ECRONICON OPEN ACCESS

EC MICROBIOLOGY
Research Article

Coinfection of HIV-1 with *Schistosoma* spp. and with Intestinal Parasites in Patients Attending Boane Health Center, Maputo Province, Mozambique

Lucas Banze[1,2], Ana Carina Madureira[2], Borges Cerveja Zacarias[1,2], Noémia Nhacupe[1,2], Carmen Mascaro-Lazcano[3], Constance A Benson[4], Robert T Schooley[5] and Emilia Virginia Noormahomed[1,2,5]*

[1]*Department of Microbiology, Parasitology Laboratory, Faculty of Medicine, Eduardo Mondlane University, Maputo, Mozambique*

[2]*Mozambique Institute for Health Education and Research, Maputo, Mozambique*

[3]*Department of Parasitology, Universidad de Granada, Granada, Spain*

[4]*Department of Medicine, Division of Infectious Diseases and Global Public Health, University of California, San Diego, USA*

[5]*Department of Medicine, Infectious Diseases Division, University of California, San Diego, USA*

***Corresponding Author:** Emilia Virginia Noormahomed, Department of Microbiology, Faculty of Medicine, Eduardo Mondlane University, Av Salvador Allende, nº 702, Maputo, Mozambique.

Received: December 03, 2020; **Published:** April 28, 2021

Abstract

Background: It is hypothesized that schistosomiasis and intestinal parasites increase susceptibility to HIV-1 infection and enhance AIDS progression by immunomodulation. This study aims to compare the prevalence and risk factors for schistosomiasis and intestinal parasites in HIV-1 infected and uninfected persons and to evaluate the association between HIV-1 induced immunosuppression and risk factors for parasite infection.

Methods: This was a cross-sectional study conducted at Boane Health Center in Boane village, Maputo Province from April to June 2017 in 280 patients aged over 5 years. From each of 140 HIV-1 infected or 140 HIV-1 uninfected persons, demographic and clinical data were collected as well as one stool and urine sample for parasitological analysis. All stool samples were processed using direct wet mount and Ritchie method for detection of common parasites, and modified Ziehl-Neelsen staining techniques to identify *Cryptosporidium* spp., *Cystoisospora belli* and *Cyclospora* spp. oocysts from children stools. The urine was sedimented and analyzed for *S. haematobium* eggs detection.

Results: The overall prevalence of parasitism in the study population was 46.8% (131/280). Fifty six percent of the HIV-1 infected persons (78/140) were infected by at least one parasite compared to 38% (53/ 140 of the HIV-1 uninfected persons (odds ratio [OR] 2.0, 95% confidence interval [CI] 1.2-3.3).

Further, HIV-1 infected persons were more likely to be infected by *S. mansoni* (OR 5.6, 95% CI 1.8-15.8) when compared to HIV-1 uninfected person and HIV-1 infected women were more likely to be infected by *S. mansoni* (OR 6.7 CI 95% 1.8-22.8%) when compared to HIV-1 uninfected women (p< 0.001). HIV-1 serostatus (OR 7.0, 95% CI 1.5-31.2). Multivariate logistic regression revealed that HIV-1 infected status (OR=1.813575), the use of river or lake as water sources either for drinking (OR=7.289245) or domestic chores (OR=9.16205) were significant risk factor for parasitic infection. Partcipants with secondary and higher school (OR=0.379) were less likely to have a parasitic infection compared with primary school or illiterate participants.

Conclusions: It is possible that the a high prevalence of schistosomiais and intestinal parasites in this region plays an important role on the transmission and pathogenesis of HIV.

Keywords: *Neglected Tropical Diseases; Enteroparasites; Intestinal Parasites; Water Born Parasites; Co-Infection HIV-1 And Schistosoma Mansoni; Co-Infection HIV-1 And Schistosoma Haematobium; Synergism HIV-1 And Parasitism; Mozambique*

Abbreviations

CD4: Cluster of Differentiation 4; FGS: Female Genital Schistosomiasis; HAART: Highly Active Antiviral Treatment;

HIV-1: Human Immunodeficiency Virus 1; NTDS: Neglected Tropical Diseases; PI: Principal Investigator

Introduction

Schistosomiasis, a waterborne disease, and intestinal parasitosis are neglected tropical diseases (NTDs) that impose significant health and socioeconomic burdens, especially in sub-Saharan Africa. It was estimated that over 229.2 million people globally needed preventive chemotherapy for schistosomiasis in 2018 [1], and that about 2 billion people were infected with at least one helminthic specie, of which 90% of cases occur in sub-Saharan Africa [2-6]. Their geographical distribution in Africa overlaps substantially with Human Immunodeficiency Virus 1 (HIV-1) distribution, suggesting that infection with specific helminths may contribute to or be influenced by HIV-1 infection [2,3,5,7-14].

The most prevalent species of *Schistosoma* in Africa are *S. haematobium* and *S. mansoni* causing urogenital and intestinal schistosomiasis respectively. *S. mansoni* eggs can be also found in the urogenital tract of women [6,15-17]. Infection by *S. haematobium* and less often by *S. mansoni* may cause female genital shistosomiasis (FGS), a special condition associated with mucosal inflammation induced by the presence of *Schistosoma* eggs in the genitalia of women. This results in enhanced expression of CD4 T-cell receptors and may increase the risk of HIV-1 transmission following sexual exposure [3,18-20]. In addition, *S. mansoni* infection is associated with a higher density of HIV-1 co-receptors CCR5 and CXCR4 on monocytes and CD4 T-cells, thus perhaps further influencing HIV-1 pathogenesis in patients infected with this parasite [21].

Mozambique, together with other nearby South East African surrounding countries such as Eswatini, South Africa, Zimbabwe, Zambia and Malawi are among the top 10 countries affected by HIV-1 [22,23].

In 2018, with an HIV prevalence among adults (15-49 years) of 12.6%, 2,200,000 people were living with HIV in Mozambique. The HIV incidence per 1000 uninfected among all people of all ages of 5.25 resulted in 150 000 new HIV infections. Mozambican women are disproportionally affected by HIV in Mozambique: of the 2,200,000 adults living with HIV, 1,200,000 (60%) are women [24].

Further, the country is highly endemic for numerous NTDs, including schistosomiasis with an estimated country prevalence of more than 50% [25]. One study in Cabo Delgado Province documented that 63% of children in the first year of school, 66% children from 9 to 12 years of age and 44.8% of adults aged 20 to 55 years were infected by *S. haematobium* [26]. For intestinal parasites the global prevalence varied from 1.2%- 93%. The most prevalent helminths were *Trichiuris trichiura, (*36.06% to 93%), *Ascaris lumbricoides (*35.69% to 56%), *Strongyloides stercoralis* (5.5% to 48%), and *Ancylostoma duodenale* (1.86 to 38%) [8,27]. Concerning protozoans, the most frequently found were *Giardia intestinalis* (5.6% to 37%), *Entamoeba histolytica/Entamoeba dispar (*4.83% to 10%), *Entamoeba coli* (10.41% to 34%), and *Cryptosporidium* spp. (2.5% to 9%) [27,28].

However, information remains limited on the bidirectional interactions between HIV-1 and *Schistosoma*, or relationships among HIV-1 and intestinal parasites in Mozambique. In particular, the roles played by these NTDs on the acquisition of HIV-1 infection and progression to AIDS are uncertain. A prior study conducted in Maputo city found that the prevalence and intensity of intestinal parasites in HIV-1 infected persons was related to the degree of immunosuppression as assessed by CD4 cell count, while antiretroviral treatment (ART) was associated with lower levels of parasitic infection [8].

We conducted a study of the prevalence of these NTDs in HIV-1 infected and HIV-1 uninfected persons attending the Boane Village Health Center in Maputo province, south Mozambique in an effort to better understand relationships among NTDs and HIV/AIDS in Mozambique and neighboring countries. The study also examined risk factors associated with parasitic infection and examined associations

between levels of immunosuppression and parasitism.

Materials and Methods

Study design and setting

We conducted a descriptive, cross-sectional study at Boane Health Centre from April to June of 2017. This Health Centre is located in the Boane district in the southeast corner of Maputo province (26˚02'36S 32˚19'36E) which has a HIV-1 prevalence rate of 22.9% [29,30].

Study population, sample and data collection

We recruited a total of 280 persons equally distributed as 140 HIV-1 infected and 140 HIV-1 uninfected.

The sample size for this study was calculated based on previously published estimates of the prevalence of schistosomiasis in the Boane region [29] of 61.4% considering a confidence level of 95% and using the following equation:

$$n = \frac{\sigma^2 * p * q * U}{\varepsilon^2 * (U-1) + \sigma^2 * p * q}$$

Where:

n: sample size;

σ: confidence level chosen, in number of deviations;

p: proportion of characteristics surveyed in the universe;

q: proportion of the universe that does not have the researched characteristic (q = 1-p) or q = 100% -p

ε: allowed estimation error;

U: universe.

Recruited population and study workflow

Persons over 5 years of age seeking care at Boane Health Center were systematically recruited by collaborating physicians and the principal investigator while performing their daily healthcare activities. The principal investigator, a research nurse or a collaborating physician approached the patient or relative, explained the aims and methodology of the study and obtained informed consent. Individuals aged 5 to 14 years old were classified as children and the remaining as adults. Study participants were prospectively enrolled until the expected sample size n=280 was achieved. Consenting study participants were assigned a study number and all data and samples were handled using this study number.

Sociodemographic and clinical data were collected using a standardized questionnaire that included age, sex, education, profession, water source and time of residence in Boane. In addition, clinical data were obtained, including history of haematuria, hematemensis, fecal blood, HIV-1 serostatus, CD4 cell count and highly active antiviral treatment (HAART) in the case of patients with HIV-1 infection, and history of prior antiparasitic drug treatment. Participants were asked to provide a stool sample and a urine sample for detection of *S. mansoni* eggs in the stool, and *S. haematobium* in the urine. All detected parasites were recorded, and the presence in faeces of visible blood in faeces was also noted.

Sample collection and copromicroscopy analysis

The stool samples were divided into two aliquots each at the study site. One aliquot was used for direct microscopic examination. The Ritchie technique was used for *S.mansoni* eggs and for intestinal parasites. The other aliquot was kept at 4ºC and sent the same day to the Parasitology Laboratory of the Universidade Eduardo Mondlane Faculty of Medicine for further processing within 48 hrs using the same techniques as in the study site [31].

A subsample of stools from patients aged under 14 years old was separated and stained using a modified Ziehl-Neelsen method [32] for detection of *Cryptosporidium* spp., *Cystoisospora belli* and *Cyclospora* spp. oocysts (Figure 1). Each stool sample was examined by two laboratory technicians, as well as by the principal investigator, with 94% concordance among the three observations.

Urine Analysis

Urine samples were also primarily examined in the clinical laboratory at the study site after concentration by centrifugation (284 g for 5 minutes). The supernatant was discarded and 10% formalin was added to the pellet which was observed microscopically for the detection of *S. haematobium* eggs. The remainder of the sample was sent to the Parasitology Laboratory at the Faculty of Medicine for examination by the same procedure (Figure 1).

Setlement for Figure 1.

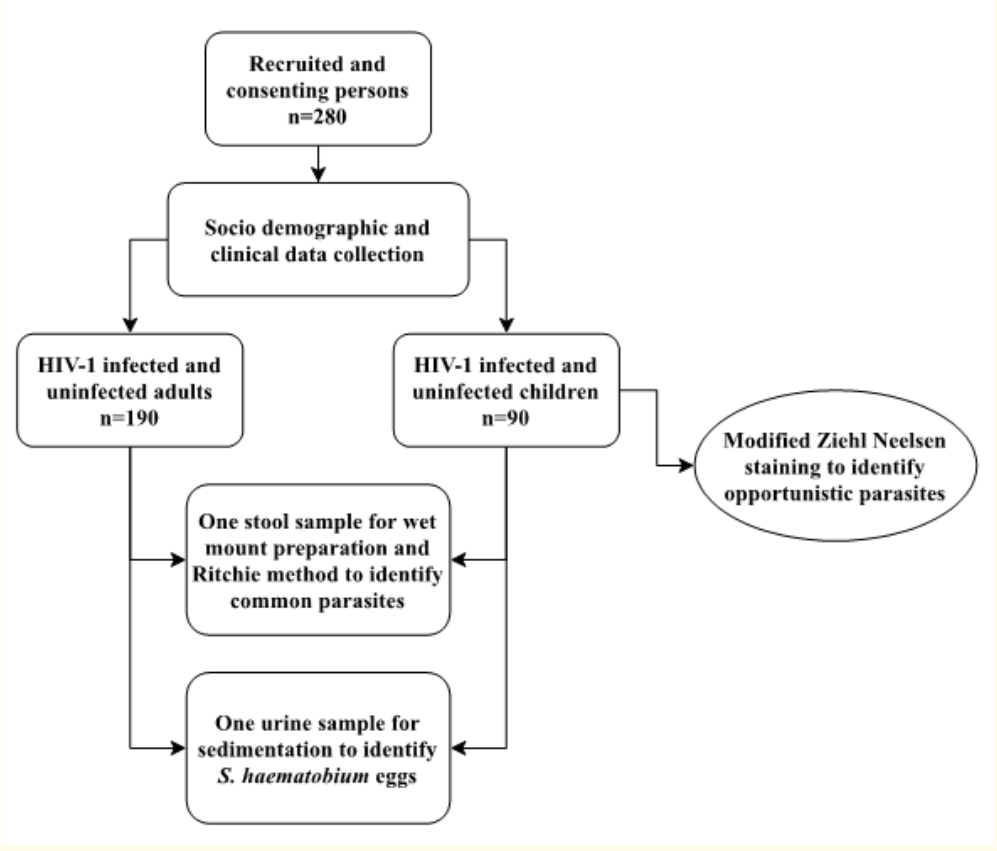

Figure 1: *Workflow Chart.*

Ethical considerations

The study was approved by the National Bioethics Committee of Mozambique, and the Human Research Protections Program of the University of California, San Diego, USA. The survey was conducted according to the National Bioethics Committee of Mozambique guidelines. The purpose of the study and the non-invasiveness methods were explained to all participants. Informed consent were obtained from all patients. In the case of children and illiterate participants the informed consent was obtained from their parents or legal guardians or a witness who signed on their behalf.

Statistical data analysis

The Epi-info™ version 7.2.1 (Public Software, Center for Disease Control, United States) was used to establish a database for manual double-entry of data by two different researchers. After database validation, two identical datasets were obtained, of which one was used for all subsequent analyses with Statistical Package for Social Science (SPSS) version 20.0 statistical software.

The differences in the proportion of HIV-1 infected patients with a CD4 cell count within specific ranges and stool examination results showing characteristic findings were tested using Fisher's exact test. p-values of < 0.05 were considered to be statistically significant. Multivariate logistic regression modeling was employed to analyze the relationship of socio-demographic and clinical and immunological variables with parasite infection and HIV-1 serostatus.

Results and Discussion

This was a study that aimed to estimate and compare the prevalence of schistosomiasis and intestinal parasites in HIV-1 infected and uninfected persons receiving health care at the Booane Village Health Center in southern Mozambique. We also sought to delineate risk factors associated with parasitism, and to examine associations between the degree of immunosuppression and the risk of acquisition of schistosomiasis and intestinal parasites in the HIV-1 infected population.

Sociodemographic characteristics of the study population

The sociodemographic data of the study population are summarized in table 1. We enrolled a total of 280 patients, with a mean age of 23.7± 13.3 years, equally distributed as HIV-1 infected (140) and HIV-1 uninfected (140) persons.

Variables		HIV-1 Infected N =140 (%)	HIV-1 Uninfected N=140 (%)	Total N=280 (%)
Age	Children 5-14 years old	45 (32.1)	45 (32.1)	90 (32.1)
	Adults >14 years old	95 (67.9)	95 (67.9)	190 (67.9)
Gender	Female	109 (77.9)	99 (70.7)	208 (74.3)
	Male	31 (22.1)	41 (29.3)	72 (25.7)
Education	Illiterate	37 (26.4)	39 (27.9)	76 (27.1)
	Primary school	87 (62.1)	71 (50.7)	158 (56.4)
	Secondary school and higher	16 (11.4)	30 (21.4)	46 (16.4)
Occupation	Unemployed	53 (37.9)	65 (46.4)	118 (42.1)
	Farmer	72 (51.4)	45 (32.1)	117 (41.8)
	Trading/others	15 (10.7)	30 (21.4)	45 (16.1)
Water source for domestic chores	Piped	40 (28.6)	59 (42.1)	99 (35.4)
	River and lake	100 (71.4)	81 (57.9)	181 (64.6)
Water source for drinking	Piped	56 (40.0)	45 (32.1)	101 (36.1)
	River and lake	54 (38.6)	76 (54.3)	130 (46.4)
	Well	30 (21.4)	19 (13.6)	49 (17.5)

Table 1: *Sociodemographic characteristics of the study population.*

Most of the study participants were women and a third were children. The majority were illiterate or with primary school, were unployed or farmers and use river or lake water for drinking and/or domestic chores. The socio demographic profile observed in our atudy area, is similar to many other sub-Saharan African countries, which are characterized by low levels of education, poor environmental sanitation, inadequate access to safe water basic living standards and overcrowding. These factors contribute to the proliferation of NTDs, diarrheal and respiratory diseases, HIV and malaria which causes significant morbidity and mortality in the region [22,23,25,33].

Prevalence and profile of *Schistosma* spp. infection and intestinal parasites in the study population

We found an high prevalence of infection by any parasite amongst the study partcipantes (46.8% (131/280). When stratified according to age, both children (52.2%) and adults (44.2%) presented highy prevalence of parasitic infection, though this differences were not statistically significant.

HIV-1 infected study participants were more likely to be infected by one or more parasites than HIV-1 uninfected study participants (OR 2.0, 95% CI 1.2 - 3.3), ($p < 0.004$). While HIV-1 infected adults were more likely to be parasitized by any parasite (OR 2.3 95% CI1.3 - 4.3) compared to HIV-1 uninfected adults ($p < 0.005$). No other significant differences were found regarding the prevalence of parasitism in children and adults either infected or not infected by HIV-1.

		Children n (%)	Adults n (%)	OR (95% CI)	*p* value	Total n (%)	OR (95% CI)	*p* value
HIV serostatus	Yes	26/45 (57.8)	52/95 (54.7)	2.3 (1.3 – 4.3)	0.005	78/140 (55.7)	2.0 (1.2 – 3.3)	0.004
	No	21/45 (46.7)	32/95 (33.7)			53/ 140 (37.9)		
	Total	47/90 (52.2)	84/190 (44.2)			131/280 (46.8)		

Table 2: *Prevalence of parasitism in children and adults related with their HIV-1 serostatus.*

The profile and prevalence of each species of parasites detected in the patients stratified according to HIV-1 serostatus are shown in figure 2. Overall, we identified 10 parasite species including larvae and eggs of helminths and protozoa cysts and oocysts. The most frequently observed parasites were *G. intestinalis* (13.6%), *E. coli* (10.7%), *S. mansoni* (8.6%), *A. duodenale* (5.4%) and *E. histolytica* (5.0%). *Cryptosporidium spp*. oocysts were found in only one HIV-1 infected child. *Cystoisospora* and *Cyclospora* were not found.

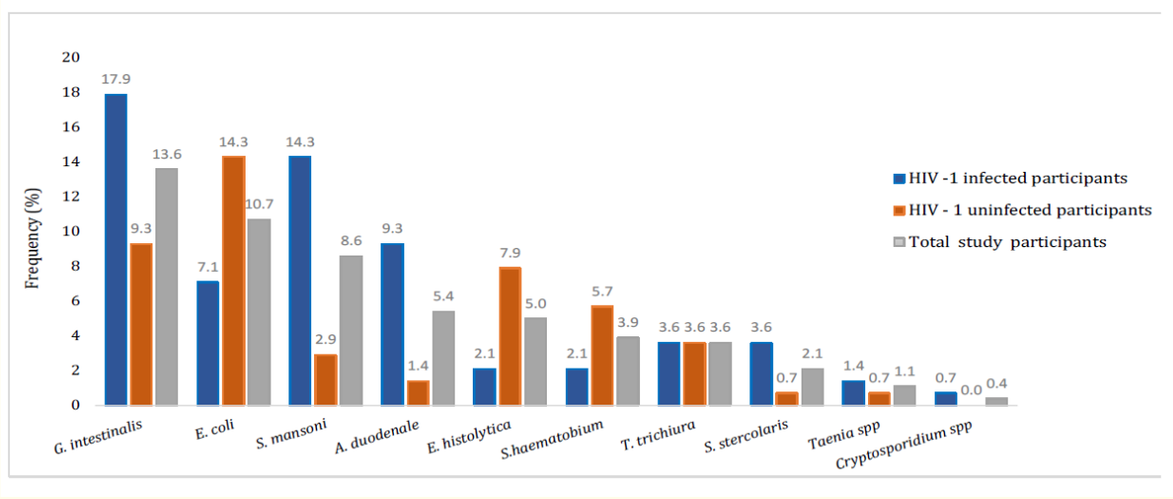

Figure 2: *Profile and Prevalence of Intestinal Parasites in the Study Persons.*

Table 3 summarizes the prevalence of each parasite in children according to HIV-1 serostatus. In children, we identified 7 diferent parasitic species. The most frequently detected parasites were *G. intestinalis* 33.3% (30/90), *E.coli* 14.4% (13/90), *T.trichiura* 5.6% (5/90). However we did not find any statistically significant diferences in parasitism between HIV-1 infected and HIV-1 uninfected children.

Parasites		CHILDREN		Total n=90 (%)	p value
		HIV-1 infected n=45 (%)	HIV-1 uninfected n =45(%)		
S. mansoni	Yes	1 (1.1)	0 (0.0)	1 (1.1)	1.000
	No	44 (48.9)	45 (50.0)	89 (98.9)	
S. haematobium	Yes	0 (0.0)	0 (0.0)	0 (0.0)	1.000
	No	45 (50.0)	45 (50.0)	90 (100.0)	
T. trichiura	Yes	1 (1.1)	4 (4.4)	5 (5.6)	0.360
	No	44 (48.9)	41 (45.6)	85 (94.4)	
S. stercoralis	Yes	0 (0.0)	0 (0.0)	0 (0.0)	1.000
	No	45 (50.0)	45 (50.0)	90 (100.0)	
A. duodenale	Yes	0 (0.0)	0 (0.0)	0 (0.0)	1.000
	No	45 (50.0)	45 (50.0)	90 (100.0)	
Taenia spp.	Yes	1 (1.1)	0 (0.0)	1 (1.1)	1.000
	No	44 (48.9)	45 (50.0)	89 (98.9)	
E. coli	Yes	4 (4.4)	9 (10.0)	13 (14.4)	0.229
	No	41 (45.6)	36 (40.0)	77 (85.6)	
E. histolytica	Yes	2 (2.2)	2 (2.2)	4 (4.4)	1.000
	No	43 (47.8)	43 (47.8)	86 (95.6)	
G. intestinalis	Yes	18 (20.0)	12 (13.3)	30 (33.3)	0.263
	No	27 (30.0)	33 (36.7)	60 (66.7)	
Cryptosporidium spp.	Yes	1 (1.1)	0 (0.0)	1 (1.1)	1.000
	No	44 (48.9)	45 (50.0)	89 (98.9)	

Table 3: *Prevalence of each parasite in children according to HIV-1 serostatus.*

S. mansoni was found only in one HIV-1 infected female child aged 13 years who started HAART at the age of 8 years. *S. haematobium* was not found in any children in this study.

We also found that HIV-1 infected children tend to have higher prevalence of *Giardia* infection compared to HIV-1 uninfected children. Though these differences were not statistically significant nor related to the degree of inmunossupression they rise a concern because of parasitic infections effects on nutritional status of the children and their cognitivite development [27,33]. There are several studies documenting that AIDS status predisposes to increased intensity and persistence of *G. intestinals* infection, due to humoral immune defect observed in these patients [34,35].

The prevalence data from adult participants according to their HIV-1 serostatus are summarized in table 4. In total, we identified 9 diferent parasitic species. The most frequently detected parasites were *S. mansoni* 12.1% (23/190), *E. coli* 8.9% (17/190), *A. duodenale* 7.9% (15/190), *S. haematobium* 5.8% (11/190) and *E. histolytica* 5.2% (10/190). We found that HIV-1 infected study participants were more likely to be infected with *S. mansoni* 10.0% (19/95) and *Ancylostoma duodenale*, 6.8%(13/95) than HIV-1 adult participants

(p=0.001 and p=0.005 respectively). *E. histolytica* was found more frequently in HIV-1 uninfected study participants 4.8% (9/95) than in the HIV-1 infected adult population 1.0% (1/95) (p= 0.018).

Parasites		ADULTS		Total n =190 (%)	*p* value
		HIV-1 infected n =95 (%)	HIV-1 uninfected n=95 (%)		
S. mansoni	Yes	19 (10.0)	4 (2.1))	23 (12.1)	0.001
	No	76 (40.0)	91 (47.9)	167 (87.9)	
S. haematobium	Yes	3 (1.6)	8 (4.2)	11 (5.8)	0.212
	No	92 (48.4)	87 (45.8)	179 (94.2)	
T. trichiura	Yes	4 (2.1)	1 (0.5)	5 (2.6)	0.368
	No	91 (47.9)	94 (49.5)	185 (97.4)	
S. stercoralis	Yes	5 (2.6)	1 (0.5)	6 (3.2)	0.211
	No	90 (47.4)	94 (49.5)	184 (96.8)	
A. duodenale	Yes	13 (6.8)	2 (1.1)	15 (7.9)	0.005
	No	82 (43.2)	93 (48.9)	175 (92.1)	
Taenia spp.	Yes	1 (0.5)	1 (0.5)	2 (1.1)	1.000
	No	94 (49.5)	94 (49.5)	188 (98.9)	
E. coli	Yes	6 (3.2)	11 (5.8)	17 (8.9)	0.309
	No	89 (46.8)	84 (44.2)	173 (91.1)	
*E. histolytica**	Yes	1 (0.5)	9 (4.8)	10 (5.2)	0.018
	No	94 (49.5)	86 (45.3)	180 (94.7)	
G. intestinalis	Yes	7 (3.7)	1 (0.5)	8 (4.2)	0.064
	No	88 (46.3)	94 (49.5)	182 (95.8)	

Table 4: *Prevalence of each parasite in adult patients according to HIV-1 serostatus.*

In addition to that, infection by one parasite specie in the study participants only was present in 84% (110/131) of study participants. Mixed infection by two parasitic species was present in 21 study participants and the most common combinations were *E. coli* and *T. trichiuria* (19%) and *E. coli* and *G. intestinalis* (14.3%).

These findings either in children participants or in adults should be viewed in context of similar studies done in Mozambique and in other countries including Tanzania, Zambia, Zimbabwe and Ethiopia, Nigeria, Uganda, Brasil, where the prevalence varied according to the geographical region, to each parasite species and age groups [1,4,6,8,9,20,25,27,28,36-40]. They also reflect differences in the level of exposure and susceptibility to infection by age. Young children do not go to rivers or lakes for recreational activities as frequently as the older children and adults. In fact, the only child infected by *S. mansoni* was a 13 year old HIV-1 infected girl.

On the other hand, in our study we found a higher prevalence of infection with *E. coli* (14.3%) and *E. histolytica* (7.9%) in the HIV-1 uninfected patients than in HIV-1 infected persons. This could be because, HIV-1 infected patients are more exposed to health care where anti-parasitic drugs such as albendazole, metronidazole and prazinquantel are routinely used as prophylaxis or to treat parasitic diseases and in case of metronidazole also for gastroenteritis, sexually transmited diseases or related conditions such as pelvic inflammatory disease.

Bivariate analyses of each parasite identified, either in stools or in urine according to gender and HIV-1 serostatus from adult patients

Bivariate analyses of each parasite identified, either in stools or in urine according to gender and HIV-1 serostatus from adult patients are shown in table 5.

Parasite	HIV-1 infected	Female n=154	Male n=36	OR (95%-CI)	*p* value	Total N=190	OR (95%-CI)	*p* value
S. mansoni	Yes	18 (11.7)	1 (2.7)	6.7 (1.8 - 22.8)	0.001	19 (10.0)	5.6 (1.8 – 15.8)	0.001
	No	3 (1.9)	1 (2.7)			4 (2.1)		
S. haematobium	Yes	2 (1.3)	1 (2.7)	0.2 (0.04 – 1.1)	0.086	3 (1.6)	0.3 (0.09 – 1.2)	0.212
	No	7 (4.5)	1 (2.7)			8 (4.2)		
T. trichiura	Yes	4 (2.6)	0 (0.0)	3.7 (0.5 – 46)	0.370	4 (2.1)	4.1 (0.6 – 51)	0.368
	No	1 (0.6)	0 (0.0)			1 (0.5)		
S. stercolaris	Yes	4 (2.6)	1 (2.7)	3.7 (0.5 – 46)	0.370	5 (2.6)	5.2 (0.6 – 62)	0.211
	No	1 (0.6)	0 (0.0)			1 (0.5)		
A. duodenale	Yes	9 (5.8)	4 (11.1)	4.4 (1.1 - 20.9)	0.059	13 (6.8)	7.3 (1.8 – 33)	0.005
	No	2 (1.3)	0 (0.0)			2 (1.1)		
Taenia spp.	Yes	1 (0.6)	0 (0.0)	0.9 (0.04 – 17)	1.000	1 (0.5)	1.0 (0.05 -19)	1.000
	No	1 (0.6)	0 (0.0)			1 (0.5)		
E. coli	Yes	6 (3.9)	0 (0.0)	0.8 (0.2 – 3.0)	1.000	6 (3.2)	0.5 (0.1 – 1.4)	0.309
	No	6 (3.9)	5 (13.9)			11 (5.8)		
E. histolítica	Yes	1 (0.6)	0 (0.0)	0.1 (0.01 - 0.7)	0.027	1 (0.5)	0.1 (0.0 – 0.6)	0.018
	No	7 (4.5)	2 (5.6)			9 (4.7)		
G. intestinalis	Yes	4 (2.6)	3 (8.3)	3.7 (0.5 – 46)	0.370	7 (3.7)	7.4 (1.2 – 85)	0.064
	No	1 (1.1)	0 (0.0)			1 (0.5)		

Table 5: *Results of bivariate analyses of parasitism according to gender and HIV-1 serostatus in adult patients.*

Overall, HIV-1 infected adult participants were more likely to be infected by *S. mansoni* (10.0%) and *A. duodenale* (6.8%) (OR 5.6, 95% CI 1.8-15.8) and (OR 7.3 95% CI 1.8-33) respectively ($p < 0.005$), but less likely to be infected by *E. histolytica* (0.5%) (OR 0.1 95% CI 0.0-0.6). In addition, *S. mansoni* infection was more likely associated with HIV-1 infection in adult women (OR 6.7 95% CI 1.8-22.8) compared with HIV-1 uninfected women. No other differences were found regarding HIV-1 serostatus and gender.

Previous studies in Zimbabwe and Tanzania demonstrated a three or six-fold increased risk of HIV-1 infection in women infected with *S. mansoni*, concluding that *S. mansoni* infection was a risk factor for HIV-1 infection in women [18,37,38,41]. Although there are studies demonstrating *S. haematobium* infection to be a risk factor for acquisition of HIV-1 in women, we did not demonstrate this association in our study [12,13]. Our sample size and the relatively low prevalence of *S. haematobium* in this region may have contributed to this dif-

ference between our study and several others in the literature [12,18,19]. Going forward, research on regional variation regarding the prevalence of *S. mansoni* and *S. haematobium* are required in order to clarify the role of the infection by these parasites and its association or not with HIV-1 infection.

Furthermore, analysis between selected parasites and the presence of blood in the stools revealed that HIV-1 infected patients were more likely to have visible blood in their stools when parasized by *S. mansoni* (OR 2.9 CI 95% 1.1 - 7.3), *A. duodenalis* (OR 13.8 CI 95% 2.2 - 148), and *E. coli* (OR 6.9 CI 95% 2.5 - 18) and *E. histolytica* (OR12.7 CI 95% 1.9 - 136) when compared to HIV-1 uninfected patients ($p > 0.005$). Intestinal parasites cause high morbidity and mortality of individuals, particularly sub-Saharan countries, and they have been associated with low educational performance, stunting, and physical weakness. This and other factors may explain why schistosomiasis and intestinal parasites may contribute to progression of HIV-1 infection [33,42].

Relationships among CD4 cell count, HAART and parasitic burden

CD4 T cell count information was available in 89.3% (125/140) of HIV-1 infected patients. The average CD4 cell count was 608 (52-1675; SD 315) cells/ul. Table 6 shows a bivariate analysis of CD4 cell count stratification and HAART intake in relation to parasitic infection in general, and infection by *S. mansoni*. We did not find any differences in parasitism according to the CD4 cell count stratification. However, HIV-1 infected patients with CD4 cell count lower or equal to 200 cells/µl were more likely to be infected by *S. mansoni* (OR 7.0 CI 95% 1.5 - 31.2) compared to patients with CD4 cell count > 200 - 500 (< 0.031).

Variables		Total	Parasitism		*S. mansoni*		OR (95%CI)	*p* value
		Yes	No	Yes	No			
CD4	≤200	7 (5.6)	6 (4.8)	1(0.8)	4 (3.2)	3 (2.4)	7.0 (1.5 -31.2)	0.031
	201-500	44 (35.2)	24 (19.2)	20 (16.0)	7 (5.6)	37 (29.6)		
	>501	74 (59.2)	39 (32.2)	35 (28.0)	8 (6.4)	66 (52.8)		
	Total	**125 (100)**	**69 (55.2)**	**56 (44.8)**	**19 (15.2)**	**106 (84.8)**		
HAART intake	Yes	127 (64.8)	69 (49.2)	58 (41.4)	19 (13.6)	108 (77.1)	2.1 (0.3-23-7)	0.693
	No	13 (35.2)	9 (6.4)	4 (2.8)	1 (0.7)	12 (8.6)		
	Total	**140 (100.0)**	**78 (55.7)**	**62 (44.3)**	**20 (14.3)**	**120 (85.7)**		

Table 6: *Analysis of CD4 cell counts, HAART intake and association with parasitism and S. mansoni infection.*

With regard to HAART intake, we found that 64.8% (127/140) of HIV-1 infected patients were on HAART and 35.2% (13/140) were not on HAART. Patients on HAART were more likely to be infected by *S. mansoni* (OR 2.1 CI 95%, 0.3-23.7), however these differences were not statistically significant for $p>0.05$. This could be due to the fact that the two populations likely share the same environmental risk factors, the average CD4 cell count in the HIV-1 infected study participants was 607.95 cells/ul, indicating that our HIV-1 infected population was relatively immunocompetent.

We also analysed the effect of prazinquantel on the rates of parasitism in our study population and found that 62.9% (176/280) had previously taken prazinquantel. The prevalence of parasitism was higher in participants who were not previously treated 32.5% (91/280) compared to those treated with praziquantel 14.3% (40/280) ($p < 0.0001$). This difference was found in both the HIV-1 infected and un-

infected populations ($p < 0.005$), suggesting that prazinquantel intake has a protective effect on decreasing the rates of parasitic infection. A study done in Ugandan adult women infected by *S. mansoni* found that treatment of their infection with prazinquantel, substancially reduced HIV acquisition for at least two months. This is attributed to the improvement of local genital tract and global immunological effects, suggesting that treatment of neglected parasitic infection can potentuially reduce the risk of female HIV [37]. This is even true taking into account the growing evidences sugesting the existence of considerable interaction between parasitic infections and HIV transmission [2,3,5,7-12,14].

Despite Mozambique's efforts to control schistosomiasis and intestinal parasites according to the WHO recommendation since 2010 directed to school-age children, the prevalence of these infections is still very high in Mozambique and in South East African countries in general [4,8,25,27,28]. Meta- analysis studies of HIV-1 infected individuals indicated substantial changes in HIV viral load after treatment of co-infections. Thus, the control strategies for these parasites, needs to be extended to adults deserves to be revisited with inclusion of adults, especially those on high risk of infection with NTDs. This is especially true in the context of climate change where we expect to see significant impacts of heat and drought on the parasitic lifecycles and that will also affect the biology of their hosts [8,39].

Multivariate logistic regression

Results from multivariate logistic regression shown in table 7, revealed that HIV-1 infected patients were more likely to be infected by any parasite (OR = 1.813575) than HIV-1 uninfected patients. In addition, those using river or lake as water sources either for drinking (OR = 7.289245) or domestic chores (OR = 9.16205) were more likely to be infected by any parasite, than those whose water source was from pipes. A lower level of education was also identified as a significant risk factor for parasitic infection, as noted in many other studies [27,33,42]. Participants with secondary/higher education were found to be less likely to have a parasite infection that those with primary or no education (OR = 0.379).

Variables	Estimate	OR (95% CI)	*p* value
(Intercept)	-2.90766		<0.0000
Sex (Ref=Female)			
Male	0.07879	1.081977	0.8232
HIV-1 status (Ref=Negative)			
Positive	0.5953	1.813575	0.0468
Time of residence in Boane (Ref= less than 5 years)			
More than 5 years	0.28913	1.335265	0.3937
Age (Ref= >14)			
5-14 years	0.38264	1.46615	0.3207
Education (Ref=illiterate)			
Primary	-0.57594	0.562176	0.09
Secondary	-0.96931	0.379345	0.0399
Occupation (Ref=unemployed)			
Farmer	-0.02686	0.973498	0.9471
Trading/others	-0.52604	0.59094	0.224
Water source (Ref=piped)			
River/Lake	1.9864	7.289245	<0.0000
Well	2.28807	9.855897	<0.0000
Garments, bed linen (Ref=home)			
River/Lake	2.21507	9.16205	<0.0000

Table 7: *Multivariate logistic regression in relation to some selected risk factors.*

Our study had several limitations that deserve to be highlighted. First, our study population represented a convenience sample among those seeking health care in Boane Health Center, so the results obtained cannot be extrapolated to the general population of the country. Secondly, we only collected one stool and urine sample for each patient, and it is possible that the results obtained underestimate parasite prevalence in the stools, mainly due to intermittent excretion of parasite eggs or cysts, or to the limitations regarding sensitivity of the microscopic techniques used [43].

Conclusions

In women HIV-1 status was associated with higher rates of infection by *S. mansoni*, suggesting that chronic infection with schistosomiasis is a risk factor for HIV-1 acquisition in our study population. Further we were able to demonstrate that in our group the infestation by *S. mansoni* was associated with degree of inmunosupresion.

Given the negative effect of these parasitic infections and the high rates of HIV/AIDS in Mozambique and in South East Africa, the control strategy for these infections should be extended to this high risk group and adults in general, as an additional tool to control HIV transmition. Moreever, these strategy should also take into account that climate changes may further influence rates of infection by these parasites.

Future studies in the region should be targeted on defining the role of each parasite identified in relation to HIV-1 infection, as well as in identification of human immunogenetic determinants of schistosomiasis susceptibility and severity, thus open insigths for rational development of novel therapeutic and vaccine targets for schistosomiasis.

Acknowledgements

The study was funded by the US National Institutes of Health through an International Pilot Grant from the UCSD Center for AIDS Research, (5P30AI036214-15). The manuscript writing and publication was supported by Fogarty International Center, Office of the Director, Eunice Kennedy Shriver National Institute of Child Health and Human Development and National Institute of Neurological Disorders and Stroke of the National Institutes of Health under Award Number D43TW010135. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Fogarty International Center or the National Institutes of Health.

We express our gratitude to all patients who contributed to this study. We also acknowledge to the staff of the Boane Health Center where the study was done. We also thank Professor Virgílio do Rosario, retired Professor from Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa, for helping to draft and edit the manuscript.

Conflict of Interest

The authors declare that they not have competing interests.

Bibliography

1. World Health Organization. "Schistosomiasis". (2020).
2. Von Braun A., *et al*. "Schistosoma and Other Relevant Helminth Infections in HIV-Positive Individuals-an Overview". *Tropical Medicine and Infectious Disease* 4.2 (2019).
3. Downs JA., *et al*. "Effects of schistosomiasis on susceptibility to HIV-1 infection and HIV-1 viral load at HIV-1 seroconversion: A nested case-control study". *PLOS Neglected Tropical Diseases* 11.9 (2017): e0005968.
4. Gebrewahid T., *et al*. "Intestinal parasitosis in relation to CD4 count and anemia among ART initiated patients in St. Mary Aksum general hospital, Tigray, Ethiopia". *BMC Infectious Diseases* 19.1 (2019): 350.

5. Hodges MH., *et al*. "Mass drug administration significantly reduces infection of Schistosoma mansoni and hookworm in school children in the national control program in Sierra Leone". *BMC Infectious Diseases* 12 (2012): 16.

6. Mazigo HD., *et al*. "Co-infection of Schistosoma mansoni/hepatitis C virus and their associated factors among adult individuals living in fishing villages, north-western Tanzania". *BMC Infectious Diseases* 17.1 (2017): 668.

7. Downs JA and DW Fitzgerald. "No more neglect of helminths and HIV". *Lancet* 388.10054 (2016): 1857-1859.

8. Cerveja BZ., *et al*. "Prevalence of Intestinal Parasites Among HIV Infected and HIV Uninfected Patients Treated at the 1º De Maio Health Centre in Maputo, Mozambique". *EC Microbiology* 9.6 (2017): 231-240.

9. Agbolade OM., *et al*. "Intestinal helminthiases and schistosomiasis among school children in an urban center and some rural communities in southwest Nigeria". *The Korean Journal of Parasitology* 45.3 (2007): 233-238.

10. Kaniyarakkal V., *et al*. "Intestinal Parasite Profile in the Stool of HIV Positive Patients in relation to Immune Status and Comparison of Various Diagnostic Techniques with Special Reference to Cryptosporidium at a Tertiary Care Hospital in South India". *The Advanced Medical* 2016 (2016): 3564359.

11. Assefa S., *et al*. "Intestinal parasitic infections in relation to HIV/AIDS status, diarrhea and CD4 T-cell count". *BMC Infectious Diseases* 9 (2009): 155.

12. Mbah MLN., *et al*. "HIV and Schistosoma haematobium prevalences correlate in sub-Saharan Africa". *Tropical Medicine and International Health* 18.10 (2013): 1174-1179.

13. Mbabazi PS., *et al*. "Examining the relationship between urogenital schistosomiasis and HIV infection". *PLOS Neglected Tropical Diseases* 5.12 (2011): e1396.

14. Yegorov S., *et al*. "Impact of Endemic Infections on HIV Susceptibility in Sub-Saharan Africa". *Tropical Diseases, Travel Medicine and Vaccines* 5 (2019): 22.

15. Feldmeier H., *et al*. "Female genital schistosomiasis as a risk-factor for the transmission of HIV". *International Journal of STD and AIDS* 5.5 (1994): 368-372.

16. Poggensee G., *et al*. "Presence of Schistosoma mansoni eggs in the cervix uteri of women in Mwanga District, Tanzania". *Transactions of the Royal Society of Tropical Medicine* 95.3 (2001): 299-300.

17. Secor WE. "The effects of schistosomiasis on HIV/AIDS infection, progression and transmission". *Current Opinion in HIV and AIDS* 7.3 (2012): 254-259.

18. Downs JA., *et al*. "Urogenital schistosomiasis in women of reproductive age in Tanzania's Lake Victoria region". *The American Journal of Tropical Medicine and Hygiene* 84.3 (2011): 364-369.

19. Brodish PH and K Singh. "Association Between Schistosoma haematobium Exposure and Human Immunodeficiency Virus Infection Among Females in Mozambique". *The American Journal of Tropical Medicine and Hygiene* 94.5 (2016): 1040-1044.

20. Wall KM., *et al*. "Schistosomiasis is associated with incident HIV transmission and death in Zambia". *PLOS Neglected Tropical Diseases* 12.12 (2018): e0006902.

21. Secor WE., *et al*. "Increased density of human immunodeficiency virus type 1 coreceptors CCR5 and CXCR4 on the surfaces of CD4(+) T cells and monocytes of patients with Schistosoma mansoni infection". *Infection and Immunity* 71.11 (2003): 6668-6671.

22. World Atlas. "Countries with the highest rates of HIV/AIDs". (2019).

23. Manuel L., *et al*. "Human toxoplasmosis in Mozambique: gaps in knowledge and research opportunities". *Parasites Vectors* 13.1 (2020): 571.

24. UNAIDS. "Mozambique".

25. Grau-Pujol B., *et al*. "Frequency and distribution of neglected tropical diseases in Mozambique: a systematic review". *Infectious Diseases of Poverty* 8.1 (2019): 103.

26. Phillips AE., *et al*. "Urogenital schistosomiasis in Cabo Delgado, northern Mozambique: baseline findings from the SCORE study". *Parasites Vectors* 11.1 (2018): 30.

27. Noormahomed EV., *et al*. "Seroprevalence of anti-cysticercus antibodies among the children living in the urban environs of Maputo, Mozambique". *Annals of Tropical Medicine and Parasitology* 97.1 (2003): 31-35.

28. Meurs L., *et al*. "Diagnosing Polyparasitism in a High-Prevalence Setting in Beira, Mozambique: Detection of Intestinal Parasites in Fecal Samples by Microscopy and Real-Time PCR". *PLOS Neglected Tropical Diseases* 11.1 (2017): e0005310.

29. Serviço Distrital de Saúde, Mulher e Acção Social (SDSMAS) Boane. Balanço das actividades realizadas durante o ano (2016).

30. Ministério da Saúde (MISAU), Instituto Nacional de Estatística (INE), and ICF. Inquérito de Indicadores de Imunização, Malária e HIV/SIDA em Moçambique 2015 (IMASIDA). Maputo, Moçambique; Rockville, Maryland, EUA: INS, INE, and ICF (2018).

31. Katz DE and DN Taylor. "Parasitic infections of the gastrointestinal tract". *Gastroenterology Clinics of North America* 30.3 (2001): 797-815.

32. Henriksen SA and JF Pohlenz. "Staining of cryptosporidia by a modified Ziehl-Neelsen technique". *Acta Veterinaria Scandinavica* 22.3-4 (1981): 594-596.

33. Gedle D., *et al*. "Intestinal parasitic infections and its association with undernutrition and CD4 T cell levels among HIV/AIDS patients on HAART in Butajira, Ethiopia". *Journal of Health, Population and Nutrition* 36.1 (2017): 15.

34. Heyworth MF. "Immunological aspects of Giardia infections". *Parasite* 21 (2014): 55.

35. Moolasart P. "Giardia lamblia in AIDS patients with diarrhea". *Journal of the Medical Association of Thailand* 82.7 (1999): 654-659.

36. Augusto G., *et al*. "Geographic distribution and prevalence of schistosomiasis and soil-transmitted helminths among schoolchildren in Mozambique". *The American Journal of Tropical Medicine and Hygiene* 81.5 (2009): 799-803.

37. Yegorov S., *et al*. "Schistosoma mansoni infection and socio-behavioural predictors of HIV risk: a cross-sectional study in women from Uganda". *BMC Infectious Diseases* 18.1 (2018): 586.

38. Kjetland EF., *et al*. "Association between genital schistosomiasis and HIV in rural Zimbabwean women". *AIDS* 20.4 (2006): 593-600.

39. Shimelis T., *et al*. "Cryptosporidium and other intestinal parasitic infections among HIV patients in southern Ethiopia: significance of improved HIV-related care". *Parasit Vectors* 9.1 (2016): 270.

40. Belo VS., *et al*. "Fatores associados à ocorrência de parasitoses intestinais em uma população de crianças e adolescentes". *Revista Paulista de Pediatria* 30.2 (2012): 195-201.

41. Downs JA., *et al*. "Association of Schistosomiasis and HIV infection in Tanzania". *The American Journal of Tropical Medicine and Hygiene* 87.5 (2012): 868-873.

42. Nokes C., *et al*. "Parasitic helminth infection and cognitive function in school children". *Proceedings of the Royal Society* 247.1319 (1992): 77-81.

43. Van Lieshout L and M Roestenberg. "Clinical consequences of new diagnostic tools for intestinal parasites". *Clinical Microbiology and Infection* 21.6 (2015): 520-528.

Volume 17 Issue 5 May 2021