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Prevalence and Associated Factors of Intestinal Parasitic Infections Among Pulmonary Tuberculosis Patients in Harar Town, Eastern Ethiopia

Ukash Umer[1, *], Teferi Eshetu[2], Abebaw Tiruneh[2], Belay Merkeb[3], Mulugeta Getachew[4], Kinfu Yazachew[5]

[1]School of Medical Laboratory Sciences, College of Health and Medical Sciences, Haramaya University, Harar, Ethiopia
[2]School of Medical Laboratory Sciences, Institute of Health, Jimma University, Jimma, Ethiopia
[3]Department of Medical Laboratory Science, College of Health Science, Salale University, Fiche, Ethiopia
[4]Department of Medical Laboratory Science, College of Medicine and Health Science, Ambo University, Ambo, Ethiopia
[5]Department of Medical Laboratory Science, Institute of Health Science, Wallaga University, Nekemte, Ethiopia

Email address:

ukashumer123@gmail.com (Ukash Umer), teferies@yahoo.com (Teferi Eshetu), abebawtiruneh@gmail.com (Abebaw Tiruneh), belaymerkeb19@gmail.com (Belay Merkeb), mulgetagetachew71@gmail.com (Mulugeta Getachew), kinfugdr@gmail.com (Kinfu Yazachew)

[*]Corresponding author

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Abstract: Co-infection of intestinal parasites (IPs) and tuberculosis (TB) in humans is an important public health problem in developing countries where both diseases are common. However, there are limited studies on the epidemiology of this co-infection elsewhere in Ethiopia and particularly none in the current study area. Therefore, the aim of this study was to determine the prevalence and associated factors of intestinal parasitic infections (IPIs) among pulmonary tuberculosis (PTB) patients in Harar Town, Eastern Ethiopia. Health facility based cross-sectional study was carried out from July 01 to August 30, 2021. PTB patients were enrolled in the study using non-random consecutive sampling technique. A structured questionnaire using face to face interview and checklist were used to collect data on socio-demographic, clinical and associated factors to IPIs. Height and weight were measured to calculate body mass index (BMI). About 3-5grams of stool sample was collected and processed using direct saline mount, formol-ether concentration, modified Ziehl-Neelsen staining and Kato-Katz technique following standard procedures. All data were entered into Epi-Data version 3.1 and exported to SPSS version 25.0 software for analysis. Descriptive statistics, binary logistic regression, odds ratio and 95% confidence interval were used during data analysis. A p-value of <0.05 was considered as statistically significant. The overall IPI rate among a total of 277 PTB patients included in the study was 28.5%. Intestinal helminths and protozoa infections accounted 16.2% and 12.3%, respectively. Double parasite species infection was observed in 1.8% of study participants. *A. lumbricoides* accounted for the highest frequency (7.2%), followed by *G. lamblia* (5.4%) and *E. histolytica/dispar* (4.3%). Presence of dirt in fingernail (AOR=3.04, 95% CI: 1.12-8.22, p = 0.029), having raised livestock at home (AOR=5.53, 95% CI: 1.58-19.38, p = 0.016) and BMI < 18.5 (AOR = 8.56, 95% CI: 3.88-18.88, p = 0.000) were associated factors for IPIs among PTB patients. High infection rate of IPs, predominantly *A. lumbricoides* was observed among PTB patients. Therefore, routine screening and prompt treatment for IPIs among PTB patients was recommended in order to ensure good TB prognosis.

Keywords: Intestinal Parasitic Infection, Pulmonary Tuberculosis, Harar, Ethiopia

1. Background

Intestinal parasitic infections (IPIs) caused by protozoa and helminths are among the most widespread human infectious diseases throughout the world affecting around 3.5 billion people; of whom 450 million are ill as a result of the infections [1]. Majority of this parasitic infections accounted by developing countries, mainly sub-Saharan Africa due to low socio-economic status, inadequate water supply, poor environmental sanitation and fast population growth [2]. Globally, it is estimated that more than 10.5 million new cases are reported annually and *Ascaris lumbricoides* (*A. lumbricoides*), hookworms, *Trichuris trichiura* (*T. trichiura*), *Giardia lamblia* (*G. lamblia*), *Entamoeba histolytica* (*E. histolytica)* and *Schistosoma* species are found to be the most common intestinal parasites (IPs) detected [2]. In developing regions, particularly in Africa, more than 173 million people are infected with *A. lumbricoides* while 198 million and 162 million people are infected with hookworms and *T. trichiura*, respectively [3]. In Ethiopia, around 81 million people live in soil-transmitted helminth (STH) endemic areas [4].

Similarly, tuberculosis (TB) is another infectious disease mainly caused by *Mycobacterium tuberculosis* (Mtb) that typically affects the lungs (pulmonary TB), but it can also affect other body parts (extra-pulmonary TB) [5]. TB still continuous as one of the top ten leading causes of mortality that affecting around one-fourth of the world's population [6]. Based on recent World Health Organization (WHO) report, in 2020, globally there were around 10.0 million new TB cases and the death toll was 1.5 million from all forms of TB. About a quarter of this reported TB cases were from African regions. Currently, although there is some progress in Ethiopia in terms of reducing incident rate of TB, the country still remains as one of the top 30 high TB burden nations [6].

Control of infection with Mtb is mainly dependent on the success of the interaction between innate and adaptive immune responses of the host. It was known that the host cell mediated immunity primarily determines the outcome of Mtb infection [5, 7] and in most immuno-competent individuals, the infected macrophages interact with both CD4+ and CD8+ T cells and control the infection mainly via T helper (Th)-1 type inflammatory response [7, 8]. However, individual whose immunity is suppressed or shifted toTh2 type are more susceptible to develop active TB infection and more acute morbidity. Malnutrition, diabetes mellitus, human immunodeficiency virus (HIV), parasites (particularly, helminths) infection, different forms of cancer and prolonged use of steroid drugs are among the factors which suppress/shift the immune response [7-9]. Helminths induce a strong Th2 type immune response characterized by production of cytokines like IL-4, IL-5, IL-9, and IL-13 and increased levels of circulating immunoglobulin IgE antibodies and eosinophils [7]. Thus, prolonged Th2 response is followed by activation and expansion of both natural and inducible regulatory T cells [9, 10]. All of these immune-modulations induced by parasitic infections could favor the survival, multiplication and dissemination of Mtb which in turn result in the development of active TB and the associated sequale [11, 12]. Such independent immune-modulation by parasites, particularly helminths and Mtb determines the pathogenesis and outcome of both infections [13].

Geographically, the distribution of IPIs and TB are overlapping extensively to a large extent and both infections affect primarily low social and economic level populations, living clustered in precarious habitational settings [14, 15]. Thus, co-infection with IPs and TB in humans is an important public health problem in co-endemic areas, especially in developing countries [5, 16] including sub-Saharan Africa [17]. Available evidence suggested that more than 50% of people with latent or active TB infections in the world have IPIs, which is also common in high TB burden nations [18]. In Africa, one-third of TB patients have IPIs [19] that contributes to the high therapeutic failure rate among PTB patients [20]. Moreover, it is expected that this co-infection would increase the complexity of control and prevention of both diseases in co-endemic areas [16, 21]. Therefore, understanding epidemiology of IP/TB co-infection and associated factors is vital to design and implement appropriate intervention tools at different levels of one's country or in nationwide forms.

In Ethiopia, like in other developing countries, IPs are highly prevalent and causing a significant number of infections [22] that also more likely to overlap with TB in co-endemic areas. Limited studies were done in the country and reported varying degrees of IP co-infection rate among TB patients which ranges from 2% to 41% with identification of some factors that increase the risk of having these parasitic infections [23-26]. However, the parasite species and rate of co-infection with PTB vary from one area to another across the country and climatic conditions, socio-demographic factors and living standards of the population are expected to determine the type of parasites existing in various TB endemic areas. As to the best of our knowledge, no similar study has been conducted so far in the current study area. This initiates further study to be conducted on the local epidemiology and associated factors of IPIs among PTB patients, since the data obtained from this study may enable policy makers and program planners to integrate screening and prompt treatment of IPIs into the existing TB management system. Thus, the current study aimed to determine the prevalence and associated factors of IPIs among PTB patients attending selected health facilities in Harar Town, Eastern Ethiopia.

2. Materials and Methods

2.1. Study Design, Area and Period

Health facility based cross-sectional study was conducted in Harar town, which is the capital city of Harari National Regional State and East Hararge Zone. Harar is located at 526km East of Addis Ababa and the town is found at an altitude ranging from 1300-2200m above sea level with annual rainfall ranging from 400-500mm. The average annual temperature of the town ranges from 18-30°C. Based on the census report done in 2007 by the Central Statistical Agency (CSA) of Ethiopia, the town has an estimated total population of 226,412. Harar town has 6 woredas and 19 administrative kebeles. With regard to health facilities; there are 5 hospitals including one private hospital, 8 health centers and 26 health posts. Almost all of the above mentioned hospitals and health centers have TB diagnosis laboratory and treatment clinics with other routine health services. Thus, the study was conducted at three purposively selected health facilities, namely: Hiwot Fana Comprehensive Specialized Haramaya University Hospital (HFCSHUH), Jugol General Hospital (JGH) and Jenela Health Center (JHC) from July 01 to August 30, 2021.

2.2. Study Population and Eligibility Criteria

All age PTB patients who were newly diagnosed based on the current national TB diagnosis guideline and also on treatment follow up patients attending selected TB clinics during the study period, volunteered and had given written informed consent/assent to take part in the study were included. PTB patients who had taken any anti-parasitic treatment in the past 3 months prior to data collection, with severe illness and unable to provide stool specimen were excluded.

2.3. Sample Size Determination and Sampling Procedure

The minimum required sample size (n) for this study was determined using single population proportion formula; $n = (Z_{\alpha/2})^2 \times p\ (1-p)/d^2$ with the following assumptions: estimated IP/TB co-infection rate (p) of 26.3% that taken from previous study done in Arba Minch, Ethiopia [26], 1.96 (standard normal value ($Z_{\alpha/2}$)) for 95% confidence interval and 4% margin of error (d). Accordingly, n was found to be 456.

Since, the source population (N= 627) for this study was <10,000 and n/N was >0.05, a finite population correction formula; $n_{corrected} = N \times n/N+n$ was used to minimize n. The source population for the study was estimated and taken from the data obtained on PTB patients attending health facilities in Harar town during the past consecutive 4 months (last quarter data). Thus, $n_{corrected} = 627 \times 456/627+456 = 264$.

In addition, sample size calculation for associated factors of IPIs among PTB patients was also done using Epi-Info version 7.0 as shown below:

Table 1. *Sample size calculation for factors associated with IPIs among PTB patients by Epi-Info statcalc.*

Variables	Power (%)	OR	CI (%)	Ratio (unexposed / exposed)	% outcome in unexposed	Calculated sample size	Reference
Residence	80	3.18	95	3.53	27.7	162	[26]
Habit of eating unwashed raw vegetables/fruits	80	2.21	95	0.45	39.1	260	[26]
Presence of dirty materials in fingernail	80	8.99	95	3.33	14.3	54	[25]
Laboring barefoot in farmlands	80	4.54	95	1.93	4.0	239	[27]

After considering non-response rate of 10%, the largest sample size obtained out of all calculation was taken as optimum sample size to answer all objectives of the study. Thus, a final sample size of 290 that obtained from prevalence was used for the study.

Regards to sampling procedure; first baseline information on PTB patient flow at each health facility (five hospitals and eight health centers) was collected. Relatively, two hospitals (HFCSHUH and JGH) and one health center (JHC) were found with high PTB patient flow. Accordingly, TB clinics of these three health facilities were purposively selected for data collection and then, brief description about the study was provided whenever eligible individuals visit those TB clinics. A written informed consent or assent was obtained from those volunteer to participate in the study. Non-random consecutive sampling technique was then employed to enroll both newly diagnosed and on treatment follow up PTB patients visiting selected TB clinics during the study period and fulfill inclusion criteria until the required sample size was obtained. Sub-division of patients to each of the three selected health facilities was done based on their respective data obtained from the past consecutive two months.

2.4. Data Collection Tools and Procedure

A structured questionnaire and information sheet for the study were prepared in English after reviewing relevant literatures. The questionnaire was then translated into both Afan Oromo and Amharic languages. It was also pre-tested on 15 PTB patients (5% of the total sample size) in HFCSHUH one week prior to the actual data collection and then, revised and formatted accordingly. Moreover, checklist and laboratory result record format were also prepared and used to record few clinical data and stool sample result, respectively.

Data was collected by trained nurses and laboratory technologists working at those selected TB clinics and laboratories. A total of three BSc nurses and three BSc laboratory technologists were selected from respective TB clinics and laboratories and then, trained for a day by principal investigator. Training was given to equip the data collectors with basic knowledge and skills on data collection instruments and related laboratory procedures.

Data related with socio-demographic, clinical characteristics and associated factors for IPIs were collected using a structured questionnaire via face to face interview by trained nurse during patient visit. During interview, participants' fingernail and foot wear status were inspected. Few clinical data, such as HIV status were also collected by using checklist from patients' log book. Data regarding anthropometric variables such as height (to the nearest 0.1cm without shoes), and weight (to the nearest 0.1 kg) were measured and recorded by trained nurses following anthropometric measurements protocol using calibrated instruments (digital weight scale with stadiometer). BMI of the study participants was then calculated as individuals' weight in kilograms divided by height in meter squared. After an interview, review of records and anthropometric measurement was completed by trained nurses, the study participants were sent to a respective laboratory where stool sample was collected for parasite examination.

2.5. Stool Sample Collection and Laboratory Procedures

All participants were given a stool cup with a tight fitting lid, which was clean, dry, leak proof and labeled with a unique identification number and also with an applicator stick in order to collect about 3-5 grams of stool samples for parasite detection. A small portion (about a match stick head size) of stool sample was processed immediately after collection using direct saline mount at respective health facility laboratory in order to identify motile trophozoites of intestinal protozoa and larva of *S. stercoralis.* A single Kato-Katz thick smear per all stool samples was also prepared using a template delivering 41.7 mg of feaces. The remaining fresh stool sample was preserved by 10% formalin and transported to medical parasitology teaching laboratory of Haramaya University (HU), College of Health and Medical Sciences (CHMS) on the same day of specimen collection following standard sample collection and transportation procedures by principal investigator. This was done for further sample processing through formol-ether concentration (FEC) and modified Ziehl-Neelsen (ZN) staining technique for microscopic examination of parasites.

For direct saline mount, a small amount of faeces was mixed with one drop of normal saline (0.85%) placed on a clean slide. A uniform thin suspension was made using an applicator stick and covered with a clean coverslip. Then, the entire area under the coverslip was screened systematically using the 10X and 40X objective lenses for detection of protozoan trophozoites and cysts as well as helminth ova and larvae [26].

FEC technique is considered as the most sensitive technique for the detection of most intestinal helminths ova/larvae and protozoan cysts. About 1 gram of faeces was added to a clean 15 ml conical test tube containing 7 ml of 10% formalin and the contents was mixed thoroughly using applicator stick. The resulting suspension was filtered through a sieve into another conical centrifuge tube. The debris trapped onto the sieve was discarded. After 3 ml of diethyl ether was added to the formalin solution in the second conical test tube, the contents were centrifuged at medium speed (2,500 rpm) for 5 minutes. The supernatant was poured off and smear was made from the sediment on a clean slide and then, covered with a clean coverslip. Finally, the smear was examined in the same way as that of the direct saline method [25].

Modified ZN staining method was performed for the detection of oocysts of opportunistic intestinal coccidian parasites, such as; *Cryptosporidium* species, *Isospora belli* and *Cyclospora cayetanensis* in stool sample. Proper faecal thin smear was made from the remaining sediment prepared during FEC technique and allowed to air dry. The dried smear was then fixed with methanol for 3 minutes and stained with 1% carbol-fuchsin for 15-20 minutes. After that the smear was decolorized in 1% acid alcohol (HCl in methanol) for 15-20 seconds and counterstained with 0.25% malachite green and left for 1 minute. Finally, the stained smears were dried and examined microscopically using oil immersion (100X) objective lense after back of the slide was wiped and dried through dry cotton/gauze. (Notice: In between each staining steps, the stained smears were washed with clean water and drained) [28].

Kato-Katz technique was carried out at respective health facility laboratory for both detection and quantification of the eggs of intestinal helminths, mainly STHs (*A. lumbricoides*, *T. trichiura*, hookworm) and *S. mansoni*. Quantification of the egg load for evaluation of the intensity of infection was performed following standard operating procedures (SOPs) and a multiplication factor of 24 was used to convert the egg count into eggs per gram of stool [29].

The intensity of infection was estimated from the number of eggs per gram of faeces (epg) and then accordingly, cut-off values for the classification of intensity of infection were used. Thus, the intensity of *S. mansoni* infection is classified as: light (1-99 epg), moderate (100-399 epg) and heavy (≥400 epg). Similarly, for *A. lumbricoides*: light infection (1-4,999 epg), moderate infection (5,000-49,999 epg) and heavy infection (≥50,000 epg). Intensity of *T. trichiura* infection: light (1-999 epg), moderate (1,000-9,999 epg) and heavy (≥10,000 epg). For hookworm: light infection (1-1,999 epg), moderate infection (2,000-3,999 epg) and heavy infection (≥4,000 epg) [29].

2.6. Data Quality Control

Questionnaire was prepared in English and translated into both Afan Oromo and Ahmaric and then, re-translated back to English by an expert who was fluent in both languages to maintain its consistency. Questionnaire was pre-tested on 15 study participants who were not included in the study. Training was also given for data collectors and laboratory technologists prior to actual data collection.

The overall activities of data collection were monitored regularly by the principal investigator to keep validity of the data during data collection. The collected data was also checked for its completeness, clarity and consistency by the principal investigator on daily basis.

The quality of the study results was assured by applying and following quality control measures during the overall process of laboratory procedures (pre-analytical, analytical and post-analytical quality control steps were strictly followed). All materials, equipment and procedures were adequately controlled.

2.7. Statistical Analysis

The collected data was checked, coded and entered into

Epi-Data version 3.1 statistical software and then, exported to Statistical Package for Social Sciences (SPSS) version 25.0 (IBM Corporation, USA) program for analysis. Descriptive statistical analysis including frequency and percentage was computed to descriptively summarize the data. Binary logistic regression analysis was employed and all variable with p-value less than 0.25 during the bivariate analysis were entered into a multivariate analysis to outline the independently associated factors of IPIs among PTB patients. To assess the presence and strength of association between dependent and independent variables, odds ratio (OR) was computed. A p-value of <0.05 at 95% confidence interval (95% CI) was considered as statistically significant.

2.8. Ethical Consideration

Ethical clearance was obtained from the Institutional Review Board (IRB) of Jimma University, Institute of Health with letter protocol number IHRPGn/161/20. A supporting letter was written to HFCSHUH, JGH and Harari Regional Health Bureau in order to get permission to conduct the study. A written informed consent/assent was obtained from each study participants' and for participation of children less than 18 years; consent was obtained from their respective parents'/guardians' after giving a full description about the study. To ensure data confidentiality, the study participants were identified by codes instead of using individual names and only responsible persons were able to access the collected data. Any positive results for IPIs were communicated promptly to the respective clinicians'/health care providers' who were working in TB clinics for proper management of the patients as per the national protocol.

3. Results

3.1. Socio-Demographic Characteristics

A total of 277 PTB patients were included in this study with response rate of 95.5%. One hundred forty-seven of the study participants were from HFCSHUH while 98 and 32 were recruited from JGH and JHC, respectively. Out of 277 participants, 153 (55.2%) were males. The mean age of the study subjects were 31±16.3 (SD) years with majority of the patients (177, 63.9%) belonged to the age group 19-45 years. More than half (159, 57.4%) of the patients were from urban residences (Table 2).

Table 2. *Socio-demographic characteristics of PTB patients attending selected health facilities in Harar Town, Eastern Ethiopia, 2021 (n=277).*

Variables	Categories	Frequency	
		Number	Percent
Sex	Male	153	55.2
	Female	124	44.8
Age	5-18	51	18.4
	19-45	177	63.9
	46-65	40	14.4
	>65	9	3.2
Residence	Urban	159	57.4
	Rural	118	42.6
Occupation	Gov't employee	38	13.7
	Student	82	29.6
	Merchant	42	15.2
	Farmer	33	11.9
	Housewife	57	20.6
	Daily labourer	25	9.0
Educational status	No formal education	66	23.8
	1^0 school	96	34.7
	2^0 school	53	19.1
	College and above	62	22.4
Marital status	Single	123	44.4
	Married	124	44.8
	Divorced	15	5.4
	Widowed	15	5.4

3.2. Behavioral and Clinical Characteristics

In this study, most of the respondents (266, 96.0%) reported that they use latrine. Similarly, 271 (97.8%) of the study participants had no swimming habit. All of the study participants had a shoe wearing habit with 218 (78.7%) of them always wear a shoe. Majority of the patients (189, 68.2%) and (170, 61.4%), used tap water for bathing and drinking purpose, respectively. Most of the participants, 275 (99.3%) and 272 (98.2%), had a habit of hand washing before meal and after defecation, respectively. During the time of interview, 79 (28.5%) of the patients were inspected as having dirt in their fingernails. Similarly, nearly half (142, 51.3%) of the study participants had a habit of eating unwashed raw vegetables/fruits. Moreover, 95 (34.3%) and 100 (36.1%) of the respondents reported that they have a raised livestock (cattle, sheep, goat, chicken, equine/camel) and pets (cat/dog) at their homes, respectively (Table 3).

Out of 277 participants, 35 (12.6%) and 45 (16.2%) reported that they had history of diarrhea and other GIT discomfort in the past 3 weeks before this data was collected, respectively. During the time of interview, 207 (74.7%) of the study participants have already started anti-TB treatment. All of the study subjects were tested for HIV and among them, 38 (13.7%) were positive. The mean BMI of the study participants was 18.7$\pm$3.33 (SD) kg/m^2 and 125 (45.1%) of them had BMI<18.5 (Table 4).

Table 3. *Behavioral characteristics of PTB patients attending selected health facilities in Harar Town, Eastern Ethiopia, 2021 (n=277).*

Variables	Categories	Frequency	
		Number	Percent
Latrine usage	Yes	266	96.0
	No	11	4.0
Swimming habit	Yes	6	2.2
	No	271	97.8
Swimming habit frequency	Always	2	0.7
	Often	1	0.4
	Occasional	3	1.1
Shoe wearing habit	Yes	277	100.0
	No	0	0.0
Shoe wearing habit frequency	Always	218	78.7
	Often	46	16.6
	Occasional	13	4.7
Water source for bathing	Tap water	189	68.2
	Stream/river/lake	82	29.6
	Ground water	6	2.2
Hand washing habit before meal	Yes	275	99.3
	No	2	0.7
Hand washing habit before meal frequency	Always	259	93.5
	Often	11	4.0
	Occasional	5	1.8
Hand washing habit after defecation	Yes	272	98.2
	No	5	1.8
Hand washing habit after defecation frequency	Always	238	85.9
	Often	31	11.2
	Occasional	3	1.1
Source of water for drinking	Tap water	170	61.4
	Stream/river/lake	80	28.9
	Highland water	26	9.4
	Ground water	1	0.4
Water source for washing utensils	Tap water	191	69.0
	Stream/river/lake	74	26.7
	Ground water	12	4.3
Presence of dirt in fingernail	Yes	79	28.5
	No	198	71.5
Unwashed raw vegetables/fruit eating habit	Yes	142	51.3
	No	135	48.7
Unwashed raw vegetables/fruit eating habit frequency	Always	39	14.1
	Often	69	24.9
	Occasional	34	12.3
Habit of eating raw meat	Yes	60	21.7
	No	217	78.3
Eating raw meat habit frequency	Always	1	0.4
	Often	20	7.2
	Occasional	39	14.1
Presence of raised livestock at home	Yes	95	34.3
	No	182	65.7
Presence of raised pet (cat/dog) at home	Yes	100	36.1
	No	177	63.9

Table 4. *Clinical and physical baseline conditions of PTB patients attending selected health facilities in Harar Town, Eastern Ethiopia, 2021 (n=277).*

Variables	Categories	Frequency	
		Number	Percent
Diarrheal history in the past 3 weeks	Yes	35	12.6
	No	242	87.4
Other GIT discomfort history in the past 3 weeks	Yes	45	16.2
	No	232	83.8
Anti-TB treatment start	Yes	207	74.7
	No	70	25.3
Duration of anti-TB treatment (in months)	<2	50	18.1
	2-4	43	15.5
	>4	114	41.2
HIV status	Positive	38	13.7
	Negative	239	86.3
BMI	<18.5	125	45.1
	≥18.5	152	54.9

3.3. Prevalence of Intestinal Parasites

Among 277 PTB patients included in the study, IPs was detected in 79 (28.5%). A total of 84 IPs (50 intestinal helminths and 34 intestinal protozoans) were identified in 79 PTB patients. Thus, intestinal helminths and protozoa infections accounted for 45 (16.2%) and 34 (12.3%), respectively. Infection with single and double parasite species were observed in 74 (26.7%) and 5 (1.8%) of study participants, respectively. *A. lumbricoides* accounted for the highest frequency (20, 7.2%) followed by *G. lamblia* (15, 5.4%), *E. histolytica/dispar* (12, 4.3%), *H. nana* (9, 3.2%), hookworm species (8, 2.9%), *C. parvum* (5, 1.8%), *T. trichiura* (4, 1.4%), Teania species (3, 1.1%), *S. stercoralis* (3, 1.1%), *E. vermicularis* (3, 1.1%) and *I. belli* (2, 0.7%), respectively. Moreover, *S. mansoni* was observed in 7 (2.5%) patients (Table 5, Figures 1 and 2).

In addition to prevalence determination for intestinal helminths, particularly STHs and *S. mansoni*, their intensity of infection was also determined from the number of eggs per gram of feaces by Kato-Katz method. All of the intensities of *A. lumbricoides,* hookworm species and *T. trichiura* infections were light, whereas for *S. mansoni* infections; only one case (0.4%) had light infection (<100 epg), and the other six cases (2.2%) were found to have moderate-intensity infection (100-400 epg) (Table 6).

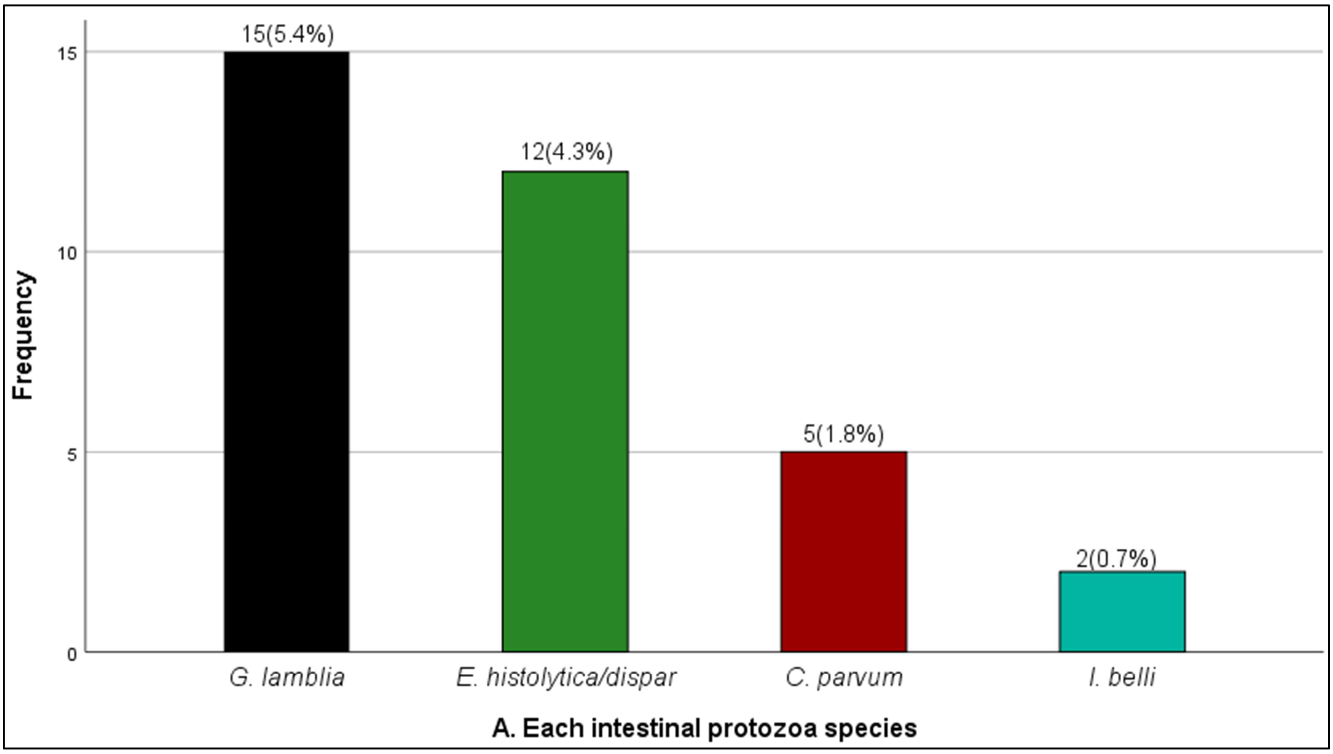

Figure 1. *Distribution of intestinal protozoa among PTB patients attending selected health facilities in Harar Town, Eastern Ethiopia, 2021.*

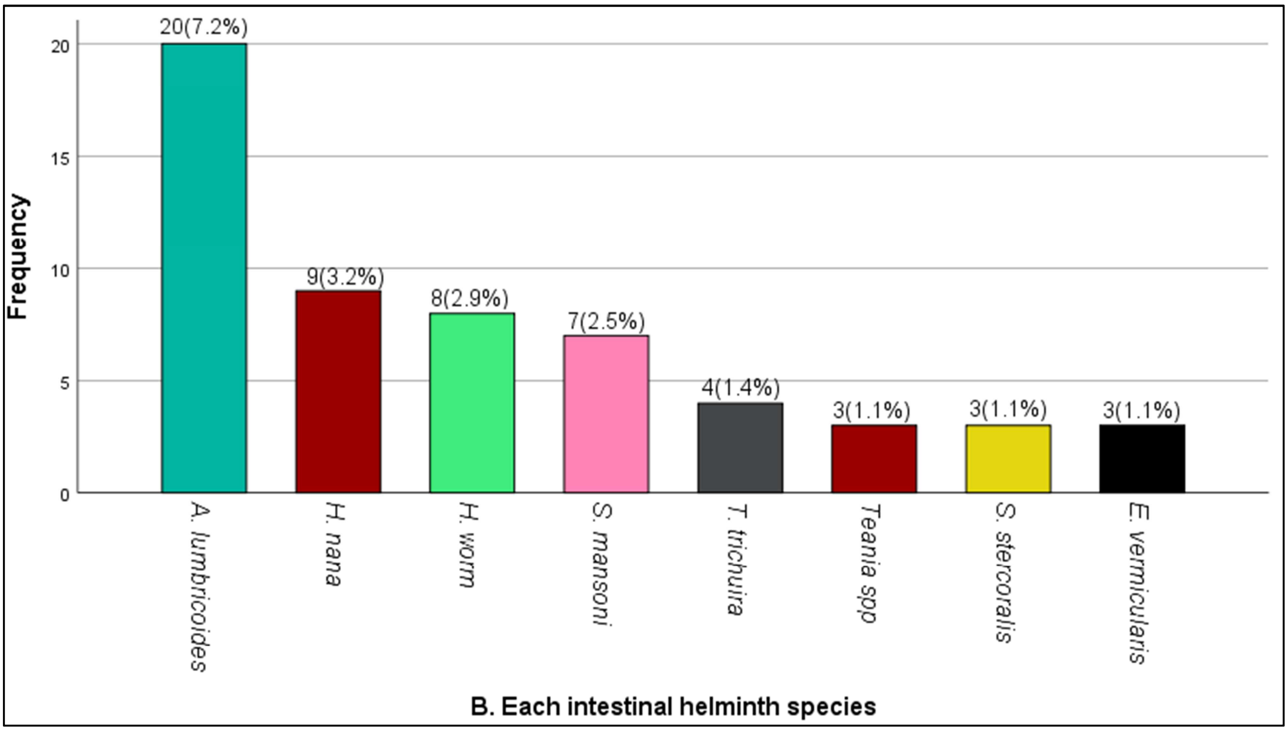

Figure 2. *Distribution of helminth parasites among PTB patients attending selected health facilities in Harar Town, Eastern Ethiopia, 2021.*

Table 5. *Prevalence of IPs among PTB patients attending selected health facilities in Harar Town, Eastern Ethiopia, 2021 (n=277).*

Variables	Categories	Frequency	
		Number	Percent
Overall IPs (I. helminths + I. protozoa)	Not infected	198	71.5
	Infected	79	28.5
I. helminths (mono-infections only)	Not infected	237	85.6
	Infected	40	14.4
I. protozoa (mono-infections only)	Not infected	246	88.8
	Infected	31	11.2
No of parasite species detected per patients	Single (1)	74	26.7
	Double (2)	5	1.8
Double parasite species infection	*A. lumbricoides* + *E. vermicularis*	1	0.36
	Hookworm species + *G. lamblia*	1	0.36
	E. histolytica/dispar + *H. nana*	2	0.72
	G. lamblia + *S. stercoralis*	1	0.36

Table 6. *Proportion of the intensity of STHs and S. mansoni infections among PTB patients attending selected health facilities in Harar Town, Eastern Ethiopia, 2021 (n=277).*

Helminth species	Intensity of infection: No (%)			
	Light	Moderate	Heavy	Total
S. mansoni	1 (0.4)	6 (2.2)	-	7 (2.5)
A. lumbricoides	20 (7.2)	-	-	20 (7.2)
T. trichiura	4 (1.4)	-	-	4 (1.4)
Hookworm species	8 (2.9)	-	-	8 (2.9)

"-"=not present

3.4. Statistical Analysis on Associated Factors of Intestinal Parasitic Infections

In this study, results from bivariate logistic regression analysis showed that being male in sex, age, living in rural area, occupation, educational level, latrine usage, shoe wearing habit frequency, water source for bathing and washing utensils, frequency of hand washing after defecation, having dirt in fingernail, habit of eating unwashed raw vegetables/fruits, eating raw meat habit, having raised livestock and pets at home, diarrheal history in the past 3 weeks, duration of anti-TB treatment and BMI had significant association with IPIs at p-value of <0.25. However, after all these variables were entered into multivariate logistic regression analysis, only 3 of them showed significant association with IPIs at p-value of <0.05. Those include; presence of dirty materials in fingernail

(AOR=3.04, 95% CI: 1.12-8.22, p=0.029), having raised livestock at home (AOR=5.53, 95% CI: 1.58-19.38, p=0.016) and BMI<18.5 (AOR=8.56, 95% CI: 3.88-18.88, p=0.000) (Tables 7 and 8).

Table 7. *Statistical analysis on socio-demographic characteristics and associated risk factors of IPIs among PTB patients attending selected health facilities in Harar Town, Eastern Ethiopia, 2021.*

Variables	Categories	No examined	IPI rate No (%)	COR (95%CI)	P-value	AOR (95%CI)	P-value
Sex	Male	153	53 (34.6)	2.00 (1.16-3.45)	0.013	1.07 (0.20-7.84)	0.084
	Female	124	26 (21.0)	1.000		1.000	
Age	5-18	51	20 (39.2)	1.29 (0.29-5.76)	0.215	3.00 (0.31-28.64)	0.588
	19-45	177	48 (27.1)	0.74 (0.18-3.10)		1.68 (0.21-13.30)	
	46-65	40	8 (20.0)	0.50 (0.10-2.45)		0.96 (0.11-8.56)	
	>65	9	3 (33.3)	1.000		1.000	
Residence	Urban	159	25 (15.7)	1.000	0.000	1.000	0.063
	Rural	118	54 (45.8)	4.52 (2.58-7.92)		3.10 (0.10-8.76)	
Occupation	Merchant	42	8 (19.0)	1.000	0.060	1.000	0.666
	Gov't employee	38	11 (28.9)	1.73 (0.61-4.91)		0.37 (0.07-2.07)	
	Housewife	57	13 (22.8)	1.26 (0.47-3.37)		0.25 (0.03-1.81)	
	Farmer	33	17 (51.5)	4.51 (1.61-12.64)		0.48 (0.06-3.63)	
	Student	82	23 (28.0)	1.66 (0.67-4.11)		0.27 (0.05-1.37)	
	Daily laborer	25	7 (28.0)	1.65 (0.52-5.29)		0.27 (0.03-2.14)	
Educational status	No formal education	66	24 (36.4)	2.65 (1.16-6.03)	0.128	1.66 (0.23-12.23)	0.203
	1^0 school	96	27 (28.1)	1.81 (0.82-4.00)		1.36 (0.25-7.31)	
	2^0 school	53	17 (32.1)	2.19 (0.92-5.23)		3.50 (0.79-15.55)	
	College and above	62	11 (17.7)	1.000		1.000	
Marital status	Single	123	38 (30.9)	2.91 (0.63-13.52)	0.486	–	–
	Married	124	36 (29.0)	2.66 (0.57-12.38)			
	Divorced	15	3 (20.0)	1.63 (0.23-11.46)			
	Widowed	15	2 (13.3)	1.000			
Latrine usage	Yes	266	74 (27.8)	1.000	0.214	1.000	0.594
	No	11	5 (45.5)	2.16 (0.64-7.30)		0.57 (0.07-4.56)	
Swimming habit	Yes	6	1 (16.7)	0.50 (0.06-4.30)	0.524	–	–
	No	271	78 (28.8)	1.000			
Shoe wearing habit frequency	Always	218	53 (24.3)	1.000	0.013	1.000	0.767
	Often	46	20 (43.5)	2.40 (1.24-4.63)		0.65 (0.20-2.11)	
	Occasional	13	6 (46.2)	2.67 (0.86-8.29)		0.66 (0.07-6.41)	
Water source for bathing	Tap water	189	40 (21.2)	1.000	0.000	1.000	0.814
	Stream/river/lake	82	37 (45.1)	3.06 (1.75-5.35)		0.88 (0.06-12.49)	
	Ground water	6	2 (33.3)	1.86 (0.33-10.54)		2.95 (0.03-16.03	
Hand washing habit before meal	Yes	275	78 (28.4)	1.000	0.514	-	-
	No	2	1 (50.0)	2.53 (0.16-40.88)			
Hand washing habit before meal frequency	Always	259	71 (27.4)	1.000	0.499	-	-
	Often	11	5 (45.5)	0.83 (0.04-16.99)			
	Occasional	5	2 (40.0)	0.67 (0.03-18.06)			
Hand wash habit after defecation	Yes	272	78 (28.7)	1.000	0.673	-	-
	No	5	1 (20.0)	0.62 (0.07-5.65)			
Hand wash habit after defecation frequency	Always	238	62 (26.1)	1.000	0.087	1.000	0.249
	Often	31	15 (48.4)	3.75 (0.38-37.47)		2.13 (0.01-12.75)	
	Occasional	3	1 (33.3)	2.00 (0.08-51.59)		1.26 (0.41-26.19)	
Source of water for drinking	Tap water	170	40 (23.5)	0.61 (0.20-1.88)	0.002	1.18 (0.01-4.11)	0.744
	Stream/river/lake	80	36 (45.0)	2.75 (1.56-4.85)		1.89 (0.51-7.03)	
	Ground water	1	1 (100.0)	3.14 (1.81-6.33)		2.64 (0.10-4.01)	
	Highland water	26	2 (7.7)	1.000		1.000	
Water source for washing utensils	Tap water	191	41 (21.5)	1.000	0.000	1.000	0.279
	Stream/river/lake	74	35 (47.3)	3.28 (1.85-5.82)		1.10 (0.09-14.16)	
	Ground water	12	3 (25.0)	1.22 (0.32-4.71)		0.11 (0.00-4.67)	
Presence of dirt in fingernail	Yes	79	34 (43.0)	2.57 (1.47-4.48)	0.001	3.04 (1.12-8.22)	0.029
	No	198	45 (22.7)	1.000		1.000	
Raw vegetable/fruit eating habit	Yes	142	49 (34.5)	1.84 (1.08-3.14)	0.024	0.51 (0.20-1.26)	0.143
	No	135	30 (22.2)	1.000		1.000	
Habit of eating raw meat	Yes	60	13 (21.7)	0.65 (0.33-1.29)	0.216	1.16 (0.36-3.74)	0.808
	No	217	66 (30.4)	1.000		1.000	
Presence of livestock at home	Yes	95	44 (46.3)	3.62 (2.10-6.26)	0.000	5.53 (1.58-19.38)	0.016
	No	182	35 (19.2)	1.000		1.000	
Presence of pet (cat/dog) at home	Yes	100	33 (33.0)	1.40 (0.82-2.40)	0.215	1.45 (0.64-3.27)	0.374
	No	177	46 (26.0)	1.000		1.000	

COR=crude odds ratio, AOR=adjusted odds ratio, CI=confidence interval, "-"=Not done

Table 8. *Statistical analysis on clinical factors and health status baseline conditions associated with IPIs among PTB patients attending selected health facilities in Harar Town, Eastern Ethiopia, 2021.*

Variables	Categories	No examined	IPI rate No (%)	COR (95%CI)	P-value	AOR (95%CI)	P-value
Diarrheal history in the past 3 weeks	Yes	35	15 (42.9)	2.09 (1.01-4.32)	0.048	1.52 (0.50-4.63)	0.465
	No	242	64 (26.4)	1.000		1.000	
Other GIT discomfort in the past 3 weeks	Yes	45	15 (33.3)	1.31 (0.66-2.60)	0.435	–	–
	No	232	64 (27.6)	1.000			
Anti-TB treatment start	Yes	207	62 (30.0)	1.000	0.365	–	–
	No	70	17 (24.3)	0.75 (0.40-1.40)			
Anti-TB treatment course	First	203	60 (29.6)	1.000	0.330	–	–
	Retreatment	4	2 (50.0)	0.43 (0.06-3.12)			
Anti-TB treatment duration	<2	50	15 (30.0)	0.55 (0.28-1.08)	0.137	0.40 (0.15-1.06)	0.232
	2-4	43	8 (18.6)	0.79 (0.39-1.62)		0.64 (0.23-1.82)	
	>4	114	39 (34.2)	1.000		1.000	
HIV status	Positive	38	8 (21.1)	0.63 (0.28-1.44)	0.276	–	–
	Negative	239	71 (29.7)	1.000			
BMI	<18.5	125	59 (47.2)	5.90 (3.28-10.61)	0.000	8.56 (3.88-18.88)	0.000
	≥18.5	152	20 (13.2)	1.000		1.000	

COR=crude odds ratio, AOR=adjusted odds ratio, CI=confidence interval, “-”=Not done

4. Discussion

In this study, the overall prevalence of IPIs among PTB patients was 28.5%. Similar findings were reported from studies done at Arba Minch (26.3%) [26], Gondar (33.3%) [30] and India (27.1%) [31]. However, our finding showed lower co-infection rate than studies conducted in Gondar: (40.5%) [23], (37.3%) [32] and Brazil (57.8%) [33]. This might be due to the difference in the time when these studies were conducted and currently throughout the country, there is health extension workers engaged in the primary health care activities. In addition, the laboratory procedure followed might also justify this variation. In those previous studies, 3 consecutive stool specimens were collected and examined from each study participant before ruling out parasitic infections. However, in the present study, we have collected and examined a single stool specimen. On the other hand, our study revealed higher co-infection rate than studies done in Adama (21.4%) [34], Addis Ababa (22.0%) [25], Oromia Special Zone of Amhara Region and South Wollo Zone (10.8%) [35], Gondar (2%) [24], Brazil (19.6%) [16] and China (14.9%) [17]. This might be due to the difference in study area, sample size, study population and the type of laboratory techniques used. Moreover, differences in socio-economic status and level of awareness regarding parasitic infection transmission and prevention might also be essential determinant factors for the low prevalence observed in Brazil and China compared to our study results [16, 17].

Multiple parasitic infections and repeated infections are common in areas where parasites are highly prevalent, and this might make people susceptible to other infections such as TB. Studies revealed that individuals with high worm burden or multiple infections had an increased risk of developing TB [7, 25]. In line with this, the current study detected double parasite species infection in five (1.8%) of PTB patients. Similarly, mixed or more than one species of IPs among TB patients were reported from previous studies done in Arba Minch [26], Gondar [30], Tanzania [20] and China [27]. Moreover, in this study, the intensity of STHs and *S. mansoni* infection were determined so that all of the study participants infected with *A. lumbricoides, T. trichiura* and hookworms had light infection, whereas, most of the patients (6, 2.2%) infected with *S. mansoni* had moderate infection and only one case (0.4%) had light infection. This finding was in agreement with the study conducted in Tanzania [20] where most of the infected study participants had light-intensity helminthic infection. The mostly observed light-intensity helminthic infection in our study might be due to those majorly on treatment follow up PTB patients enrolled into the study so that drugs & other health care services may in turn result in improved immune status against helminthic infection and cause low worm (egg) load.

Among the 11 species of IPs and *S. mansoni* identified in this study, *A. lumbricoides* (7.2%) was the predominant parasite species followed by *G. lamblia* (5.4%) and *E. histolytica/dispar* (4.3%). Our results in this case was supported by the existing evidence suggesting that *A. lumbricoides* is the most prevalent helminth in Ethiopia with around 33% of the population being infected [36, 37]. Some cross-sectional studies conducted among TB patients in different parts of Ethiopia also revealed similar findings [23, 24, 26, 32, 38]. However, there are other studies presenting other parasite species as a predominant parasite in PTB patients. Thus, *E. histolytica* (8.1%) [34], *G. lamblia* (8.8%) [25], *S. mansoni* (4.3%) [35] and hookworms (11.1%) [30] were reported as the most frequently detected parasites in Ethiopia. *S. stercoralis*; (7.3%) [16], (17.0%) [20], hookworms (16.5%) [21] and *Blastocystis hominis* (6.0%) [17] were also reported as the most prevalent parasite in Brazil, Tanzania, Egypt and China, respectively. The observed variation in predominant parasite species among these studies might be due to the difference in study area or geographical locations, climate conditions, socio-demographic characteristics and living standards of the population that believed to determine the type of parasites existing in various TB endemic areas. In the present study, we used modified Ziehl-Neelsen staining method to identify intestinal coccidian parasites and, *C. parvum* and *I. belli* were detected in 1.8% and 0.7% PTB patients, respectively. Similar findings were reported from previous studies conducted in Ethiopia [25, 39].

In the current study; presence of dirty materials in fingernail, having raised livestock at home and BMI<18.5 were associated factors of IPIs among PTB patients. In this study, out of 79 study participants who had dirty material in their fingernails, 34 (43.0%) had IP/PTB co-infection. Thus, participants who had dirt in their fingernails were three times more likely to have IPI as compared to those with clean fingernail. Our finding in this case was supported by studies done at Addis Ababa [25] and Tilili [40] where 47.9% of students who had dirty material in their fingernails were infected with helminths. Infective helminth ova or protozoan cysts/oocysts are ingested with contaminated food, water or hands to initiate infection so that individuals with dirty material in their fingernails are more likely to be infected with IPs. Moreover, in this study, out of 95 PTB patients that reported the presence of raised livestock at home, 44 (46.3%) were co-infected with IPs. Thus, participants who raised livestock at homes were about six times more likely to be infected by IPs than their counterparts. For this case supportive findings were reported from previous studies conducted in Ethiopia [41] and China [27]. The observed association between IPI and presence of raised livestock at home in our study might be due to the role of zoonotic transmission for *C. parvum* detected.

Screening, assessment and management of nutrition are integral components of TB treatment and care. Therefore, WHO recommended that patients with TB should be assessed for nutrition and receive nutritional care and support [42]. In this study, we identified 125 (45.1%) of PTB patients with malnutrition and among them, 59 (47.2%) had IP co-infection. Thus, patients with BMI<18.5 were nearly nine times at higher risk of acquiring IPI as compared to those with BMI ≥18.5. This finding was consistent with studies done in Ethiopia [25, 26, 34] and China [17, 27]. This is expected as IPs, especially helminths cause undernutrition [43, 44]. In general, our finding in this case indicates that parasitic infections affect nutritional status of the individual which in turn result in immunological alterations. Thus, immunological alterations again promote a decrease in the efficacy of immune response and then favor the occurrence of other infections such as TB [16].

5. Limitations

Limitations of this study were; single stool sample was collected and examined for each study participant to rule out parasitic infection, which was done for the sake of time and logistic problems. Immunological parameters and nutritional assessments except BMI were also not done in this study so that their role on TB pathogenesis could be justified.

6. Conclusion and Recommendation

6.1. Conclusion

High prevalence of IPIs among PTB patients was observed in this study. *A. lumbricoides* was the predominant parasite identified. Double parasite species infection was also observed in this study. Presence of dirty materials in fingernail, having raised livestock at home and BMI<18.5 were significantly associated with IPIs among PTB patients.

6.2. Recommendation

Based on the current study findings, it is recommended that PTB patients should protect their personal hygiene by regular trimming and cleaning of their fingernail, avoiding unwanted contact with livestock and their fecal contaminated materials. Health care provider, particularly those working on TB program should screen TB patients for IPI and also provide health education on good hygiene practice as preventive measures of IPI among PTB patients which may lead to good TB prognosis. Moreover, other researcher should undergo further large scale study accompanying the impacts of this parasitic infection on TB treatment outcomes. Lastly, the integration of routine screening and prompt treatment of IPIs among PTB patients into the existing TB management system should also be considered by policy makers to enhance better control of both infections simultaneously.

Acronyms and Abbreviations

BMI: Body Mass Index; FEC: Formol Ether Concentration; GIT: Gatro-Intestinal Tract; HFCSHUH: Hiwot Fana Comprehensive Specialized Haramaya University Hospital; HIV: Human Immunodeficiency Virus; HU: Haramaya University; CHMS: College of Health and Medical Sciences; Ig: Immunoglobulin; IRB: Institutional Review Board; IL: Interleukin; JHC: Jenela Health Center; JGH: Jugol General Hospital; IPI: Intestinal Parasitic Infection; Mtb: Mycobacterium-tuberculosis; PTB: Pulmonary Tuberculosis; SOP: Standard Operating Procedure; SPSS: Statistical Package for Social Sciences; STH: Soil Transmitted Helminth; TB: Tuberculosis; Th: T helper; WHO: World Health Organization; ZN: Ziehl Neelsen.

Authors' Contributions

U. U., T. E., A. T., B. M., M. G. and K. Y. are involved in the conception of the research idea, design and data collection, analysis and interpretation of the finding. U. U. wrote the manuscript and then all authors reviewed it and contributed their intellectual content. Final manuscript was read and approved by all authors.

Competing Interests

The authors declared that they have no competing interests with respect to research, authorship and/or publication of this article.

Availability of Data and Supplemental Materials

The original data and supportive materials for the study are available from the corresponding author.

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