National Burden of Intestinal Parasites and Its Determinants Among People Living with HIV/AIDS in Ethiopia: A Systematic Review and Meta-analysis

Tadesse Yirga Akalu (✉ tadesseyirga680@gmail.com)
Debre Markos University

Yared Asmare Aynalem
Debre Markos University

Wondimeneh Shibabaw Shiferaw
Debre Markos University

Yoseph Merkeb Alamneh
Debre Markos University

Asmamaw Getnet
Debre Markos University

Abtie Abebaw
Debre Markos University

Aytenew Atnaf
Debre Markos University

Abebe Abate
Debre Markos University

Melkamu Tilahun
Debre Markos University

Bekalu Kassie
Debre Markos University

Yibeltal Aschale
Debre Markos University

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Abstract

Background: Intestinal parasites are a group of opportunistic gastrointestinal diseases commonly encountered among people living with human immunodeficiency virus (HIV). Intestinal parasites increased the risk of morbidity and mortality among these vulnerable populations. Therefore, to design appropriate prevention strategies, up-to-date information concerning prevalence of intestinal parasite is crucial. However, studies assessing the prevalence and associated factors of intestinal parasite in Ethiopia are inconsistent and widely varied. Therefore, this systematic review and meta-analysis is designed to assess the pooled prevalence and determine risk factors.

Methods: International databases; PubMed, Web of Science, Cochrane Library, Scopus, PsycINFO, African Journals Online, and Google Scholar were systematically searched. A funnel plot and Egger’s regression test were used to determine publication bias. The $I^2$ statistic was used to check heterogeneity between the studies. DerSimonian and Laird random-effects model was applied to estimate the pooled effect size. Subgroup and meta-regression analyses were conducted. Sensitivity analysis was done to see the effect of a single study on the overall estimation. STATA version 14 statistical software was used for meta-analysis.

Results: A total of 27 studies with 8,946 individuals were used to estimate the pooled prevalence of intestinal parasitosis among people living with HIV. The estimated pooled prevalence of intestinal parasitosis was 40.24% (95% CI: 33.8–46.6). Subgroup analysis of this study revealed that the highest prevalence was observed in Tigray region 45.7% (95% CI: 7.9-83.5), followed by Oromia region 42.2% (95% CI: 28.8–55.6). Availability of latrine (OR: 26.6, 95% CI: 2.8-15.8), presence of animal (OR: 2.7, 95% CI: 1.2-5.8) and source of drinking water (OR: 3.2, 95% CI: 1.3-7.5) were significantly associated with intestinal parasitosis.

Conclusion: The prevalence of intestinal parasite was high in Ethiopia. There should be a need to work for improving the hygienic standard on quality of drinking water and regular utilization of latrine among people living with HIV/AIDS.

Background

Human immunodeficiency virus (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 stage 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 the opportunity offered by a weakened immune system[1, 2]. About 80% of deaths of AIDS patients are related to opportunistic infections rather than the virus itself, and of these, more than 47% happen due to opportunistic intestinal parasitic infections which usually affect gastrointestinal system[3].
Opportunistic infection typically began to manifest when the CD4 Lymphocytes count of an infected person declines below critical level, i.e. 800 cells/mm$^3$ of which the normal value is 1200 cells/mm$^3$. When immune system is severely suppressed in this manner infection can be fatal usually resulting to death in less than two years, unless the patient receives specific therapy for HIV infection highly active anti-retroviral treatment (HAART)[2].

Intestinal parasites are the major source of morbidity and mortality in many tropical countries including Ethiopia where HIV/AIDS is endemic[4]. Protozoan infections such as: *Toxoplasma gondii, Isospora belli, cryptosporidium parvum, Entameoba histolytica* and *Giardia lamblia* and helminthic infections such as *strongyloidesstercoralis*are some of the most common opportunistic intestinal parasites[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, intensity of infection depends on parasite factors (parasite species, length of infection, coinfection), host factors (nutritional and immunological status) and socioeconomic factors[8].

The incidence and prevalence of infection with a particular enteric parasite in HIV/AIDS patients is likely to depend upon the endemicity of that particular parasite in the community. *Cryptosporidium parvum, I. belli, S.stercolaris*and *Toxoplasma gondii*have been reported as the most frequently 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 parasitosis as a great health burden in the regions. However, inconsistent and wide variation was observed among these studies. Therefore, this systematic review and meta-analysis aimed to estimate the pooled prevalence of Ips and its determinants among people living with HIV/AIDS in Ethiopia.

**Method**

**Study design and setting**

A systematic review and meta-analysis were conducted to estimate the prevalence and its determinants of intestinal parasitosis among people living with HIV in Ethiopia. It 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]. Currently, 20.9% of the population of Ethiopia is urban (23,376,340 people in 2019)[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 obtain primary studies. Studies were searched from 1st of May to the 1st of July, 2020. Google hand searching was also performed and the search of the reference list of already identified articles was done to retrieve additional articles. All explorations 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, like Addis Ababa Digital Library were searched. Studies identified by our search strategy were retrieved and managed using Endnote X7 software. The search used the following keywords “prevalence”, “proportion”, “parasitosis”, “magnitude”, “and people living with HIV”, “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

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 parasitosis 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 exclusion of these 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 parasitosis and its determinants among people living with HIV/AIDS. This study has two main outcomes. Intestinal parasitosis was defined as having recorded positive for any stage of intestinal parasites seen during microscopic examination of stool [5]. The second outcome of this study was to identify the determinants of intestinal parasitosis among People living with HIV (PLWHIV). For the second outcome, we determined the association between intestinal parasitosis 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: presence of pet animals (Yes versus No), availability of latrine (Yes versus No), CD4 count of the patient, eating uncooked vegetables (Yes versus No), source of drinking water (pipe versus other), and residence (urban versus 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 author/s name, year of publication, study region, study design, sample size, prevalence of intestinal parasites. 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 [15]. 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. [16]. Representativeness of the sample, response rate, measurement tool used, comparability of the subject, appropriateness of the statistical test used to analyze the data are some of the key criteria in the Newcastle – Ottawa scale. Two authors independently assessed the quality of each article. Whenever necessary other reviewers were involved. Any disagreement was resolved through discussion and consensus.

Data processing and analysis

Data were extracted in 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 Cochrane Q-test and I^2 statistics[17]. As the test statistic showed there is 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, arcsine-transformed proportions were used. The pooled prevalence was estimated by 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 [18]. Egger’s and Begg’s tests at 5% significant level were significant for publication bias[19]. Point estimation of intestinal parasitosis, 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 to 95% confidence interval. For the second outcome, the odds ratio was utilized to ascertain the association between determinant factors and intestinal parasitosis in the included articles.

Result

This systematic review and meta-analysis have been reported following the PRISMA statement [20]. Initially, 579 articles related to intestinal parasitosis were accessed. Of these, 286 duplications and 257 unrelated articles were excluded. Second, from the rest 36 impending articles, 27met eligibility for the review and included in the analysis. Nine full-text articles were excluded due to unmet outcomes of interest or study area (Fig. 1).

Characteristics of included studies

This systematic review and meta-analysis were conducted with a total sample of 8,946 people living with HIV/AIDS. The main features of the incorporated articles are described in Table 1. All of the included studies were cross-sectional in their design. Eight (29.6%) of the studies included in this review were from
the Oromia region[21–27], seven (25.9%) were from the Amhara regional state[6, 9, 28–32], seven (25.9%) were from Southern Nations Nationalities and People's (SNNPs) regional state[33–39], Two (7.4%) studies were from Tigray regional state[26, 40] and the remaining three (11.1%) were from Addis Ababa[41], Harar[42] and whole Ethiopia[43]. Reported burden of intestinal parasitosis ranged from 13.9% in Oromia[27] to 80.3% in Amhara regional state[9]. The reported sample size ranged from 150 [24] to 1034[43].

**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 [6, 9, 21–44] [supplementary file_1]. None of the studies were excluded based on the quality assessment criteria (Table 1).
Table 1
the characteristics of included studies for a meta-analysis of intestinal parasitosis among people living with HIV/AIDS in Ethiopia

| Authors name/Year | Region    | publication year | Study Design | Sample size | Prevalence with 95% CI | Quality |
|-------------------|-----------|------------------|--------------|-------------|------------------------|---------|
| Alemu et al., 2011[9] | Amhara    | 2011             | cross-sectional | 248         | 80.3(75.3–85.3)        | 9       |
| Fekadu et al., 2013[33] | SNNRs    | 2013             | cross-sectional | 343         | 47.8(42.5–53.1)        | 10      |
| Zeynudin et al., 2013[21] | Oromia   | 2013             | cross-sectional | 91          | 39.56(29.5–49.6)       | 8       |
| Assefa et al., 2009[34] | SNNRs    | 2009             | cross-sectional | 378         | 55(50.0–60.0)          | 10      |
| Girma et al., 2014[35] | SNNRs    | 2014             | cross-sectional | 268         | 34.3(28.6–40.0)        | 9       |
| Missaye et al., 2013[28] | Amhara   | 2013             | cross-sectional | 136         | 17.6(11.2–24.0)       | 9       |
| Gebrecherkos et al., 2019[29] | Amhara | 2019             | cross-sectional | 150         | 45.3(37.3–53.3)        | 9       |
| Awole et al., 2003[22] | Oromia    | 2003             | cross-sectional | 372         | 51.1(46.0–56.2)        | 10      |
| Gebrewahid et al., 2019[40] | Tigray | 2019             | cross-sectional | 242         | 26.4(20.8–32.0)        | 9       |
| Shimelis et al., 2016[36] | SNNRs | 2016             | cross-sectional | 491         | 35.8(31.6–40.0)        | 10      |
| Gedle et al., 2017[23] | Oromia    | 2017             | cross-sectional | 323         | 35.9(30.7–41.1)        | 10      |
| Adamu et al., 2013[44] | Oromia    | 2013             | cross-sectional | 378         | 63.5(58.6–68.4)        | 10      |
| Eshetu et al., 2017[30] | Amhara    | 2017             | cross-sectional | 223         | 29.1(23.1–35.1)        | 9       |
| Alemu et al., 2018[37] | SNNRs    | 2018             | cross-sectional | 220         | 28.81(22.8–34.8)       | 9       |
| Gebretsadik et al., 2018[6] | Amhara | 2018             | cross-sectional | 223         | 13.9(9.4–18.4)         | 9       |
| Getaneh et al., 2010[38] | SNNRs    | 2010             | cross-sectional | 384         | 25(20.7–29.3)          | 10      |
| Gerzmu et al., 2015[39] | SNNRs    | 2015             | cross-sectional | 209         | 45.4(38.6–52.2)        | 9       |
| Authors name/Year | Region | publication year | Study Design | Sample size | Prevalence with 95% CI | Quality |
|-------------------|--------|------------------|--------------|-------------|------------------------|---------|
| Kindie and Bekele, 2016[24] | Oromia | 2016 | cross-sectional | 150 | 45(37.0–53.0) | 8 |
| Kiros et al., 2015[31] | Amhara | 2015 | cross-sectional | 399 | 30.6(26.1–35.1) | 9 |
| Mariam et al., 2008[25] | Oromia | 2008 | cross-sectional | 160 | 62.5(55.0–70.0) | 8 |
| Mahmud et al., 2014[26] | Tigray | 2014 | cross-sectional | 384 | 65(60.2–69.8) | 10 |
| Mahmud et al., 2014 | Oromia | 2014 | cross-sectional | 520 | 26.9(23.1–30.7) | 10 |
| Taye et al., 2014[41] | Other | 2014 | cross-sectional | 546 | 33.9(29.9–37.9) | 10 |
| Teklemariam et al., 2013[42] | Other | 2013 | cross-sectional | 371 | 33.7(28.9–38.5) | 9 |
| Dufera et al., 2008[27] | Oromia | 2008 | cross-sectional | 296 | 13.9(10.0-17.8) | 9 |
| Adamu et al., 2010[43] | Other | 2010 | cross-sectional | 1034 | 52(49.0–55.0) | 10 |
| Yabsira et al.2019[32] | Amhara | 2019 | cross-sectional | 407 | 49.1(44.2–54.0) | 9 |

The burden of intestinal parasitosis among people living with HIV/AIDS in Ethiopia

Generally, the pooled prevalence of intestinal parasitosis among people living with HIV/AIDS in Ethiopia was 40.24% (95% CI: 33.8–46.6) (Fig. 2). The lowest (13.9%) and highest (80.3%) prevalence of intestinal parasitosis was reported in Oromia[27]and Amhara region respectively[9]. 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 socio-economic backgrounds, we fitted a DerSimonian and Laird random-effect model to estimate the pooled prevalence of intestinal parasitosis [45, 46]. The study with the largest weight was 3.78% [43] and a slightly smaller weight of 3.48% was given to a study conducted in Oromia regional state[21]. In the sub-group analysis by region, the highest pooled prevalence of intestinal parasitosis 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 SNNRs 38.8% (95% CI: 30.5, 47.2) and the lowest pooled prevalence was in Amhara regional state 37.99% (95% CI: 20.1, 55.9) (Fig. 3). The sub-group analysis indicated the presence of heterogeneity across the studies. To identify
the source of heterogeneity, we conducted meta-regression and sensitivity analysis. The meta-regression analysis was performed using publication years, sample size, and the region as study covariates. However, the results showed that the sample size was a statically significant source of heterogeneity. We also performed sensitivity analyses to assess the effect of each study on the overall effect size. 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 ($I^2 = 97.7\%$), we executed a subgroup analysis by region to adjust and decrease heterogeneity (Fig. 3). Additionally, to distinguish the potential source of heterogeneity, we performed meta-regression analysis using sample size, study setting/region, and publication year as covariates (Table 2). However, none of them significantly affected heterogeneity between studies. We assessed publication bias using both Begg's and Egger’s test and these tests showed that there was no statistical evidence of publication bias with p-value greater than 0.05 and the funnel plot was symmetry (Fig. 4). Besides, in sensitivity analysis 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 (Fig. 5).

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

### Determinants of intestinal parasitic infection in Ethiopia

**The association of drinking water source and intestinal parasitosis:** In this meta-analysis, the association of intestinal parasitosis with source of drinking water had been seen using eight studies conducted in Ethiopia[6, 23, 24, 28, 29, 36, 37, 41]. The meta-analysis of these studies revealed that intestinal parasitosis among people living with HIV/AIDS was significantly associated with the drinking water from unprotected sources (OR: 3.15, 95%CI: 1.32–7.5). Specifically, the likelihood of getting intestinal parasitic
infection was around three times higher among HIV/infected people who drink unprotected water source compared to HIV infected people drinking from pipe water. The test result of this meta-analysis revealed heterogeneity among ten studies ($I^2 = 74.9.0\%$, $p < 0.001$). So, the random effect meta-analysis model was used to see the association of drinking water source and intestinal parasitosis in Ethiopia (Fig. 6).

**The association between availability of latrine and intestinal parasitic infection:** Besides, the association of availability and intestinal parasitosis was examined using eight studies conducted in Ethiopia[6, 23, 24, 29, 30, 36, 37, 41]. In this meta-analysis availability of latrine was found to be significantly associated with occurrence of intestinal parasitosis (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 compared to counterparts who had latrine. The test statistics of these thirteen studies showed significant heterogeneity among studies ($I^2 = 78.4\%$, $P < 0.001$). As a result, a random effect meta-analysis method was used (Fig. 7).

**The association between intestinal parasitosis and presence of animal in home:** Four studies were included to examine the association between the intestinal parasitosis among people living with HIV/AIDS and presence of animals in home[23, 28, 36, 37]. The meta-analysis of these studies revealed that the presence of animals in home was found to be significantly associated with intestinal parasitosis (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 be infected with intestinal parasites compared to those who had no animals in their home (Fig. 8).

**Discussion**

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

The finding of this study was found to be comparable with studies conducted in Saudi Arabia 39.7%, and Ghana (35%) [47]. It is higher compared to studies conducted in Nepal 32%[48] Nigeria 28.3%, 22.7%, 5.3% [49–51], India 35% [52], Senegal 10.6%[53], Democratic Republic of Congo(15.4%)[54], and Cameroon (14.64%) [1]. These variations in findings among the studies might be explained by differences in geographical locations, socioeconomic conditions and cultural practices of the population. The methods exercised for stool examination and the time of the study might also have contributed for the differences. The higher proportion of intestinal parasites in this study might also be due to the difference in geographical and environmental conditions. In addition, the lower access to water supply and sanitation in Ethiopia may contribute to the high magnitude of intestinal parasites. High prevalence of IP infections among the study participants may call for better follow-up through laboratory tests and more
comprehensive actions by the patients themselves in adopting prevention measures against intestinal parasites. But the current finding is significantly lower than study conducted in Brazil 63.9% [55], Cameroon 82.6%[56], India 62.7%[57] Thailand 50%[58], Democratic republic of Congo 49.7% [54], Kenya (50.9%)[59]. This lower prevalence of parasite in this study could be due to the variation in sample size, and the environmental difference. It might be also due to 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 visit to ART clinic could contribute for lowering prevalence of intestinal parasitic infection.

Based on this Mata-analysis and systematic review, absence of toilet was found to be significantly associated with the occurrence of intestinal parasitosis. 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 counter parts that have 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]. They reported absence of latrine was an independent predictor of intestinal parasitic infection. This is due to the fact that failure to access latrine causes in unguarded defecation and environmental contamination. Thus, it facilitates the likelihood transmission of intestinal parasitic infections (IPIs). In addition, the source of drinking water was found to be significantly associated with high prevalence of intestinal parasitic infection. Specifically, People living with HIV/AIDS who do not use pipe water 3.15 times more likely to be infected by intestinal parasites compared to people living with HIV/AIDS who use pipe water. This finding was supported by studies conducted in Malaysia [60]and Nigeria [49] which stated source of drinking water was a significant determinant of intestinal parasitic infection. It is fact that, river/unprotected water is highly contaminated with animals and human excreta since people is usually bathing and washing their clothes under river. These habits have been practiced in developing countries particularly in Ethiopia due to scarcity or inadequate distribution of safe/clean water. So, using untreated/unsafe water contributes to be infected with one or more intestinal parasitic infections [62, 63].

The most prevalent waterborne intestinal parasites producing diarrhea were Cryptosporidium parvum, G.lamblia, and E. histolytica. These parasitic infections have been commonly reported in immune-compromised patients, particularly in HIV/AIDS patients [62].

Besides, a significant association was found between presence of animal in home and intestinal parasitic infection. Specifically, people living with HIV/AIDS who had pet animal living in their home were 2.69 times more likely to be infected with intestinal parasites compared to those who did not have animals in their home. This finding was in line with studies in India [57, 64] which revealed the presence of animals was a significant risk factor of intestinal parasitic infection. The association might be due to living of human with domestic animals which increases a tendency to contact with pet or domestic animal excretion and consuming their products. So, those patients will be more vulnerable to be infected with one or more intestinal parasites [65, 66].

Limitations of the study
One of the limitations of this systematic review and meta-analysis was only studies written by 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, Somalia and Benishangul-Gumuz.

**Conclusion And Recommendations**

A high prevalence of intestinal parasitic infections was observed in people living with HIV. There is a need for awareness creation towards better access for safe water, separation of animals from home and to have latrine in their vicinity for the prevention of intestinal parasites.

**Abbreviations**

AIDS Acquired Immune Deficiency Syndrome

ART Anti-Retroviral Therapy

CD4 Cluster for Differentiation

CI Confidence Interval

IPs Intestinal Parasite

HIV Human Immunodeficiency Virus

OR Odds Ratio

OIPi Opportunistic Intestinal parasitic infection

WHO World Health Organization

**Declarations**

**Ethics approval and consent to participate**

Not applicable

**Consent for publication**

Not applicable

**Availability of data and material**

The datasets analyzed during the current study are available from the corresponding author upon reasonable request.
Competing interests

We have confirmed that we have no competing interests.

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No funding was obtained for this study.

Authors' 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.

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