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HIV prevalence correlates with *Schistosoma haematobium* in sub-Saharan Africa

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Abstract

Objective—*Schistosoma haematobium*, the primary cause of genital schistosomiasis, is highly prevalent in sub-Saharan Africa. Epidemiological studies have observed that genital schistosomiasis increases the risk of HIV infection among young women in rural Africa. We analyzed whether *S. haematobium* prevalence is correlated with HIV prevalence across sub-Saharan Africa countries.

Design—A regression analysis across sub-Saharan African countries of HIV and *Schistosomiasis haematobium* prevalence.

Methods—We compiled country-level *S. haematobium* prevalence, HIV prevalence, and other demographic and economic data from published sources. We used univariate and multivariate regression models to assess the correlations between *S. haematobium* prevalence and HIV prevalence while controlling for risk factors for each infection.

Results—Among 43 sub-Saharan African countries, the mean prevalence of *S. haematobium* and HIV were 22.4% and 6.21%, respectively. In multivariate analysis, *S. haematobium* prevalence was a significant correlate of the HIV prevalence. Additional significant correlates were prevalence of male circumcision, years since a country's first HIV/AIDS diagnosis, geographic region, and immunization coverage. Each *S. haematobium* infection per 100 individuals was associated with a 2.9% (95% CI: 0.2-5.8%) increase in HIV prevalence.

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Conflicts of Interest: None

Conclusions—*S. haematobium* prevalence is associated with HIV prevalence among sub-Saharan Africa countries. Therefore, controlling *S. haematobium* may be an effective means of reducing HIV transmission in sub-Saharan Africa.

Keywords

HIV; genital schistosomiasis; sub-Saharan Africa; *Schistosoma haematobium*; *Schistosoma mansoni*; regression analysis; male circumcision

Introduction

Schistosoma haematobium is highly prevalent in sub-Saharan Africa, with an estimated 112 million people infected [1, 2]. In *S. haematobium* endemic areas, up to 75% of infected individuals suffer from genital schistosomiasis [3], acquired primarily during childhood [4]. Female genital schistosomiasis causes ulcerative lesions and inflammation on the cervix and vagina [4], while male genital schistosomiasis is associated with both leukocytospermia and gross hematospermia [5]. In both sexes, these conditions result in that activation of the immune system which may facilitate HIV viral entry and binding to HIV-susceptible cells [6,7]. The biologic plausibility of the association between female genital schistosomiasis and HIV infection, as well as cross-sectional studies that have reported strong statistical associations between female genital schostosomiasis and HIV [4,7] suggest that genital schistosomiasis is a risk factor for HIV [8].

In this paper, we analyze whether *S. haematobium* is a correlate of HIV prevalence, across sub-Saharan African countries. For comparison, we evaluated the relationship between HIV and *Schistosoma mansoni*, which is also highly prevalent in sub-Saharan Africa but not known to cause urogenital ulcers [2,9]. We build upon existing research by examining the association between *S. haematobium* and HIV at the national level, addressing multiple potential confounders, and incorporating a natural control in the form of another schistosome.

Methods

We obtained country-specific *S. haematobium* and *S. mansoni* prevalence data on 43 sub-Saharan African countries [2]. As described previously [2], the data were compiled from published and unpublished survey data [10], using species-specific models of age- and spatial-distribution of infection to estimate prevalence in regions with less comprehensive sampling. We corroborated the data with additional sources, using the most recent prevalence data when sources differed [1, 11].

We collected additional country-level statistics as previously described by Drain *et al.* [12, 13]. Country-specific HIV prevalence data (% population ages 15–49) was obtained from the database of Joint United Nations Programme on HIV/AIDS [14]. Additional statistics included population structure, indicators of development, economic status, education, religion, reproductive health, health services, and other infectious diseases [12, 13]. Major sources for these data were the United Nations Development Programme, World Health Organization, United Nations Children's Fund, and United Nations Statistics Division [12,

13]. We used the country-level prevalence of male circumcision as previously categorized as "low" (<20%), "medium" (20—80%), or "high" (>80%) by Drain *et al.* [11]. Countries were categorized into four African regions (Eastern, Central, Southern, Western) based on the World Health Organization classification, due to differences in the severity and character of the HIV epidemic [13].

HIV prevalence was log-transformed to create a more normal distribution. We weighted country-level data by the adult population of each country to avoid privileging data from less populous countries. We summarized *S. haematobium* and HIV prevalence by geographical region, and used analysis of variance (ANOVA) to compare these prevalences across African regions. All regression statistics were performed using a robust variance to account for unmeasured ecologic and population differences. Stata version 9.0 was used for conducting statistical analyses [15].

We used univariate linear regression statistics to analyze the relationship between *S. haematobium* prevalence, HIV prevalence, and other infectious and non-infectious variables. We then assembled a multivariate model with HIV prevalence as the dependent variable. The multivariate model was constructed by backwards removal of non-significant (at the $p = 0.05$ level) independent variables from an initial model that included the prevalence of *S. haematobium* and *S. mansoni*, along with independent variables which we found to be significant in predicting HIV prevalence in our previous studies [12, 13].

Results

Country-level *S. haematobium* prevalence was 22.4 ± 9.8% among 43 countries in sub-Saharan Africa (Table 1). Mean *S. haematobium* prevalence differed significantly by region (p-value: 0.03), and was highest among 15 western African countries and lowest among 13 eastern African countries. Country-level HIV adult prevalence was 6.21 ± 5.7% among all 43 countries, and differed significantly by region ($p < 0.0001$). In univariate analysis, *S. haematobium* was not significantly associated with HIV prevalence ($p = 0.7$).

Among other infectious disease indicators, an increase in *S. haematobium* prevalence of 1 infection per 100 people was associated with a decrease of 0.15 infections per 100 people in Hepatitis C prevalence in univariate analysis (p: 0.03). *S. haematobium* was not significantly associated with cervical cancer incidence, tuberculosis, herpes simplex virus type-2, malaria, or syphilis prevalence. *S. haematobium* was also not significantly associated with *S. mansoni* prevalence.

In univariate regression analyses among non-infectious health care indicators, the number of *S. haematobium* infections per 100 individuals was positively correlated with infant mortality rate (0.12 infections per death per 1000 births, p: 0.01), child mortality rate (0.06 infections per death per 1000 births, p: 0.009), and number of midwives (0.25 infections per midwife per 100,000 population, $p < 0.0001$). *S. haematobium* prevalence was negatively correlated with age of the HIV epidemic (−2.1 infections per year prior to 2000 in which first HIV or AIDS diagnosis occurred, p: 0.04), male use of condoms with non-regular partners (−0.22 infections per percent of men using condoms, p: 0.02), breast feeding (−0.10

infections per percent of women exclusively breast-feeding for first four months , p: 0.045), cigarette consumption (−0.007 infections per cigarette per year per adult, p: 0.05), and access to essential medicines (−0.15 infections per percent with access, p: 0.01).

In multivariate analyses, significant, independent correlates of HIV prevalence were *S. haematobium* prevalence, male circumcision prevalence, age of the HIV epidemic, geographical region, and percent of the population immunized for diphtheria, tetanus, and pertussis (DTP) (Table 2). When controlling for the other predictors, each *S. haematobium* infection per 100 people was significantly associated with a 2.9% increase (95% CI: 0.2-5.8% p = 0.038) in HIV prevalence.

In contrast, the prevalence of *S. mansoni* was not a significant predictor of HIV prevalence, either in univariate or multivariate analysis. It suggests that the correlative factor between *S. haematobium* and HIV is the urogenital ulcerations caused by *S. haematobium*, rather than a common feature of schistosomiasis. In fact, *S. haematobium* is much more frequently associated with genital schistosomiasis than are other schistosomes [6], and the rare genital schistosomiasis caused by *S. mansoni* generally involve lesions of the ovaries, rather than the cervix and vagina which are expected to increase HIV susceptibility [9].

Discussion

Increasing evidence supports that *Schistosoma haematobium* infection is a risk factor for HIV transmission in sub-Saharan Africa [4]. We used regression models to assess the correlations between *S. haematobium* and HIV prevalence in sub-Saharan African countries, while controlling for specific HIV risk factors and for general health care indicators. We showed that HIV prevalence is positively correlated with *S. haematobium*, the major cause of urogenital schistosomiasis, across 43 sub-Saharan African countries. These results agree with epidemiological studies that have reported strong statistical associations between female genital schistosomiasis and HIV among rural African women [16, 17].

We found that the magnitude of correlation between HIV infection and *S. haematobium* (2.9% per *S. haematobium* infection per 100 people) is similar to that between HIV and male circumcision (−84% per category, with categories of <20, 20—80, and >80 circumcised men per 100 men). This magnitude of effect is plausible, given the similarities in proposed mechanisms by which these factors affect HIV transmission [4,18].

S. haematobium is usually regarded as a rural and peri-urban disease [22]. But it has established itself in urban areas across Africa [22,23], most probably through infected migrants [22], with the presence of endemic foci in many large cities such as in Bamako, Mali, Dar el Salam, Tanzania, and Kampala, Uganda [22]. On the other hand, HIV is often considered as an urban infection, but there are also important and emerging foci of HIV epidemic in African rural communities [24,25]. *S. haematobium* and HIV meet in migrating populations, travelers, commuting spouses and roadside rural and peri-urban communities [22,24]. Urban migration and spatial overlap are plausible explanatory mechanisms of the observed correlation between *S. haematobium*, which is mainly a rural disease, and country-level HIV prevalence in sub-Saharan Africa.

Schistosomiasis control programs have made use of mass drug administration of praziquantel [19]. For prevention of genital schistosomiasis to be effective, praziquantel administration should start in childhood, when exposure to schistosomiasis through water contact is highest and adaptive immunity is weakest [19]. A prospective study to test the effect of praziquantel treatment on HIV incidence has been proposed as a necessary step toward developing a new protocol to treat schistosomiasis for HIV prevention [20]. However, such a study will be complicated by the ethical imperative to treat schistosomiasis for prevention of the urinary tract consequences of infection, the burden of which is significant [19, 21].

Our results suggest that *S. haematobium* prevalence enhances HIV transmission throughout sub-Saharan Africa, and support the hypothesis that urogenital schistosomiasis is a risk factor for sexual transmission of HIV. Thus, public health programs to control *S. haematobium* may not only reduce morbidity due to urinary tract disease, but may also reduce HIV transmission in sub-Saharan Africa.

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Table 1

Schistosoma haematobium and HIV prevalence by geographical region within sub-Saharan Africa.

Sub-Saharan African Region	No. Countries	*S. haematobium* Prevalence per 100 People[1]	HIV prevalence per 100 Adults[2]
		Mean ± SD	Mean ± SD
Eastern Africa	13	17.7 ± 9.6	4.69 ± 3.04
Central Africa	8	20.5 ± 8.1	4.10 ± 1.79
Southern Africa	7	23.7 ± 11.9	18.47 ± 1.78
Western Africa	15	27.7 ±7.7	3.31 ± 1.62
Total	43	22.4 ± 9.8	6.21 ± 5.71

[1] $p=0.037$ using one-way analysis of variance between groups.

[2] $p<0.0001$ using one-way analysis of variance between groups.

Table 2

Model of HIV: multivariate linear regression analysis of HIV prevalence within sub-Saharan Africa.

HIV prevalence as dependent variable[1]	**Regression Coefficient**	**p-value**
Schistosoma haematobium prevalence (%)	0.029	0.038
Male Circumcision prevalence by category[2]	−0.84	<0.001
Age of HIV Epidemic (years)	0.30	<0.001
Geographical regions (west, central, east, south)	0.19	0.012
Children fully immunized for diphtheria, pertussis, and tetanus (%)	−0.0077	0.017

[1] In the model, number of countries was 35 and R-squared was 0.66.

[2] Male circumcision prevalence was categorized as low (<20%), intermediate (20-80%), or high (>80%).