variation was observed among these studies. Therefore, this systematic review and meta-analysis aimed to estimate the pooled prevalence of intestinal parasites and its determinants among people living with HIV/AIDS on anti-retroviral therapy (ART) in Ethiopia. Ethiopia is bounded by Eritrea to the north, Djibouti, and Somalia to the east, Sudan and South Sudan to the west, and Kenya to the south.\(^11\) According to 2019 worldometers report, 20.9% of the population of Ethiopia is urban (23,376,340 people).\(^12\)

**Search strategies**

We organized and reported this meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis protocols (PRISMA).\(^13\) International electronic web-based searches of PubMed, Web of Science, Cochrane Library, Scopus, PsycINFO, African Journals Online, and Google Scholar were searched for studies to find primary studies. Studies were searched from the 1st of May to the 1st of July 2020 which were published between 2008 and 2019. Google hand searching was also performed and the search of the reference list of already identified articles was done to retrieve additional articles. All searches were limited to articles written in English given that such language restriction does not alter the result of the systematic reviews and meta-analysis.\(^14\) Gray kinds of literature observational studies were assessed through the review of reference lists. Besides, to find unpublished papers important to this systematic review and meta-analysis, some research centers of Higher Academic and Research institutions Digital Library in Ethiopia were searched. Studies identified by our search strategy were retrieved and managed using Endnote X8 software. The search used the following keywords “prevalence,” “proportion,” “intestinal parasitic infections,” “magnitude,” “and people living with HIV/AIDS,” “determinants,” “associated factors,” and “Ethiopia.” The search terms were used individually and in combination using Boolean operators like “OR” or “AND.”

**Eligibility criteria**

**Inclusion criteria**

**Study area.** Studies conducted in Ethiopia were included.

**Population.** Only studies involving adult people living with HIV/AIDS on ART.

**Publication condition.** Both published and unpublished studies were included.

**Study design.** All observational study designs (cross-sectional and case–control) reporting the prevalence of intestinal parasitic infections and associated factors among people living with HIV/AIDS were eligible for this systematic review and meta-analysis.

**Exclusion criteria**

Articles, which were not wholly accessible, after at least two-email contact with the primary authors, were excluded.
The reason for excluding the articles is because of the difficulty to evaluate the quality of articles without getting full text. Moreover, studies which had poor quality according to the appraisal tool were also excluded.

**Measurement of outcome variables**

The outcomes of interest included the prevalence of intestinal parasitic infections and its determinants among people living with HIV/AIDS on ART. This study has two main outcomes. Intestinal parasitic infections were defined as having recorded positive for any stage of intestinal parasites seen during microscopic examination of stool specimen. The second outcome of this study was to identify the determinants of intestinal parasitic infections among people living with HIV/AIDS. For the second outcome, the association between intestinal parasitic infections and determinants in the form of the odds ratio. For major determinants, the odds ratio was calculated based on binary outcomes from the primary studies. The determinant factors included in this review were as follows: the presence of animals in home (Yes vs No), availability of latrine (Yes vs No), CD4 count of the patient, eating uncooked foods (Yes vs No), source of drinking water (pipe vs unprotected water), and residence (urban vs rural).

**Data extraction and quality assessment**

Data were extracted using a pre-piloted data extraction format prepared in a Microsoft Excel spreadsheet. The tool consisted of information regarding the author/s name, year of publication, study region, study design, sample size, the prevalence of intestinal parasites, and associated factors. The data were extracted by three independent authors. The quality of included studies was evaluated using the Joanna Briggs Institute (JBI’s) critical appraisal checklist for prevalence studies. Moreover, the methodological quality of studies was evaluated using a customized version of the Newcastle–Ottawa Scale (NOS) for cross-sectional studies adapted from Modesti et al. Representativeness of the sample, response rate, measurement tool used, comparability of the subject, and appropriateness of the statistical test used to analyze the data are some of the key criteria in the Newcastle–Ottawa scale. The quality of each article was checked by two authors independently. Other reviewers were involved and any disagreement was resolved through discussion and consensus.

**Statistical analysis**

Data were extracted in the Microsoft Excel format, followed by analysis using Stata version 14 statistical software. The standard error for each original study was calculated using the binomial distribution formula. Heterogeneity among reported prevalence was assessed by computing p-values of Cochran’s Q-test and F statistics. As the test statistic showed there was significant heterogeneity among the studies. As a result, a random-effects meta-analysis model was used to estimate the DerSimonian and Laird’s pooled effect. In the current meta-analysis, the pooled prevalence was estimated using the back-transform of the weighted mean of the transformed proportions, using arcsine variance weights for the fixed-effects model and DerSimonian–Laird weights for the random-effects model. Egger’s and Begg’s tests at 5% significant level were significant for publication bias. Point estimation of intestinal parasitic infections, as well as 95% confidence intervals, was reported in the forest plot format. The result of the forest plot, the size of the respective box showed the weight of each study, whereas each crossed line indicates 95% confidence interval. For the second outcome, the odds ratio was utilized to determine the association between determinant factors and intestinal parasitic infections in the included articles.

**Results**

This systematic review and meta-analysis have been reported following the PRISMA statement. Initially, 579 articles related to intestinal parasitic infections were accessed. Of these, 286 duplications and 257 unrelated articles were excluded. Second, from the rest 36 impending articles, 9 full-text articles were excluded due to unmet outcomes of interest or study area. Finally, 27 articles fulfill the eligibility criteria for the review and are included in the analysis (Figure 1).

**Characteristics of included studies**

This systematic review and meta-analysis were conducted with a total sample of 8946 people living with HIV/AIDS on ART. The main features of the incorporated articles are described in Table 1. All of the included studies were cross-sectional in their design. The regional distribution of articles included in this review showed that eight (29.6%) of the studies were from the Oromia region, seven (25.9%) were from the Amhara regional state, seven (25.9%) were from the Southern Nations, Nationalities, and Peoples’ (SNNPs) regional state, and two (7.4%) studies were from Tigray regional state and the remaining three (11.1%) were from Addis Ababa, Harar, and whole Ethiopia. The reported prevalence range of intestinal parasitic infections was from 13.9% in Oromia to 80.3% in Amhara regional state. The reported sample size ranged from 1596 to 103443 (Table 1).

**Quality assessment of individual studies**

Twenty-seven studies were assessed using the Joanna Briggs Institute Meta-Analysis of Statistical Assessment and Review Instrument (JBI-MAStARI) checklist for cross-sectional studies (Supplemental Material).
None of the studies were excluded based on the quality assessment criteria (Table 1).

**The burden of intestinal parasitic infections among people living with HIV/AIDS in Ethiopia**

Generally, the pooled prevalence of intestinal parasitic infections among people living with HIV/AIDS on ART in Ethiopia was 40.24% (95% confidence interval (CI) = 33.8–46.6) (Figure 2). Among the included articles, the lowest (13.9%) and highest (80.3%) prevalence of intestinal parasitic infections was reported in Oromia and Amhara region, respectively. The result of $I^2$ test static for heterogeneity indicated that the studies varied significantly ($I^2 = 97.7\%$, $p < 0.001$) and because hypothetically we supposed large differences in the study settings and socioeconomic backgrounds, we fitted a DerSimonian and Laird random-effect model to estimate the pooled prevalence of intestinal parasitic infections. The study with the largest weight was 3.78% and a slightly smaller weight of 3.48% was given to a study conducted in Oromia regional state. The sub-group analysis by region showed that the highest pooled prevalence of intestinal parasitic infection was found in the Tigray regional state 45.7% (95% CI = 7.9–83.5), followed by Oromia regional state 42.2% (95% CI = 28.8–55.6), and in SNNPs regional state 38.8% (95% CI = 30.5–47.2), whereas the lowest pooled prevalence was observed in Amhara regional state 37.99% (95% CI = 20.1–55.9) (Figure 3). The sub-group analysis indicated the presence of heterogeneity across the studies. To identify the source of heterogeneity, meta-regression and sensitivity analysis were conducted. The meta-regression analysis was performed using publication years, sample size, and the region as study covariates. The results showed that the sample size was a statically significant source of heterogeneity. The sensitivity analyses to assess the effect of each study on the overall effect size were done, but no single study significantly affected the overall pooled estimate.

**Heterogeneity and publication bias**

Given that the result of this meta-analysis revealed statistically significant heterogeneity among studies ($I^2 = 97.7\%$), a sub-group analysis was performed by region to adjust and decrease heterogeneity (Figure 3). In addition, to distinguish
the potential source of heterogeneity, meta-regression analysis using sample size, study setting/region, and publication year as covariates was done (Table 2). However, none of them significantly affected heterogeneity between studies. We assessed publication bias using both Begg’s and Egger’s tests and these tests showed that there was no statistical evidence of publication bias with a \( p \)-value greater than 0.05 and the funnel plot was symmetry (Figure 4). The sensitivity analysis also showed that none of the studies had a significant effect on the pooled prevalence estimates and measures of heterogeneity within primary studies. Therefore, sensitivity analyses using the random-effects model revealed that no single study influenced the overall prevalence of intestinal parasites among people living with HIV/AIDS on ART (Figure 5).

### Determinants of intestinal parasitic infections in Ethiopia

#### The association of drinking water source and intestinal parasitic infections

The association had been seen using eight studies conducted in different part of Ethiopia.6,25,26,29,30,33,36,40 The meta-analysis of these studies revealed that intestinal parasitic infections among people living with HIV/AIDS on ART were significantly associated with drinking water from unprotected sources (odds ratio (OR) = 3.15, 95% CI = 1.32–7.5). Specifically, the likelihood of getting intestinal parasitic infections was about three times higher among HIV/AIDS-infected people who drink water from unprotected sources compared to HIV/AIDS-infected people who were drinking from pipe water. The test result of this meta-analysis revealed heterogeneity among 10 studies (\( I^2 = 74.9\% , \ p < 0.001 \)). So, the random-effect meta-analysis model was used to see the association of drinking water sources and intestinal parasitic infections in Ethiopia (Figure 6).

### The association between availability of latrine and intestinal parasitic infections

The association was done using eight studies conducted in Ethiopia.6,26,29,30,32,33,36,40 In this meta-analysis, availability of latrine was found to be significantly associated with the occurrence of intestinal parasitic infections (OR = 6.65, 95% CI = 2.79–15.84). Particularly, people living with HIV/AIDS who have no latrine in their compound were around seven times more likely to be infected with intestinal parasites.
comparatively lower compared to counterparts who had a latrine. The test statistics of these 13 studies showed significant heterogeneity among studies ($I^2 = 78.4\%, p < 0.001$). As a result, a random-effect meta-analysis method was used (Figure 7).

**The association between intestinal parasitic and presence of animals in a home**

Four studies were included to examine the association between the intestinal parasitic infection among people living with HIV/AIDS and the presence of animals in a home.25,29,30,33 The meta-analysis of these studies revealed that the presence of animals in the home was found to be significantly associated with intestinal parasitic infections (OR = 2.69, 95% CI = 1.24–5.84). In particular, HIV-infected people who had animals in their home were around three times more likely to acquire intestinal parasitic infections compared to those who had no animals in their home (Figure 8).

**Discussion**

This systematic review and meta-analysis were intended to see the pooled prevalence and determinants of intestinal parasitic infections among people living with HIV/AIDS on ART in Ethiopia. Based on the finding of this study, the
Pooled prevalence of intestinal parasitic infection was 40.24%. The sub-group analysis of this study showed that the highest prevalence of intestinal parasite was observed in the Tigray regional state 45.7%, followed by the Oromia regional state 42.2%. Availability of latrine, presence of animals in the home, and source of drinking water other than pipe were significantly associated with intestinal parasitic infections.

The finding of this study was found to be comparable with studies conducted in Saudi Arabia (39.7%) and Ghana (35%). But, the finding of this study was higher than the study conducted in Nepal (32%), Nigeria (28.3%, 22.7%,

**Figure 3.** Forest plot showing the sub-group analysis for prevalence of intestinal parasitic infections in Ethiopia.

**Table 2.** Meta-regression for the included studies to identify the source of heterogeneity for intestinal parasitic infections.

| Variables | Characteristics | Coefficient | p-value |
|-----------|-----------------|-------------|---------|
| Publication year | Publication year | −1.20 | 0.149 |
| Sample size | Sample size | 0.01 | 0.55 |
| | Amhara | −3.04 | 0.68 |
| Region | Oromia | 2.75 | 0.7 |
| | SNPPs | −1.87 | 0.8 |
| | Others | −0.38 | 0.9 |
| | Tigray | 5.9 | 0.6 |

SNPPs: Southern Nations, Nationalities, and Peoples.
and 5.3%). Studies in India (35%), Senegal (10.6%), Democratic Republic of the Congo (15.4%), and Cameroon (14.6%) have reported similar findings. These variations in findings among the studies might be explained by differences in geographical locations, socioeconomic conditions, sample size, and cultural practices of the population. The diagnostic methods exercised for stool examination and the time of the study might also have contributed to the differences. The higher proportion of intestinal parasites in this study might also be due to the difference in the strength of the health system, and intestinal parasitic infections control and prevention programs applied in the area, geographical and environmental conditions. In addition, the lower access to water supply and poor waste disposal system in Ethiopia may contribute to the high magnitude of intestinal parasites. High prevalence of intestinal parasitic infections among the study participants may call for better follow-up through highly sensitive and specific laboratory tests and more comprehensive actions by the patients themselves in adopting prevention measures against intestinal parasites. Moreover, our finding was lower than study conducted in Brazil (63.9%), Cameroon (82.6%), India (62.7%), Thailand (50%), Democratic Republic of the Congo (49.7%), and Kenya (50.9%). This lower prevalence of the parasite in this study could be due to the variation in sample size and the environmental difference. It might be also due to

Figure 4. Funnel plot to test publication bias of the included studies for prevalence of intestinal parasitic infections in Ethiopia.

Figure 5. Result of sensitivity analysis of the included studies for prevalence of intestinal parasitic infections in Ethiopia.
Figure 6. Forest plot showing the pooled odds ratio of the association between source of drinking water and intestinal parasitic infections among people living with HIV/AIDS on ART in Ethiopia.

Figure 7. Forest plot showing pooled odds ratio for the association between intestinal parasitic infections and availability of latrine among people living with HIV/AIDS on ART in Ethiopia.
better-quality care delivered to people living with HIV/AIDS and faithfulness to ART. The regular advice conveyed by healthcare providers for HIV positive patients during their frequent visits to ART clinic could contribute for lowering prevalence of intestinal parasitic infections.

In this study, the absence of latrine was found to be significantly associated with the occurrence of intestinal parasitic infections. Particularly, HIV positive individuals who had no latrine in their compound were found to be 6.65 times more likely to be infected with intestinal parasites compared to the counterparts that have a toilet in their compound. The finding of this meta-analysis and systematic review was supported by studies conducted in Nigeria and Malaysia.49,60,61 This is due to the fact that people have no latrine in their compound cause unguarded defecation and environmental contamination leads to increment of feco-oral transmission of intestinal parasitic infections. In addition, the source of drinking water was found to be significantly associated with a high prevalence of intestinal parasitic infections. Specifically, people living with HIV/AIDS who did not use pipe water were 3.15 times more likely to be infected with intestinal parasites compared to people living with HIV/AIDS who use pipe water. This finding was supported by studies conducted in Malaysia60 and Nigeria49 which stated source of drinking water was a significant determinant of intestinal parasitic infection. It is fact that unprotected water such as river is highly contaminated with animals and human excreta since people are usually drinking river waters and also bathing and washing their clothes under the river. These habits have been practiced in developing countries such as Ethiopia due to scarcity or inadequate distribution of safe/clean water. So, using untreated/unsafe water is a source of intestinal parasitic infections.62,63 The most prevalent waterborne intestinal parasites producing diarrhea were C. parvum, G. lamblia, and E. histolytica. These parasitic infections have been commonly reported in immune-compromised patients, particularly in HIV/AIDS patients.62

Another associated factor which was a significant association with intestinal parasitic infections is the presence of animals in the home. Specifically, people living with HIV/AIDS who had animals living in their homes were 2.69 times more likely to be infected with intestinal parasites compared to those who did not have animals in their homes. This finding was comparable with studies in India57,64 which revealed the presence of animals was a significant risk factor of intestinal parasitic infections. The association might be due to the living of humans with animals which increases a tendency to contact with animal excretion and consuming their products. So, those people will be more vulnerable to being infected with one or more intestinal parasites because animals act as intermediate or reservoir hosts for different parasites.65,66

Figure 8. Forest plot showing pooled odds ratio for the association between intestinal parasitic infections and presence of animals in the home among people living with HIV/AIDS on ART in Ethiopia.
Limitations of the study

One of the limitations of this systematic review and meta-analysis was only studies written in the English language were incorporated for the pooled estimate. Furthermore, the results of this study may not represent the real figure of the country, since studies had not been found in Afar, Gambela Somalia, and Benishangul-Gumuz Region.

Conclusion and recommendations

A high prevalence of intestinal parasitic infections was observed in people living with HIV/AIDS on ART in Ethiopia. There is a need for awareness creation about the transmission of intestinal parasitic infections. Concerned bodies such as community and governmental and non-governmental organizations should give emphasis on preventive methods such as increasing the accessibility of safe water, separation of animals from home, and building latrines in the community.

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; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Availability of data and material

The data sets analyzed during this study are available from the corresponding author upon reasonable request.

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Supplemental material

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