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Prevalence and Associated Factors of *Schistosoma mansoni* and Other *Intestinal Helminthes* Co-Infection Among Malaria Positive Patients in Malaria Endemic Areas of Northeast, Ethiopia: A Cross-Sectional Study

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ABSTRACT

Background and Aims: *Schistosoma mansoni* and malaria share a similar epidemiological distribution or co-endemicity. Co-infection are a global public health burden where epidemiological evidence is crucial to taking evidence-based intervention. Thus, the aim of this study was to assess the prevalence and associated factors of *Schistosoma mansoni* and other intestinal Helminthes co-infection among malaria positive patients in malaria endemic areas of Northeast Ethiopia.

Methods: A cross-sectional study was conducted from September 2018 to June 2019 among randomly recruited 145 microscopically confirmed malaria patients in Kemisse and Chefa Robit, Northeast Ethiopia. A pre-tested semi-structured questionnaire was used for sociodemographic and other risk factor data; blood samples for malaria microscopy and stool samples for *S. mansoni* and other intestinal Helminthes examinations were collected from each participant. STATA 17 was used for analysis. Chi-square and Fishers' exact test were used as required. The internal consistency and model good ness of fitness test were checked using Cronbach's alpha and Hosmer-Lemshow test, respectively. Bivariable and multivariable logistic regression model was used for analysis. Finally, variables with $p < 0.05$, their AOR and their 95% Confidence Intervals were considered statistically significant.

Results: A total of 145 patients with malaria were included in this study of which 11.3% and 49.0% respectively had poly and mono infections. From all malaria confirmed patients, 29.7% were positive for *S. mansoni*, which was significantly associated with pervious intestinal helminthic infection, history of swimming and fishing participants who lives near to river and having a history of crossing river by their legs without shoe. Moreover, compared with students; farmers merchants and housewives were found to be highly affected.

Conclusions: The co-endemicity of *S. mansoni* and malaria in the current study was considerably high. Further study is needed to explore the underlying mechanisms of interaction between malaria and *S. mansoni* with larger sample size.

1 | Introduction

Parasitic infections present a major cause of disease and morbidity in Africa. Malaria affects about 40% of the world's population [1] but the burden is huge sub-Saharan Africa where 85% and 90% respective global malaria cases and deaths have been occurred [2]. Schistosomiasis affects nearly 662 million people annually in the globe [1] and it is endemic in 76 countries globally [3]. Approximately 85% of 662 million cases of schistosomiasis were from Africa [1]. According to World Health Organization (WHO) estimates, more than one billion people are chronically infected with soil- transmitted helminths of which nearly 1.3 million cases were due to hookworm infection [1, 4]. Moreover, the burden of intestinal schistosomiasis in sub-Saharan African countries is escalating. Of all schistosomiasis cases of SSA nearly one-third of cases were due to *Schistosoma mansoni* (*S. mansoni*) [5, 6].

Both intestinal schistosomiasis (due to *S. mansoni*) and malaria becomes a global public health burden and challenges for socioeconomic development. Moreover, *S. mansoni* and malaria shares similar epidemiological distributions or have coendemicity which leads to extensive investigation of their interactive pathology [7]. The accelerated incidence of malaria was significantly associated with heavy infection of *S. mansoni* [8]. The countering effects of plasmodium species and *S. mansoni* on immunological cytokines have been known for statistically related interaction between the two diseases. However, the immunological control of malaria might be significantly decreased as a result of alteration of T helper cell immune responses by *S. mansoni* [6, 9].

S. mansoni plays an antagonistic role against malaria however, the egg intensity of *S. mansoni* and the age of infected individuals could determine the type of interaction [10, 11]. In addition to this, epidemiological concurrence and co-infection between helminthiasis and malaria is common [12–14]. In tropical countries including Ethiopia, *S. mansoni* and malaria co-infections are highly prevalent which may lead to worsening or complication of malaria such as increased malaria gametocyte carriage and risk for clinical as well as severe malaria. In addition, it might be associated with reduced heamoglobin concentration or anemia [15] and deficiency of macro and micronutrients which are responsible for the development of malnutrition as well as immune suppression and growth impairment in children. Thus, such co-infections might lead to more severe clinical symptoms and pathology than mono-infection as well as considerable health consequence. So, the interaction between helminths infection and malaria increases organomegaly and the severity of anemia which potentially create a great challenge for disease control in the tropics. Moreover, immune responses are also altered during co-infection with multiple parasites than mono-infection with a single parasitic species [1, 16].

Overlapping infections of schistosomes, soil-transmitted helminth and malaria might be mediated by the conditions which favors the survival and transmission of multiple parasitic species. Poverty, water bodies and lack of effective preventive measures and environmental contamination are the most favorable conditions for survival and transmission of infectious agents [17]. As a result, infectious diseases including malaria was a target of Ethiopian Health Sector Transformation Plan (HSTP). The death and incidence rates of malaria was decreased from 2015 to 2019 according to HSTP I evidence [18]. This reduced figure of incidence and death rate reduces the concomitant infection of the two diseases and related complications Figure 1.

On the other hand, evidence showed that individuals are commonly coinfected with helminths and malaria parasites [19]. Moreover, various epidemiological settings of Africa polyparasitism of schistosomiasis, soil-transmitted helminth and malaria have been reported [6]. Previous studies from Ethiopia were conducted in nonendemic area of malaria where *P. falciparum* infection was 4% and *S. mansoni* was not reported [12] in which the study couldn't showed co-endemicity. On behalf of this, most parasitic diseases are individually studied. So, epidemiological evidences were crucial to take evidence based public health intervention to reduce schistosomiasis

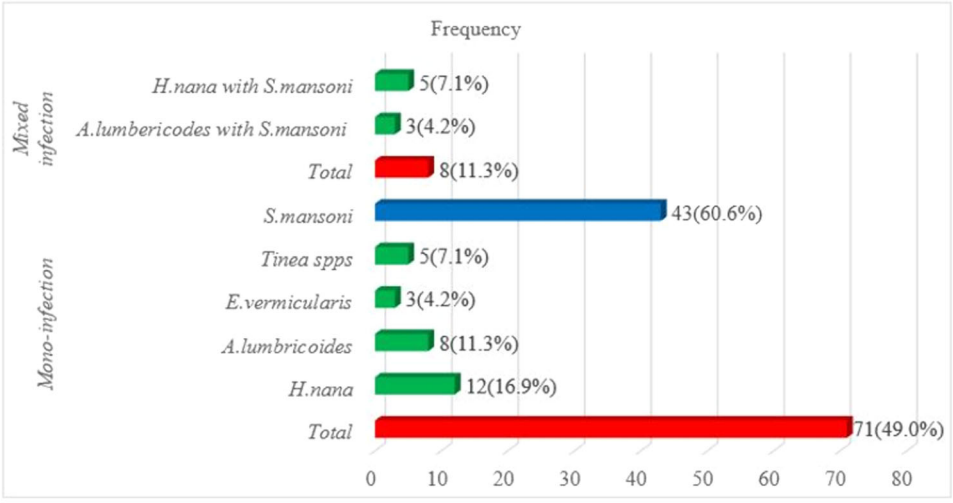

FIGURE 1 | Frequency distribution of *S. mansoni* and other *intestinal helminthes* among malaria positive patients in malaria endemic areas of Northeast Ethiopia, September 2018–June 2019.

health burden in malaria co-endemic communities and used to design better control and prevention strategies but are very limited especially in malaria endemic areas. Thus, the aim of this epidemiological study was to determine the prevalence of *S. mansion* and other intestinal helminths co-infections and associated risk factors among malaria infected patients in malaria endemic areas of Northeast Ethiopia.

2 | Methods and Materials

2.1 | Study Area, Design, Period and Population

An institution-based cross-sectional study was conducted in Kemisse and Chefa Robit towns, Northeast, Ethiopia, from September 2018 to June 2019. Kemisse and Chefa Robit are malaria endemic area which is located in the north from the capital city of Ethiopia, Addis Ababa. In these towns there are three health facilities (one health center in each and one General Hospital in Kemisse). These health facilities give different inpatient and outpatient services to the population in the surrounding area and the adjacent regions. According to District Health Bureau report, schistosomiasis (due to *S. mansoni*) and malaria (due to *P. falciparum* and *P. vivax*) are common and top five communicable disease burden in the study area. All microscopically confirmed malaria patients and who had an access to visit Kemisse Health Center and Chefa Robit Health center during the study period were enrolled in the study. However, patients who were on anti- helminthic and patients who were critically ill were excluded from the study.

2.2 | Sample Size Determination and Sampling Techniques

The minimum sample size of this study was determined by using a single population proportion formula considering the assumptions of 95% confidence level, 0.9% [20] of malaria prevalence from Ethiopian national malaria indicator survey and 5% precision. Considering 5% nonresponse rate a total of 145 all microscopically confirmed malaria patients. Systematic random sampling was employed to select 145 participants from a total of 305 malaria cases across three health facilities. The sampling interval was calculated as $305/145 \approx 2$. A random starting point was chosen to be 1. Then, in every 2nd case, a total of 145 participants were selected.

2.3 | Variables

The outcome variable of this study was *S. mansoni* and other intestinal helminths, and malaria co-infection (coded as 1 when there is *S. mansoni* co-infection while coded as 0 when there is no co-infection or negative), then the prevalence was calculated by dividing the number cases of co-infection by total participants and multiplied by 100 to express in percentage. Furthermore, socio-demographic variables (age, sex, family size, educational status, occupational status), monthly income, personal hygiene, behavioral factors (such as shoe wearing habit, swimming habit, hand washing habit etc.) were explanatory variables of the study. Moreover, family size of respondents was recategorized in to small (up to three), medium (four to six) and large family size (greater or equal to seven) [21].

2.4 | Data Collection

The data collection was undertaken after the purpose of the study, procedure, potential risks and benefits, and participants' rights using the local language were clearly explained. Using a pre-tested structured questionnaire (Supporting Information S1), trained public health officers collected the socio-demographic factors, behavioral factors, environmental related factors and other explanatory variables were collected using face to face interview after the consent was obtained. When the participants were children (age less than 15 years), the information were collected from the parents/guardian of the children after the assent was obtained. Moreover, blood specimens (for malaria case confirmation) and stool specimens (for detection of *S. mansoni* and other intestinal helminth infections) were collected and processed accordingly based on standard operating procedures of Wollo University medical parasitology laboratory by senior medical laboratory technologists working for more than 7 years from Wollo University medical parasitology laboratory. The data collection and recruitment of human participants was started on September 5, 2018 and ends on June 27, 2019.

2.5 | Laboratory Investigation of Malaria, *S. Mansoni* and Other Intestinal Helminths

2.5.1 | Detection of Malaria Parasite

For each clinical malaria cases both thin and thick blood films were prepared for the detection of malaria parasites. After the thin blood films were prefixed by absolute ethanol, Giemsa staining method was used to stain blood films. Certified malaria microscopists who had more than 10 years of experience were examined the blood films using light microscope for the detection of malaria.

2.5.2 | Detection of *S. mansoni* and Other Intestinal Helminths

Approximately 1 gm of fresh stool sample was collected from every study participant who were volunteers and had a microscopically confirmed malaria result. The stool specimens were prepared for wet mount microscopic examination and the remaining specimens was preserved using 10% formalin for further concentration technique. Formol-ether concentration techniques was performed followed by microscopic examination of the sediments under 10× and 40× objectives by three senior Medical Laboratory Technologists.

2.6 | Data Quality Management

The questionnaire was pretested before the actual data collection have been started on 5% of the total sample size and

appropriate modifications have been made on questionnaire. The collected data was checked daily for consistency (the completeness of the questionnaire, appropriateness of specimen labeling and participant identifications) and accuracy (accuracy of microscopic results). The appropriateness of the reagent was rechecked with a known positive and negative sample. Randomly positive and negative smears were blindly rechecked by an experienced laboratory technologist for quality assurance and smears from known positive and negative specimens were used as positive and negative controls for internal quality control. The analysis, reporting, and interpretation of this study was strongly followed the Guidelines for reporting of statistics for clinical research in urology" [22], SAMPL guidelines [23] and STROBE checklist for observational studies [24].

2.7 | Statistical Analysis

The data was entered in to epi-data version 3.1. Then, the data was exported and analyzed using STATA 17 statistical software (Supporting Information S2). Chi-square and Fishers' exact test were used to check the association between outcome and explanatory variables. Moreover, the internal consistency of variables was checked using Cronbach's alpha and the model good ness of fitness test was checked by using Hosmer-Lemshow test. After the assumptions of logistic regression was checked and satisfied, a bivariate analysis using binary logistic regression were done to determine the presence of a statistically significant association between explanatory variables and the outcome variables (*S. mansoni*). To control the confounding variables, all explanatory variables with a $p < 0.2$ were included in the multivariable logistic regression model. Finally, variables with $p < 0.05$, their Adjusted Odds Ratio (AOR), and their 95% Confidence Intervals (CI) were considered statistically significant.

2.8 | Ethical Considerations

Ethical approval was approved by the Institutional Review Board of the College of Medicine and Health Sciences, Wollo University. Permission letter was obtained from, Kemisse town health Department, Kemisse General Hospital, Kemisse Health Center, Chefa Robit Health office and Health center before the actual data collection was started. Written informed consent and/or assent from guardians were obtained from each patient with malaria after the purpose of the study and related risks were explained by the data collectors. Finally, those who were positive for *S. mansoni* and other intestinal helminths were treated with an appropriate treatment protocol.

3 | Results

3.1 | Sociodemographic Characteristics of Malaria Positive Patients

A total of 145 malaria confirmed cases were recruited in this study, 65 (44.8%) were females while 80 (55.2%) males. Most of the participants were between the age group of less than 11 years and 11–20 years respectively. Majority, 77 (53.1%) of participants were rural dwellers. With regard to occupational status, 48 (36.4%) of the participants were farmers of which 20 (41.7%) had *S. mansoni* infection ($p = 0.001$). The 98 (67.6%) of the study subjects were single followed by married 47 (32.4%) in their marital status. Of study participants, 86 (59.3%) of them had a family member more than 5 (Table 1).

3.2 | Behavioral Characteristics of Malaria Positive Patients

From all malaria positive patients included in the study, 93.1% (135), 90.3% (131), 97.2% (141) and 96.6% (140) participants respectively had toilet ($p > 0.05$); previous exposure to health education ($p > 0.05$); practiced hand washing before eating ($p > 0.05$) and hand washing after toilet ($p > 0.05$). Moreover, 69.0% (100) participants had a previous IH infections of which 36% of them were positive for *S. mansoni* ($p = 0.013$). Likewise, swimming history was observed among 17 malaria patients of which 13 (76.5%) had developed *S. mansoni* infection ($p < 0.001$) compared with 23.4% of *S. mansoni* infection among those who had no history of swimming. In addition, 14 (9.7%) and 63 (43.4%) respective participants had a history of fishing ($p = 0.029$) and river near to house ($p < 0.001$). Among those who had crossed rivers without shoe, 64.1% (27/44) were infected with *S. mansoni* ($p < 0.001$) compared to 15.8% (16/101) participants who had not crossed rivers without shoe (Table 2).

3.3 | Prevalence of *S. mansoni* and Other Intestinal Helminthes

In this study 71 (49%) malaria infected patients were co-infected with *S. mansoni* and other intestinal Helminthes, of which *S. mansoni* 43 (60.6%) and *H. nana* 12 (16.9%) were the first and the second predominant species detected among malaria cases with their respective order. Moreover, the least intestinal helminth was *E. vermicularis* 3 (4.2%). Additionally, 8 (11.3%) malaria cases had a mixed infection of *S. mansoni* with *H. nana* and *A. lumbericoides* (Figure 1). The overall prevalence of *S. mansoni* co-infection among malaria infected patients was 29.7% (95% CI: 22.7%–37.7%).

3.4 | Factors Associated With *S. Mansoni*

The analysis of factors associated with *S. mansoni* was computed with a classical logistic regression model. The goodness of fit test of the model was assessed by the Hosmer-Lemshow test ($p = 0.442$) and the reliability coefficient using Cronbach's alpha was 0.871. After bivariable logistic regression analysis, all variables with a $p < 0.2$ were subjected in to multivariable logistic regression analysis. While, after controlling confounding, the multivariable logistic regression analysis showed that *S. mansoni* was independently associated with pervious intestinal helminthic infection (AOR: 2.9; 95% CI: 1.2–7.4; $p = 0.020$), having a history of swimming (AOR: 5.8; 95% CI: 1.15–19.6; $p = 0.023$, and fishing (AOR: 3.5; 95% CI: 1.1–11.0; $p = 0.034$), participants who lives near to river (AOR: 2.7; 95%

TABLE 1 | Socio-demographic characteristics of *S. mansoni* co-infection among malaria positive patients in malaria endemic areas of Northeast Ethiopia, Sep 2018 to June 2019.

Variables	Category	Frequency, *N* (%)	*S. mansoni*		Chi-square test (*p* value)
			Positive, *N* (%)	Negative, *N* (%)	
Age	1–10	47 (32.4)	14 (29.8)	33 (70.2)	0.965
	11–20	44 (30.3)	16 (36.4)	28 (63.6)	
	21–30	32 (22.1)	10 (31.3)	22 (68.7)	
	> 30	22 (15.2)	7 (31.8)	15 (68.2)	
Sex	Male	80 (55.2)	24 (30.0)	56 (70.0)	0.820
	Female	65 (44.8)	19 (29.2)	46 (70.8)	
Residence	Urban	68 (46.9)	16 (23.5)	52 (76.5)	0.129
	Rural	77 (53.1)	27 (35.1)	50 (64.9)	
Marital status ($n = 107$)	Married	46 (43)	14 (30.4)	32 (69.6)	0.074
	Single	61 (57)	29 (47.5)	32 (52.5)	
Educational status ($n = 132$)	No formal education	40 (30.3)	12 (30.0)	28 (70.0)	0.677
	Formal education	92 (69.7)	31 (33.7)	61 (66.3)	
Occupational status ($n = 132$)	Farmer	48 (36.4)	20 (41.7)	28 (58.3)	0.001
	Merchant	23 (17.4)	9 (39.1)	14 (60.9)	
	House wife	30 (27.7)	13 (43.3)	17 (56.7)	
	Student	31 (23.5)	1 (3.2)	30 (96.8)	
Family size	≤ 3	46 (31.7)	17 (36.9)	29 (63.1)	0.276
	4-6	78 (53.8)	18 (23.1)	60 (76.9)	
	≥ 7	21 (14.5)	8 (38.1)	13 (61.9)	

CI: 1.1–6.4; $p = 0.024$) and having a history of crossing river by their legs without shoe (AOR: 6.4; 95% CI: 1.4–28.5; $p = 0.011$). Moreover, compared with students; farmers (AOR: 13.1; 95% CI: 2.5–115; $p = 0.006$), merchants (AOR: 14.5; 95% CI: 4.0–91.6; $p = 0.002$) and housewives (AOR: 12.2; 95% CI: 2.4–109; $p = 0.007$) were found to be highly affected (Table 3).

4 | Discussion

Malaria and schistosomiasis are co-endemic disease in sub-Saharan African countries [10]. Thus, the present study provides significant insights about patterns of polyparasitism among patients infected with plasmodium species. The present study finding revealed that intestinal helminths and malaria co-infection was alarmingly higher. Almost half (49%) of malaria cases had developed *S. mansoni* and/or other intestinal helminths infection. This statistical figure showed that, these co-endemic public health problems had extensive overlapping pattern in their transmission dynamics [25]. Furthermore, 11.3% of patients with malaria had found to develop polyparasitism involving a triple co-infection with *S. mansoni, H. nana* and *A. lumbericoides*. Evidences showed that helminth-malaria interactions promote the hosts susceptibility to the development of infection. The skewness of immune responses mediated by helminths the basic mechanism of suppressing hosts immunity through Th2/Treg pathways and anemia-induced impairment of host defenses against bacterial and malaria infections [26]. Thus, the aggregative physiological stress of polyparasitism leads to anemia, nutritional deficiencies and pulmonary hypertension. As a result, polyparasitism increases the risk of morbidity and mortality [27]. Thus, the results of the present study reinforce the need for holistic, epidemiology-tailored interventions targeting integrated management of intestinal helminthiasis and malaria for sustainable control of co-endemic parasitic diseases particularly in resource limited countries including Ethiopia.

The overall prevalence of *S. mansoni* co-infection with malaria was 29.7% (95% CI: 22.7%–37.7%). The magnitude of the co-infection was higher compared to findings reported from southern Ethiopia, 15% [12], 22.6% [28], Northwest Ethiopia 19.5% [10], surrounding areas of Addis Ababa 18.4% [29]. Moreover, this finding is consistent with the evidence of highest endemicity of *S. mansoni* throughout sub-Saharan African countries. The magnitude of high *S. mansoni* and malaria co-infection can be aggravated by the widespread distribution of its intermediate host snails in the region's freshwater bodies [30]. *S. mansoni* co-infection might be higher particularly, when the enteric phases of the parasite increase the likelihood of exposure and interaction with malaria during periodic bouts of hematuria. Thus, the overall local burden of parasitic disease

TABLE 2 | Associated risk factors of *S. mansoni* co-infection among malaria positive patients in malaria endemic areas of Northeast Ethiopia, September 2018 to June 2019.

Variable	Category	Frequency, *N* (%)	*S. mansoni* result		Chi-square test (*p* value)
			Positive, *N* (%)	Negative, *N* (%)	
Toilet	Yes	135 (93.1)	43 (31.9)	92 (68.1)	0.034[a]
	No	10 (6.9)	0 (0.00)	10 (100.0)	
Type of toilet ($n = 135$)	Private	114 (78.6)	35 (30.7)	79 (69.3)	0.504
	Common	21 (14.5)	8 (38.1)	13 (61.9)	
Health education availability	Yes	131 (90.3)	38 (29.0)	93 (71.0)	0.602
	No	14 (9.7)	5 (35.7)	9 (64.3)	
Hand washing before food eating	Yes	141 (97.2)	42 (29.8)	99 (70.2)	1.000[a]
	No	4 (2.8)	1 (25.0)	3 (75.0)	
Dirty in the nail	Yes	53 (36.6)	18 (34.0)	35 (66.0)	0.389
	No	92 (63.4)	25 (27.2)	67 (72.8)	
Previous IH infections	Yes	100 (69.0)	36 (36.0)	64 (64.0)	0.013
	No	45 (31.0)	7 (15.6)	38 (84.4)	
House style	Muddy	92 (63.4)	32 (34.8)	60 (65.2)	0.075
	Cement	53 (36.6)	11 (20.8)	42 (79.2)	
Hand washing after toilet	Yes	140 (96.6)	41 (29.3)	99 (70.7)	0.633[a]
	No	5 (3.4)	2 (40.0)	3 (60.0)	
How many times ($n = 140$)	Always	57 (39.3)	15 (26.3)	42 (73.7)	0.522
	Sometimes	83 (57.2)	26 (31.3)	57 (68.7)	
Water source	Pipe	97 (66.9)	28 (28.9)	69 (71.1)	0.875
	River	37 (25.5)	11 (29.7)	26 (70.3)	
	Burrow	11 (7.6)	4 (36.4)	7 (63.6)	
Use of raw vegetables	Yes	130 (89.7)	37 (28.5)	93 (71.5)	0.354
	No	15 (10.3)	6 (40.0)	9 (60.0)	
Frequency of raw vegetables use ($n = 130$)	Always	7 (4.8)	3 (42.9)	4 (57.1)	0.405[a]
	Sometimes	123 (84.8)	34 (27.6)	89 (72.4)	
Use of raw animal products	Yes	98 (67.6)	27 (27.6)	71 (72.4)	0.423
	No	47 (32.4)	16 (34.0)	31 (66.0)	
Frequency of raw animal products ($n = 98$)	Always	5 (3.4)	3 (60.0)	2 (40.0)	0.127[a]
	Sometimes	93 (64.1)	24 (25.8)	69 (74.2)	
Swimming behavior	Yes	17 (11.7)	13 (76.5)	4 (23.5)	< 0.001
	No	128 (84.8)	30 (23.4)	98 (76.6)	
Frequency of swimming ($n = 17$)	Always	3 (2.1)	2 (66.7)	1 (33.3)	1.000
	Sometimes	14 (9.7)	11 (78.6)	3 (21.4)	
Fishing	Yes	14 (9.7)	8 (57.1)	6 (42.9)	0.029[a]
	No	131 (90.3)	35 (26.7)	96 (73.3)	
Frequency of fishing ($n = 14$)	Always	4 (2.8)	1 (25.0)	3 (75.0)	0.245[a]
	Sometimes	10 (6.9)	7 (70.0)	3 (30.0)	
Wearing shoes	Yes	140 (96.6)	42 (30.0)	98 (70.0)	0.630
	No	5 (3.4)	1 (20.0)	4 (80.0)	
How often you wear shoes ($n = 140$)	Always	61 (42.1)	15 (24.6)	46 (75.4)	1.000[a]
	Sometimes	79 (54.5)	27 (34.2)	52 (65.8)	

(Continues)

TABLE 2 | (Continued)

Variable	Category	Frequency, *N* (%)	*S. mansoni* result		Chi-square test (*p* value)
			Positive, *N* (%)	Negative, *N* (%)	
River near to your house	Yes	63 (43.4)	30 (47.6)	33 (52.6)	< 0.001
	No	82 (56.6)	13 (15.9)	69 (84.1)	
Crossing river by leg without shoe	Yes	44 (30.3)	27 (64.1)	17 (38.6)	< 0.001
	No	101 (69.7)	16 (15.8)	85 (84.2)	

[a]Fishers' exact test was used.

TABLE 3 | Bivariable and multivariable logistic regression analysis of factors associated with *S. mansoni* co-infection among malaria positive patients in malaria endemic areas of Northeast Ethiopia, September 2018 to June 2019.

Variables	Category	S. *mansoni* infection		COR (95% CI)	P-value	AOR (95% CI)	*p* value
		Yes, *n* (%)	No, *n* (%)				
Residence	Urban	16 (23.5)	52 (76.5)	1	0.131	1	0.244
	Rural	27 (35.1)	50 (64.9)	1.76 (0.85–3.64)		1.3 (0.9–2.89)	
Occupation	Farmer	20 (41.7)	28 (58.3)	21.4 (2.69–170.3)	0.004	13.1 (2.5–115)	**0.006***
	Merchant	9 (39.1)	14 (60.9)	19.3 (2.2–167.4)	0.007	14.5 (4.0–91.6)	**0.002***
	House wife	13 (43.3)	17 (56.7)	22.9 (2.8–190.9)	0.004	12.2 (2.4–109)	**0.007***
	Student	1 (3.2)	30 (96.8)	1		1	
Previous IH infections	Yes	36 (36.0)	64 (64.0)	3.1 (1.2–7.54)	0.015	2.9 (1.2–7.4)	**0.020***
	No	7 (15.6)	38 (84.4)	1		1	
House style	Muddy	32 (34.8)	60 (65.2)	2.04 (0.92–4.49)	0.078	1.7 (1.1–6.0)	0.134
	Cement	11 (20.8)	42 (79.2)	1		1	
Swimming behavior	Yes	13 (76.5)	4 (23.5)	10.6 (3.2–35.0)	< 0.001	5.8 (1.15–19.6)	**0.023***
	No	30 (23.4)	98 (76.6)	1		1	
Fishing	Yes	8 (57.1)	6 (42.9)	3.66 (1.2–11.3)	0.024	3.5 (1.1–11.0)	**0.034***
	No	35 (26.7)	96 (73.3)	1		1	
River near to your house	Yes	30 (47.6)	33 (52.6)	4.8 (2.2–10.4)	< 0.001	2.7 (1.1–6.4)	**0.024***
	No	13 (15.9)	69 (84.1)	1		1	
Crossing river by without shoe	Yes	27 (64.1)	17 (38.6)	8.4 (3.7–18.9)	< 0.001	6.4 (1.4–28.5)	**0.011***
	No	16 (15.8)	85 (84.2)	1		1	

Note: Bold values indicate statistically significant.
*Statistically significant.

can be due to the reinforcement of the predominancy of *S. mansoni*.

H. nana was the second most frequent co-infecting helminth next to *S. mansoni* This might be due to the fact that overlapping potential of their transmission routes were increase the likelihood of co-infection in conducive areas for malaria exposure. Moreover, compared to the large sized helminths the smaller size of *H. nana* enhances the potential of interaction and rapid establishment with concurrent infections. It also decreases the host defenses against malaria as a result of its blood-feeding activity through inducing inflammatory responses in the gut and liver and by inducing the occurrence of anemia [31].

This study revealed that previous intestinal helminthic infections was statistically associated with *S. mansoni* co-infection which might be due to the co-endemicity of the parasites as a result of shared ways of transmission. Furthermore, subsequent *S. mansoni* infection might be influenced by previous soil-transmitted helminths (STH) infections due to different mechanisms. Primarily, the susceptibility of *S. mansoni* infection might be increased as a result of concurrent intestinal helminth infections through alteration of the intestinal mucosa and gut microbiota [32]. Thus, the penetration and establishment of schistosome larvae promoted due to indued inflammatory responses and damaged intestinal epithelium as a result of intestinal helminths infection. In addition, the hosts protective immunity against schistosomes might be downregulated due to

immune modulating potential of helminths. Likewise, helminths infection has a potential of host immunity modification that favors for tissue stage larvae of schistosomes by shifting the hosts immune response from Th1 to Th2. This shift of immune response is due to activation of regulatory T cell responses and alternate activation of macrophages [33]. The immune modulation might not be solely by STH infections but also as a result of anti-helminthic treatments against concurrent STH [34]. Therefore, host immunity and gut physiology alterations are the main driving forces that increases host susceptibility to *S. mansoni* infection. The existence of this interaction implies that the prevention and control of STH and schistosomiasis could be effective by designing and implementing integrated control programs targeting these two diseases.

The odds of *S. mansoni* infection was higher among individuals who had a history of swimming practice which is supported with previous finding from Cameroon [35] and Brazil [36]. This could be due to the exposure of more surface areas of the body for penetration by cercariae. The odds of acquiring infection might be varied by the difference in the time of swimming activities where the risk is high in the afternoon because of the shedding of cercariae is potentially higher in this period [37]. Moreover, the risk of infection is varied by age of exposed individual where the odds of infection is exacerbated in children especially, children who had prolonged stay in shallow area where the accumulation of cercariae is perceived to be high; those who have frequent exposure; and nonintact skin [38]. This finding implies that mass drug administration solely might not be effective for control of schistosomiasis but also it needs avoidance of high-risk water contact behaviors in endemic areas.

In addition to swimming, the odds of *S. mansoni* infection was higher among those who had a history of fishing practice. This finding revealed that the occupational risk of schistosomiasis is higher particularly in endemic areas. This relationship could be as a result of increased exposure of skin surface contact with cercariae infested water exacerbates cercarial penetration particularly during gillnets, free diving and cast nets types of fishing methods [39]. Thus, low and cost-effective water proof boots with glove can be advisable to be used as an effective physical barrier against penetration of cercariae while handling occupational activities [40]. Additionally, separating fishing and bathing area is crucial to reduce this high-risk occupation [41].

Furthermore, the likelihood of developing *S. mansoni* infection among individuals residing near to the river was significantly elevated. The finding of a strong positive association between proximity to a river and *S. mansoni* infection was supported with previous evidence from Cameroon [42]. This result reveals that the spatial distribution of the schistosomiasis greatly determined by the habitat of the fresh water snail hosts. Thus, communities who are situated or residing in lowlands near to rivers and within flooded plains [43], outdoor playing children close to rivers [44], occupational activities like farming requiring frequent contact with contaminated irrigation canals had the highest risk of developing infection [45]. The present study also revealed that majority of the participants were farmers and were significantly affected by the infection. Furthermore, the risk of *S. mansoni* infection was high among individuals who crossed the river with bare feet which was in agreement with the previous Nigerian finding [46]. The possibility of the positive correlation could be due to increasing vulnerability of the skin surfaces to be penetrated by cercariae as a result of frequent river crossing for fishing, fetching water, washing clothes and/or bathing. Additionally, the entry of the cercariae can be accelerated when minor cuts or injuries are existed [47]. The cross-sectional design and sample size were the limitations of this study which makes it difficult to draw firm conclusions from observed findings. Thus, we recommend further case control studies recruiting larger sample sizes to identify the independent determinant factors; and longitudinal studies to allow firm conclusion on causation and mechanism of *S. mansoni* co-infection with malaria and to increase the power of generalizability. Furthermore, Kato-katz technique was not performed due to lack of resources which might underestimate the intensity of *S. mansoni* and other helminths co-infection.

5 | Conclusion

Prevalence of *S. mansoni* co-infection among malaria cases in this study area was considerably high. The burden of polyparasitism was also still higher. Occupation status, history of previous intestinal helminths infections, history of swimming and fishing practice, residing in close proximity to rivers and history of crossing river by bare foot without shoe were an independent factors exacerbating *S. mansoni* infection. Further longitudinal study is required for exploring the underlining mechanisms of *S. mansoni* and malaria.

Author Contributions

Yeshi Metaferia, Abdurahaman Seid, Aderaw Adamu, and Alemu Gedefie involved in the conception and design, data collection, analysis, and interpretation of data. Yeshi Metaferia, Genet Molla Fenta, Daniel Gebretsadik Weldehanna, and Alemu Gedefie took part in drafting the article or revising it critically for important intellectual content. Finally, all authors read and approved the final version of manuscript. The corresponding author Alemu Gedefie, had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

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Consent

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The datasets used and/or analyzed during the current study available within the manuscript. If additional data are needed, it can be obtained from the corresponding authors upon request.

Transparency Statement

The lead author Alemu Gedefie affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.