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Schistosomiasis and Human Immunodeficiency Virus in Men in Tanzania

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Abstract. Schistosomiasis is a parasitic worm infection that affects over 260 million individuals worldwide. Women with schistosome infections have been demonstrated to have a 4-fold increase in the odds of human immunodeficiency virus (HIV) infection compared with women without schistosome infections. A relationship between schistosome and HIV infections has not been clearly defined in men. Among 674 men aged 18–50 years living in rural Tanzania, we identified 429 (63.6%) who had a schistosome infection as defined by serum positivity for schistosome circulating anodic antigen, visualization of parasite eggs in urine or stool, or both. HIV infection was identified in 38 (5.6%). The odds of HIV infection was 1.3 [95% confidence interval = 0.6–2.5] (P = 0.53) among men with any schistosome infection (*Schistosoma haematobium* or *Schistosoma mansoni*), and it was 1.4 [0.6–3.3] (P = 0.43) among men with *S. haematobium* infection. Men with *S. haematobium* infection were significantly more likely to report the symptom of hemospermia than men without *S. haematobium* infection. We conclude that schistosome infections appear to have little to no association with HIV infection in men.

INTRODUCTION

Schistosomiasis is a parasitic infection that affects over 260 million people worldwide, with approximately 85% of cases in Africa.[1] We have found an increased likelihood of being human immunodeficiency virus (HIV) infected among women in Tanzania with *Schistosoma haematobium* infection as compared with women without schistosomiasis.[2] Other groups have reported similar results in women, and suggested that parasite-inducted genital tract lesions may permit HIV viral entry.[3] Our additional observation that women with *Schistosoma mansoni* infection also had an increased prevalence of HIV infection[4] led us to postulate that chronic systemic inflammation caused by schistosome infection may be an additional mechanism of increased HIV risk, since *S. mansoni* primarily affects the gastrointestinal tract. Therefore, increased susceptibility to HIV infection in individuals with schistosomiasis may be due to generalized systemic immune alterations, and for this reason may affect men in addition to women.

No epidemiologic studies of HIV and schistosomiasis to date have focused solely on men. Several population-based studies in Tanzania and Uganda, which included both men and women, did not find an increased prevalence of HIV among those with *S. mansoni* infection.[5,6] Neither of these studies stratified data by gender, and both relied on schistosome egg excretion as the primary endpoint, which is less sensitive than schistosome antigen testing[7] and may be diminished in the setting of HIV infection.[8,9] Of note, in a subset of the Ugandan individuals who underwent urine schistosome antigen testing, the odds ratio (OR) for HIV infection was 1.5 with a P value of 0.19, suggesting that the study may have lacked sufficient power to detect a smaller increased risk.[6] One other study that did use schistosome antigen testing in Uganda also did not report effects of *S. mansoni* infection on men and women separately.[10]

Therefore, we conducted a large epidemiologic study to determine the relationship between *S. haematobium*, *S. mansoni*, and HIV infections among men in regions of Tanzania where schistosome infection is endemic. We predicted that both genders would experience schistosome-induced systemic immunomodulation that would increase the odds of HIV infection. We postulated that the reported ORs of 3–4 in women[2–4] were higher than would be observed in men, due to schistosome-induced epithelial breaches in the female genital tract that may facilitate HIV viral entry following sexual exposure, for which there would not be a comparable effect in men. We therefore hypothesized that the odds of HIV infection in schistosome-infected men would be increased 2-fold compared with men without schistosome infection, and we conducted interviews and additional testing to control for other factors known to be associated with HIV infection.

MATERIALS AND METHODS

Study setting and participant recruitment. This study was conducted in nine rural villages in the Mwanza region of Tanzania. Five of these were lakeside villages near Lake Victoria where *S. mansoni* is highly endemic, and four were inland villages where *S. haematobium* is highly endemic (Figure 1).[2,4,5]

The study team visited each of the health posts for 1–3 days between April 2014 and February 2016. We recruited a community-based sample of healthy outpatient men aged 18–50 years in each study villages.

Data collection. Each man provided blood, urine, and a single stool sample and completed an oral questionnaire. Men who reported current genital symptoms also underwent

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Village Name	*S. mansoni* infection	*S. haematobium* infection
Sengerema (n=43)	19 (44%)	3 (7%)
Chifunfu (n=126)	92 (73%)	0
Igombe (n=44)	35 (80%)	0
Kisesa (n=69)	34 (49%)	1 (1%)
Kayenze (n=168)	151 (90%)	2 (1%)
Lunele (n=62)	1 (2%)	28 (45%)
Shigumulo (n=42)	1 (2%)	11 (26%)
Nyamilama (n=61)	0	19 (31%)
Lumeji (n=59)	3 (5%)	31 (53%)

FIGURE 1. Map of study sites and prevalence of schistosome infections in the Lake Victoria region of northwest Tanzania. Villages noted in blue are endemic for *Schistosoma mansoni*, and villages shown in red are endemic for *Schistosoma haematobium*.

genital examination by a physician. Ten milliliters of urine were filtered and samples were read on-site by a trained parasitologist. Five Kato Katz slides were prepared from each stool sample using 41.7 mg of stool per slide, which has been demonstrated to have a sensitivity for diagnosis of *S. mansoni* that is equivalent to collecting stool on three separate days.[11] Stool slides were read by trained parasitologists at the National Institute for Medical Research (NIMR) in Mwanza, Tanzania. All study participants living in these highly endemic areas were treated with praziquantel on the day of study enrollment, in accordance with World Health Organization (WHO) treatment recommendations.[12]

Interview and examination. Men participated in a 20-minute structured interview that included demographic information, sexual history, and urogenital symptoms. The interview was administered in Kiswahili in a private setting by a male member of the study team. Men provided information about past and current genital symptoms, sexual partners, and sexual behavior. Those with current genital symptoms underwent examination, and were provided with treatment of themselves and their partners in accordance with the Tanzanian national guidelines.[13]

Syphilis. Venous blood was collected and tested for syphilis using a point-of-care *Treponema pallidum* particle agglutination assay (Crystal TP; Span Diagnostics Ltd., Surat, India). Men who tested positive for syphilis were asked to return to the study site with all of their sexual partners, and all were treated on-site with benzathine penicillin free of charge.

Human immunodeficiency virus. Men were offered on-site voluntary HIV counseling and testing in Kiswahili by a

trained nurse counselor. Rapid tests (SD Bioline; Standard Diagnostics, Inc., Kyonggi-do, South Korea) were used with confirmatory testing for positive samples (Unigold; Trinity Biotech, Bray, Ireland) as per the national testing algorithm. Patients received their results and posttest counseling on the same day. Men who were diagnosed with HIV were referred to the local HIV clinic for free care and treatment.

Laboratory testing. Schistosome circulating anodic antigen (CAA) is a glycosaminoglycan-like carbohydrate that is produced by gut epithelial cells of schistosome worms and secreted into the host bloodstream during active infection.[14] The CAA test does not distinguish *S. haematobium* from *S. mansoni* infection. The test usually becomes negative within 1 week of successful anti-schistosomal therapy.[15,16]

CAA testing was performed at the NIMR laboratory in Mwanza using the upconverting phosphor (UCP) technology lateral flow assay as previously described.[17,18] We used the strategy recommended by the WHO/the Special Programme for Research and Training in Tropical Diseases to define a composite reference standard for schistosome infection as the presence of schistosome eggs visualized microscopically and/or a serum CAA value $\geq$ 30 pg/mL.[17,19] We further defined *S. mansoni* infection as any of the following: 1) *S. mansoni* ova in stool and/or 2) CAA $\geq$ 30 pg/mL in an *S. mansoni*-endemic region in an individual with no *S. haematobium* ova in urine. We defined *S. haematobium* infection as any of the following: 1) *S. haematobium* ova in urine and/or 2) CAA $\geq$ 30 pg/mL in an *S. haematobium*-endemic region in an individual with no *S. mansoni* ova in stool.

Statistical considerations. We predicted that the prevalence of schistosome infection would be 72% among those with HIV infection, and that the prevalence of schistosome infection would be 60% in those without HIV infection. We therefore calculated that enrolling 670 men would provide 90% power to detect an OR of 2 for HIV infection in those with versus without schistosome infection.

Data were entered into Microsoft Excel (Microsoft Corp., Redmond, WA) and analyzed using Stata/IC version 13 (College Station, TX). Continuous variables were summarized by median and interquartile range (IQR), and categorical variables were summarized by frequency and percentage. For factors associated with HIV infection, we performed univariable followed by multivariable logistic regression to examine factors associated with HIV with a P value of < 0.05. We used backward elimination, sequentially removing the least-significant factor one by one until all remaining factors were significant, to arrive at the final multivariable model. Associations between factors and the endpoint were summarized using ORs with 95% confidence intervals (CIs) and associated P values.

In cases in which an outcome yielded a value less than 5 on the χ^2 analysis, we performed Fisher's exact test to determine the strength of an association. We then used Firth logistic regression with backward elimination to construct a multivariable model of factors associated with *S. haematobium* or *S. mansoni* infection due to multiple significant factors with a small number of outcomes.

Ethical considerations. The study was explained to men in a large group and subsequently one on one by a trained study team member fluent in the local language. To participate in the study, men were asked to provide written informed consent or place their mark on the consent form. At the local level, permission was obtained from the District Medical Officers and clinicians stationed at participating dispensaries and health centers. Ethical approvals were granted by the research ethics committee at Bugando Medical Center, the Medical Research Coordinating Committee of NIMR in Tanzania, and the Institutional Review Board at Weill Cornell Medical College.

RESULTS

Study population. Between April 2014 and February 2016, we invited a total of 702 men aged 18–50 years from

TABLE 1

Demographic and behavioral characteristics of 674 rural adult men screened for schistosomiasis and sexually transmitted infections in Tanzania

Characteristic	Number (%) or median [IQR]
Age in years	34 [25–42]
Residence in village endemic for *Schistosoma haematobium*	224 (33.2)
Lumeji	59 (8.8)
Lunele	62 (9.2)
Shigumulo	42 (6.2)
Nyamilama	61 (9.1)
Residence in village endemic for *S. mansoni*	450 (66.8)
Chifunfu	126 (18.7)
Igombe	44 (6.5)
Kayenze	168 (24.9)
Kisesa	69 (10.2)
Sengerema	43 (6.4)
Years attended school	
0–2 years	66 (9.8)
3–5 years	53 (7.9)
6–8 years	402 (59.6)
> 8 years	150 (22.3)
Number of people living in household	6 [4–9]
Failed to eat an afternoon or evening meal in past month due to food shortage	147 (22.4)
Prior schistosomiasis treatment	
Never	354 (52.5)
Within the past year	38 (5.6)
1 to < 3 years ago	94 (13.9)
3 to < 5 years ago	42 (6.2)
5 to < 10 years ago	62 (9.2)
More than 10 years ago	84 (12.5)
Ever been previously tested for HIV	418 (62.1)
Reports being circumcised	471 (70.3)
Age in years at first sexual encounter	18 [16–20]
Number of children	3 [1–6]
Number of sexual partners in the past 6 months	
0–1	329 (48.8)
2	160 (23.7)
3–4	119 (17.7)
5 or more	49 (7.2)
Declined to answer	17 (2.5)
Typical sexual partner $\geq$ 5 years younger	311 (51.5)
Ever given money/gifts to obtain sex (outside of marriage)	540 (81.2)
Used a condom during most recent sex	157 (23.8)
Ever treated for sexually transmitted infection	225 (33.6)
Genital symptoms in the past year	167 (24.8)
Penile discharge	64 (9.5)
Dyspareunia	106 (15.7)
Hemospermia	14 (2.1)
Painful genital ulcers	46 (6.8)
Painless genital ulcers	27 (4.0)

HIV = human immunodeficiency virus; IQR = interquartile range.
Non-missing data were included in all calculations.

TABLE 2
Clinical infections in 674 adult men in rural Tanzania

Infection	*Schistosoma mansoni*-endemic village (*N* = 450)	*Schistosoma haematobium*-endemic village (*N* = 224)
HIV	24 (5.3)	14 (6.3)
Syphilis	29 (6.4)	16 (7.1)
Any schistosome infection (CAA positive or ova positive)	335 (74.4)	94 (42.0)
S. mansoni infection (by stool ova or CAA with negative urine in endemic region)	331 (73.6)	5 (2.2)
S. haematobium infection (by urine ova or CAA with negative stool in endemic region)	6 (1.3)*	89 (39.7)
S. mansoni ova positive	227 (50.4)	5 (2.2)
S. haematobium ova positive	6 (1.3)	31 (13.8)

CAA = circulating anodic antigen.
*Two individuals living in an *S. mansoni*-endemic village had both *S. mansoni* and *S. haematobium* infection confirmed by ova.

nine different villages to participate in this study. Of these, 28 men did not consent to voluntary counseling and testing for HIV. This left a total of 674 men who completed all study procedures and were included in the analysis.

Baseline characteristics of the population are shown in Table 1. The median age was 34 years [interquartile range = 25–42]. Nearly half of the men (328, 48.7%) had had more than one sexual partner in the past 6 months, and the majority of men reported that their sexual partners were typically more than 5 years younger. One-fourth of men (167, 24.8%) had experienced genital symptoms within the past year. Nearly two-thirds of the men (418, 62.1%) had been previously tested for HIV infection, whereas 47.6% (320) had previously received treatment of schistosome infection.

Clinical outcomes. We documented HIV infection in 38/674 men (5.6%) and syphilis in 45 (6.7%, Table 2). Just under two-thirds of the total population (429, 63.6%) had schistosome infections, with the percentage approaching three-fourths among adults living in *S. mansoni*-endemic villages. *Schistosoma mansoni* and *S. haematobium* infections were sharply geographically demarcated in seven of the nine villages, with < 3% of the population in inland *S. haematobium*-endemic villages having *S. mansoni* infection, and vice versa (Figure 1).

TABLE 3
Factors associated with HIV infection in rural Tanzanian men

	HIV infected (*N* = 38)	HIV uninfected (*N* = 636)	Univariable analysis		Multivariable analysis	
Factor	Number (%) or median [IQR]	Number (%) or median [IQR]	Odds ratio [95% CI]	*P* value	Odds ratio [95% CI]	*P* value
Age in years	34 [30–40]	34 [25–42]	1.01 [0.98–1.04]	0.60		
Residence in village endemic for *Schistosoma mansoni*	24 (63.2)	426 (67.0)	0.85 [0.43–1.67]	0.63		
Years of school completed	7 [3–7]	7 [7–7]	0.84 [0.76–0.93]	**0.001**	0.86 [0.77–0.96]	0.005
Number of people living in household	5 [3–6]	6 [4–9]	0.88 [0.79–0.98]	**0.017**		
Food shortage	8 (21.1)	139 (22.5)	0.92 [0.41–2.05]	0.84		
Circumcised	21 (55.3)	450 (71.2)	0.50 [0.26–0.97]	**0.040**		
Age in years at first sex	18 [16–19]	18 [16–20]	1.02 [0.93–1.12]	0.73		
Children have more than one mother	13 (34.2)	163 (25.6)	1.5 [0.8–3.0]	0.25		
Number of sexual partners in the past 6 months	3 [1–4]	1 [1–2]	1.2 [1.1–1.3]	**0.001**	1.13 [1.05–1.23]	0.001
Typical sex partners more than 5 years younger	25 (71.4)	286 (50.3)	2.5 [1.2–5.2]	**0.018**		
Ever given money/gifts for sex (outside of marriage)	34 (91.9)	506 (80.6)	–*	0.13		
Used a condom during most recent sex	12 (31.6)	145 (23.4)	1.5 [0.7–3.1]	0.25		
Ever treated for sexually transmitted infection	19 (50.0)	206 (32.6)	2.1 [1.1–4.0]	**0.030**		
Genital symptoms in the past year						
Penile discharge	5 (13.2)	59 (9.3)	–*	0.39		
Dyspareunia	12 (31.6)	94 (14.8)	2.7 [1.3–5.5]	**0.008**	2.7 [1.3–5.7]	0.009
Hemospermia	3 (7.9)	11 (1.7)	–*	**0.039**		
Painful genital ulcers	7 (18.4)	39 (6.1)	3.5 [1.4–8.3]	**0.006**		
Painless genital ulcers	3 (8.1)	24 (3.8)	–*	0.18		
Syphilis	6 (15.8)	39 (6.1)	2.9 [1.1–7.3]	**0.026**		
Any schistosome infection (CAA positive or ova positive)	26 (68.4)	403 (63.4)	1.3 [0.6–2.5]	0.53		
S. mansoni infection (by ova or CAA in endemic region)	19 (50.0)	317 (49.8)	1.0 [0.5–1.9]	0.99		
Schistosoma haematobium infection (by ova or CAA in endemic region)	7 (18.4)	88 (13.8)	1.4 [0.6–3.3]	0.43		
S. mansoni ova positive	11 (29.0)	221 (34.8)	0.8 [0.4–1.6]	0.47		
S. haematobium ova positive	2 (5.3)	35 (5.5)	–*	1.0		

CAA = circulating anodic antigen; CI = confidence interval; HIV = human immunodeficiency virus; IQR = interquartile range.
*Unable to calculate odds ratio due to small numbers of outcomes; *P* value calculated using Fisher's exact test.
Bold *P*-values indicate *P*-values < 0.05 that were included in the multivariable model.

TABLE 4

Factors associated with egg-patent urogenital *Schistosoma haematobium* infection in rural Tanzanian men in *S. haematobium*-endemic villages

Factor	*S. haematobium* egg-positive (*N* = 31)	*S. haematobium* egg-negative (*N* = 188)	Univariable analysis		Multivariable analysis*	
	Number (%) or median [IQR]	Number (%) or median [IQR]	Odds ratio [95% CI]	*P* value	Odds ratio [95% CI]	*P* value
Age in years	24 [20–39]	33 [24–43]	0.95 [0.91–0.99]	**0.010**	0.96 [0.92–0.996]	**0.033**
Years in school	7 [7–7]	7 [7–7]	1.0 [0.8–1.1]	0.53		
Children have more than one mother	3 (9.7)	49 (26.1)	–†	0.066		
Number of sexual partners in the past 6 months	2 [1–3]	2 [1–3]	1.0 [0.9–1.1]	0.58		
Ever treated for sexually transmitted infection	4 (13.3)	52 (28.0)	–†	0.12		
Penile discharge in past year	4 (12.9)	21 (11.2)	–†	0.76		
Dyspareunia in past year	10 (32.3)	40 (21.3)	1.8 [0.8–4.0]	0.18		
Hemospermia in past year	4 (13.3)	5 (2.7)	–†	**0.023**	4.2 [1.1–16.2]	**0.038**
Painful genital ulcers in past year	5 (16.1)	13 (6.9)	2.6 [0.9–7.9]	0.093		
Painless genital ulcers in past year	0	6 (3.2)	–†	0.60		
Syphilis	2 (6.5)	14 (7.5)	–†	1.0		
HIV	2 (6.5)	12 (6.4)	–†	1.0		

CI = confidence interval; HIV = human immunodeficiency virus; IQR = interquartile range.
*Calculated using Firth logistic regression with backward elimination due to small sample sizes.
†Unable to calculate odds ratio due to small numbers of outcomes; *P* value calculated using Fisher's exact test.
Bold *P*-values indicate *P*-values < 0.05 that were included in the multivariable model.

Association of HIV with demographic and clinical factors. On univariable analysis, a number of factors were significantly associated with HIV infection, including fewer years of education, fewer people living in one's household, not being circumcised, more sexual partners in the past 6 months, having sexual partners more than 5 years younger than oneself, having been ever treated for a sexually transmitted infection, genital symptoms (dyspareunia, hemospermia, and painful genital ulcers), and having a positive syphilis test (Table 3). Factors that remained significant in the multivariable model were fewer years of education (OR per each additional year in school = 0.86 [0.77–0.96], $P = 0.005$), more sexual partners in the past 6 months (OR = 1.2 [1.1–1.3] per additional partner, $P = 0.001$), and dyspareunia (OR = 2.7 [1.3–5.7], $P = 0.009$). Schistosome infection, neither when analyzed as "any schistosome infection" nor when analyzed by the individual species, was not significantly associated with HIV infection in these men.

Association of schistosome infections with demographic and clinical factors. Men with *S. haematobium* infection, confirmed by visualization of ova in the urine, were younger and reported significantly more hemospermia in the prior year than men without schistosome infection living in the same region (Table 4, OR = 0.96 [0.92–0.996] per year older, $P = 0.033$ and OR = 4.2 [1.1–16.2], $P = 0.038$, respectively). Compared with men without *S. mansoni* infection, men with *S. mansoni* infection had less education and reported more sexual partners (OR = 0.92 [0.87–0.98] per additional year in school, $P = 0.010$ and OR = 1.15 [1.03–1.28] per additional sexual partner, $P = 0.014$, Table 5).

DISCUSSION

Men with schistosome infection did not have a higher odds of HIV infection than men without schistosome infection, even when we used a more sensitive diagnostic test

TABLE 5

Factors associated with egg-patent *Schistosoma mansoni* infection in rural Tanzanian men in *S. mansoni*-endemic villages

Factor	*S. mansoni* egg-positive (*N* = 225)	*S. mansoni* egg-negative (*N* = 219)	Univariable analysis		Multivariable analysis*	
	Number (%) or median [IQR]	Number (%) or median [IQR]	Odds ratio [95% CI]	*P* value	Odds ratio [95% CI]	*P* value
Age in years	33 [26–41]	35 [25–42]	0.99 [0.97–1.01]	0.31		
Years in school	7 [7–7]	7 [7–10]	0.91 [0.86–0.97]	**0.002**	0.92 [0.87–0.98]	**0.010**
Children have more than one mother	60 (26.7)	62 (28.3)	0.9 [0.6–1.4]	0.70		
Number of sexual partners in the past 6 months	2 [1–3]	1 [1–2]	1.2 [1.1–1.3]	**0.004**	1.15 [1.03–1.28]	**0.014**
Ever treated for sexually transmitted infection	81 (36.0)	85 (39.0)	0.9 [0.6–1.3]	0.52		
Penile discharge in past year	21 (9.3)	17 (7.8)	1.2 [0.6–2.4]	0.56		
Dyspareunia in past year	27 (12.0)	25 (11.4)	1.1 [0.6–1.9]	0.85		
Hemospermia in past year	0	5 (2.3)	–†	**0.029**		
Painful genital ulcers in past year	15 (6.7)	12 (5.5)	1.2 [0.6–2.7]	0.60		
Painless genital ulcers in past year	12 (5.4)	8 (3.7)	1.5 [0.6–3.7]	0.39		
Syphilis	19 (8.4)	9 (4.1)	2.2 [0.95–4.9]	**0.066**		
HIV	11 (4.9)	13 (5.9)	0.8 [0.4–1.9]	0.63		

CI = confidence interval; HIV = human immunodeficiency virus; IQR = interquartile range.
*Calculated using Firth logistic regression with backward elimination due to small sample sizes.
†Unable to calculate odds ratio due to small numbers of outcomes; *P* value calculated using Fisher's exact test.
Bold *P*-values indicate *P*-values < 0.05 that were included in the multivariable model.

for schistosome infections than had been used in prior studies. To the best of our knowledge, this was the first study of its kind to investigate this issue in men alone. In nearly 700 men, we found an increased odds of HIV infection of 1.3 [0.6–2.5], with an upper limit of the 95% CI of 2.5 and an upper 80% CI of 2.0. On examination of differential effects by species, *S. haematobium*-infected men had a slightly higher odds of HIV infection (1.4 [0.6–3.3]), whereas the odds of HIV infection in *S. mansoni*-infected men was below 1. Given our findings, we can be 82% certain that the true odds of HIV infection in men with *S. haematobium* infection is less than 2. Therefore, it remains possible that schistosome infections, particularly *S. haematobium* infection, may be mildly associated with HIV infection in men, but the association appears to be markedly diminished compared with that observed in women.

A recent study reported no difference in innate immune or HIV-1-specific immune responses in the blood of individuals with HIV–*S. mansoni* coinfection compared with individuals with HIV alone.[20] Our epidemiological findings support this study, suggesting that systemic schistosome-induced immunomodulation, which we hypothesized could affect interactions between HIV and schistosomiasis in men as well as women, may not lead to increased susceptibility to HIV infection. Two corollaries follow from these observations. First, our work implicates changes in the genital mucosa of women with schistosome infections as the likely reason that women, but not men, who have schistosome infections have an increased odds of HIV infection. Second, it implies that, if the impaired antiviral control that is induced by schistosomiasis in animals[21–23] leads to interactions with HIV, these parasite–virus interactions may occur after HIV infection has been acquired rather at the time of HIV exposure.

Our findings additionally offer helpful clinical clues for improved diagnosis of urogenital schistosomiasis in men, which causes tissue inflammation in the urinary and genital tracts and can be easily misdiagnosed as a sexually transmitted infection.[24] Among Tanzanian men in our study, hemospermia was strongly associated with *S. haematobium* infection. Autopsy studies in men demonstrate that the highest concentrations of *S. haematobium* ova in tissue occur in the urinary bladders, ureters, seminal vesicles, and prostate.[25] Semen of infected men frequently contains *S. haematobium* ova, together with increased seminal levels of leukocytes and the inflammatory cytokines interleukin (IL)-4, IL-6, IL-10, and tumor necrosis factor alpha (TNF-α).[26] These findings and ours support the hypothesis that men with urogenital schistosomiasis may more easily transmit HIV to their sexual partners due to tissue inflammation and bleeding, leading to higher concentrations of HIV in the semen of HIV–schistosome coinfected men than in HIV-infected men without schistosome infection.[26,27]

A recent prospective study demonstrated that men and women with the helminthic infection lymphatic filariasis had a 2-fold increased risk of incident HIV infection compared with those without filariasis.[28] Unlike schistosomiasis, filariasis is not known to have direct effects on the genital tract, suggesting that systemic immune changes induced by filariasis could increase HIV susceptibility. Our prior findings in women with *S. mansoni*, which preferentially affects the gastrointestinal tract, had led us to a similar hypothesis.[4] Now, based on our finding that schistosome-infected men do not appear to have increased odds of HIV infection, an alternate hypothesis seems plausible as well. Schistosomiasis may increase the seminal and systemic HIV viral load, thereby increasing HIV transmission from one schistosome-infected individual to another in schistosome-endemic communities. Could this also be a mechanism underlying the apparent increased HIV incidence in adults with lymphatic filariasis? Further studies to explore these possibilities are urgently needed.

In conclusion, we have used stringent methods for detection of schistosome infections to demonstrate that schistosome-infected men have little to no increased odds of HIV infection. The robustness of our work is supported by the strong associations we found between HIV and other known HIV risk factors including lack of circumcision, number of sexual partners, and syphilis infection. Given these findings, we posit that systemic immune changes provoked by schistosome infection are not likely to exert major effects on HIV susceptibility. Our data provide additional information in the ongoing discussion of the relationship between schistosomiasis and HIV infection, suggesting that post-HIV infection effects in schistosome–HIV coinfected individuals strongly merit further investigation.

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