

PREVALENCE AND PREDICTORS OF INTESTINAL HELMINTH INFECTIONS AMONG HUMAN IMMUNODEFICIENCY VIRUS TYPE 1–INFECTED ADULTS IN AN URBAN AFRICAN SETTING

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Abstract. Sub-Saharan Africa is disproportionately burdened by intestinal helminth and human immunodeficiency virus (HIV)-1 infection. Recent evidence suggests detrimental immunologic effects from concomitant infection with the two pathogens. Few studies, however, have assessed the prevalence of and predictors for intestinal helminth infection among HIV-1–infected adults in urban African settings where HIV infection rates are highest. We collected and analyzed sociodemographic and parasitologic data from 297 HIV-1–infected adults (mean age = 31.1 years, 69% female) living in Lusaka, Zambia to assess the prevalence and associated predictors of helminth infection. We found at least one type of intestinal helminth in 24.9% of HIV-infected adults. Thirty-nine (52.7%) were infected with *Ascaris lumbricoides*, and 29 (39.2%) were infected with hookworm. More than 80% were light-intensity infections. A recent visit to a rural area, food shortage, and prior history of helminth infection were significant predictors of current helminth status. The high helminth prevalence and potential for adverse interactions between helminths and HIV suggests that helminth diagnosis and treatment should be part of routine HIV care.

INTRODUCTION

Sub-Saharan Africa, a region of intestinal helminth endemicity in rural and urban settings,¹ is disproportionately burdened by infection with human immunodeficiency virus (HIV), with an estimated 70% of the world's cases² in 11% of the world's population.³ An overlapping distribution of the two pathogens becomes important because concomitant infection with HIV and helminths may potentiate the virulence of each within a coinfecting host.^{4,5} However, the few studies published to date indicate that helminth infections may occur with equal frequency and intensity in HIV-infected and HIV-uninfected persons.^{6,7} Despite increasing interest in the pathologic interactions between the two infections, few epidemiologic studies have assessed the occurrence of helminth infections and associated predictive factors in HIV-infected persons. General prevalence surveys are more commonly done in children and none, to our knowledge, have examined risk factors for intestinal helminth infection among HIV-1–infected adults in an urban sub-Saharan African setting. We analyzed baseline recruitment data from a prospective study in Lusaka, Zambia, where the background prevalence of HIV and geohelminths among adults (late teens to early 40s) was estimated in the 1990s to be 22–35%^{8,9} and 10–20%,^{10,11} respectively.

MATERIALS AND METHODS

Study design. We screened HIV-1–infected adults living in Lusaka, Zambia from March to December 2003 for a prospective study assessing the impact of helminth treatment on viral load. Baseline data from all HIV-infected screened participants were used for the present helminth prevalence survey. Adults were eligible for inclusion if they provided in-

formed consent, were confirmed to be HIV-1 seropositive by a dual rapid test algorithm (Determine® HIV-1/2; Abbott Laboratories, Abbott Park, IL and Capillus® HIV-1/HIV-2; Trinity Biotech, Wicklow, Ireland), had at least one stool sample result, were asymptomatic for HIV disease, and completed a sociodemographic questionnaire. Individuals who had received anthelmintic or antiretroviral therapy within the preceding four weeks and three months, respectively, were excluded from participation. All recruited participants were voluntarily and confidentially counseled and tested for HIV according to previously reported methods.¹²

Of 428 participants who were screened, 297 were eligible for the present survey. The primary reason for ineligibility was advanced HIV disease. Ten participants were excluded because of negative HIV serostatus (i.e., incorrect referral). Seventy-four were coinfecting with HIV-1 and geohelminths or *Schistosoma mansoni*, and 223 were infected with HIV-1 without helminth coinfection. Almost all (88.8%) participants presented clinically at stage 1 or stage 2 of the revised World Health Organization Kigali HIV staging system.¹³ Participants provided one fresh stool sample at the first visit and two preserved stool specimens at the second visit. At the second visit, a trained research nurse, masked from participant helminth status, administered a sociodemographic questionnaire to participants, who were also masked from their helminth status, to determine primary risk factors for helminth infection. Nurses used a standardized protocol to conduct the survey, given in one of the three main languages spoken in Lusaka (Bemba, Nyanja, and English) per participant preference.

Data collection. The structured interview included information regarding age, sex, occupation, education, income, prior history of helminth infection, hygienic behavior, and household parameters. A composite variable was constructed for literacy in which participants were asked to grade their capacity to read and write in any language as poor, fair, or good. Participants who did not report good literacy in any language were categorized as illiterate. Participants provided stool samples in sterilized plastic containers for fresh samples

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and 10% formalin ParaPak® vials (Meridian Diagnostics, Cincinnati, OH) for preserved specimens. Fresh and preserved samples were examined within 24 and 72 hours of collection, respectively, by formol-ether concentration techniques described elsewhere.^{14,15} Among participants whose fresh stool specimens contained helminth ova or larvae, we estimated the intensity of infection by quantitative analysis of egg load according to the Kato-Katz thick smear technique.¹⁶ From the total study population, 2 subjects had five stool samples analyzed, 9 participants had four, 261 had three, 18 had two, and 7 had only one (median = 3, mean = 2.9). For quality control purposes, 10% of study specimens were examined twice by both formol-ether concentration and Kato-Katz methods. Important discrepancies for ova identification or quantification were found in 2 (2.3%) of 86 occasions and were resolved by examination of an additional specimen.

Statistical methods. Data were entered on site, and analysis was performed using SAS software version 9.0 (SAS Institute, Cary, NC). Differences in proportions of prevalent sociodemographic parameters by helminth status and intensity of infection were assessed by Fisher's exact test. We calculated geometric means for quantitative measures of helminth load after $(x + 1)$ transformation of Kato-Katz results. Continuous variables that did not meet normality assumptions were compared using the Wilcoxon rank sum test. To determine a parsimonious set of predictors of helminth infection, we used multivariable logistic regression techniques. Variables that were statistically significant at $P < 0.2$ on univariate analysis were entered into a multivariable model using a backward elimination algorithm.¹⁷ Through this selection procedure, we calculated conditional odds ratios (ORs) and binomial 95% confidence intervals (CIs) for each parameter entered into the model. We included interaction terms for recent helminth infection by literacy and recent food shortage, as well as for frequency of wearing shoes during toilet use by type of household latrine. We used several methods to evaluate the potential influence of household cohabitants on helminth infection. We first examined the association between helminth infection and the number of school age children (6–14 years old) or young children (≤ 5 years old) living in the participant's home. We then repeated the analysis by using the absolute number of persons living in the home and the ratio of persons to rooms as an index measure of crowding. Results did not differ appreciably; therefore, we present the results of the primary analysis that included the number of school age children cohabiting with participants.

Nineteen pairs of individuals in the study cohort were either married or consanguineous relatives. To account for the potential dependency of these observations, we analyzed the data using generalized estimating equations. We assumed that the covariance matrix among correlated observations was unstructured. Because we observed only trivial differences in the results between the two regression methods, we present the results of the logistic analysis and acknowledge that the approach does not fully meet the assumption of independent observations. We also analyzed the intensity of *Ascaris lumbricoides* and/or hookworm infection, as well as the presence of multiple infections as primary outcomes, to test the hypothesis that unhygienic risk factors would correlate with heavy-intensity infections. To account for the unique life cycle and transmission route of *S. mansoni* and, therefore, a potentially unique set of risk factors, we conducted an analy-

sis that excluded persons with schistosomiasis. Both subset analyses yielded findings nearly identical to the results of the primary analysis.

Ethical considerations. Study procedures were reviewed and approved by the University of Alabama at Birmingham, the University of Zambia Research Ethics Committee for the University Teaching Hospital of Lusaka, and the Fogarty International Center of the National Institutes of Health (Bethesda, MD). Written informed consent was obtained from all study participants, and human experimentation guidelines of both institutions (University of Alabama at Birmingham and the University of Zambia Research Ethics Committee for the University Teaching Hospital of Lusaka) involved in conducting the study were followed.

RESULTS

Among participants screened and enrolled in this prevalence survey, 69% were women and 31% were men. Sixty percent were married, 15% were widowed, and 11% were divorced. The mean age of all participants was 31.1 years (SD = 6.3 years), which was the same as the mean age of helminth-infected persons (31.1 years, SD = 6.5 years) and was close to the mean of uninfected persons (30.3 years, SD = 5.8 years).

Helminth prevalence and infection intensity. Of the 297 HIV-seropositive persons screened and interviewed in the study, 24.9% were infected with at least one type of geohelminth or *S. mansoni* (Table 1). Among those with helminths, 52.7% were infected with *A. lumbricoides* and 39.2% were diagnosed with hookworm infection. The remaining helminth-positive participants were infected with *Strongyloides stercoralis*, *S. mansoni*, *Hymenolepis nana*, and *Taenia* species. Nine participants had dual infections, the majority of which were *A. lumbricoides* and hookworm ($n = 6$).

Quantitative ova counts using the Kato-Katz thick smear method were determined for all participants who had evi-

TABLE 1
Prevalence of infection with *Ascaris lumbricoides*, hookworm, *Strongyloides stercoralis*, *Schistosoma mansoni*, *Hymenolepis nana*, and *Taenia* species among human immunodeficiency virus type 1-infected Zambian adults*

Parasite	Prevalence	
	All adults (n = 297)	Helminth infected (n = 74)
<i>A. lumbricoides</i> only	32 (10.8)	32 (43.2)
With hookworm	6 (2.0)	6 (8.2)
With <i>S. mansoni</i>	1 (0.3)	1 (1.4)
Total	39 (13.1)	39 (52.7)
Hookworm only	22 (7.4)	22 (29.7)
With <i>A. lumbricoides</i>	6 (2.0)	6 (8.1)
With <i>S. stercoralis</i>	1 (0.3)	1 (1.4)
Total	29 (9.8)	29 (39.2)
<i>S. mansoni</i> only	5 (1.7)	5 (6.8)
With <i>A. lumbricoides</i>	1 (0.3)	1 (1.4)
With <i>S. stercoralis</i>	1 (0.3)	1 (1.4)
Total	7 (2.4)	7 (9.4)
<i>S. stercoralis</i> only	3 (1.0)	3 (4.0)
With hookworm	1 (0.3)	1 (1.4)
With <i>S. mansoni</i>	1 (0.3)	1 (1.4)
Total	5 (1.7)	5 (6.8)
<i>H. nana</i> only	2 (0.6)	2 (2.7)
<i>Taenia</i> spp†	1 (0.3)	1 (1.4)
Any helminth	74 (24.9)	—

* Data are no. (%) of participants. No participant had *Trichuris trichuria*.

† Participant had a dual infection of *Taenia* spp and *Giardia lamblia*.

dence of helminth infection in at least one stool sample (n = 74). Thirty-two (43.2%) of the 74 helminth-positive individuals had an infection burden below the lower detection limit of the Kato-Katz test (24 eggs per gram [epg] of feces). Fifty-nine (79.7%) of the 74 helminth-infected individuals had light-intensity infections for *A. lumbricoides* (< 5,000 epg), hookworm (<2,000 epg), and *S. mansoni* (< 100 epg) as specified by the World Health Organization classification scheme.¹⁸ The overall geometric mean of (x + 1) helminth burden was 33.2 epg. The geometric means for *A. lumbricoides* and hookworm loads were 89.5 epg and 21.8 epg, respectively. Of the 39 *A. lumbricoides* infections, 35 were of light-intensity (< 5,000 epg), 3 were of moderate intensity (5,000–49,999 epg), and 1 was of heavy-intensity (≥ 50,000 epg). Of the 29 hookworm infections, only 1 was of moderate intensity (2,000–3,999 epg); the rest were light-intensity infections (< 2,000 epg). No one presented with a heavy hookworm infection (≥ 4,000 epg). Only one of the seven participants with schistosomiasis had a detectable ova count of 120 epg. The two individuals infected with *H. nana* had egg burdens of 88 epg and 3,264 epg.

Risk factors. Prevalence of sociodemographic characteristics was largely similar between helminth-infected and hel-

minth-uninfected groups (Table 2). A lower frequency of food shortage within the previous month was reported by helminth-infected persons (*P* = 0.02).

Helminth-infected individuals reported living at their current residence for a shorter period (*P* = 0.04) and were more likely to have recently visited their home village (*P* = 0.06). Among these individuals (n = 38), helminth-infected persons tended to report a slightly longer stay (median = 10.5 days) than their helminth-uninfected counterparts indicated (median = 7 days); data were skewed by two helminth-infected persons who had lived in a rural village for several years and only recently moved to the urban districts.

We did not find any of the measured unhygienic practices to be predictive of helminth infection. We also did not find any composite variables that discriminated persons who reported any four (n = 183) or five (n = 55) of the six unhygienic practices that indicated differences in helminth status. Participants affiliated with the largest language/tribal group in Zambia (Bemba) were almost 30% more likely to be helminth negative, whereas individuals associated with the smaller Tonga tribe were twice as likely to be helminth positive (*P* = 0.2).

The multivariable logistic regression model yielded three

TABLE 2

Sociodemographic characteristics, history of helminth infection, residential information, and hygienic practices among 74 Zambian adults coinfecting with human immunodeficiency virus type 1 (HIV-1) and geohelminths and 223 Zambian adults only infected with HIV-1*

Variable	Helminth infected	Helminth uninfected	<i>P</i>
Sociodemographic characteristic			
Age, median years (range)	29 (19–44)	31 (17–46)	0.1
Sex, male	27 (37.0)	66 (29.5)	0.2
Primary education or lower†	39 (53.4)	108 (48.2)	0.5
Illiteracy	13 (17.8)	61 (27.2)	0.2
Employment			
Unemployed	40 (54.8)	124 (55.4)	0.2
Self	17 (23.3)	72 (32.1)	
Formal	16 (21.9)	28 (12.5)	
Income < 1 US dollar per day‡	50 (68.5)	138 (61.6)	0.3
In past 30 days, ≥ 1 day without food	28 (38.4)	123 (54.9)	0.02
History of helminth infection	20 (27.4)	90 (40.2)	0.05
History of housemate's helminth infection	31 (42.5)	124 (55.4)	0.06
Residential information			
Location			
West Lusaka	19 (26.4)	63 (28.0)	0.9
East Lusaka	53 (73.6)	162 (72.0)	
Duration at current residence, median years (range)	4 (0.04–31)	6 (0.02–36)	0.04
Recent visit to rural village	14 (19.2)	23 (10.3)	0.06
Rent or live in relative's home	64 (87.7)	191 (85.7)	0.8
≤ 2 rooms in household§	51 (69.9)	142 (63.3)	0.3
No. of children 6–14 years old in household			
3–6	13 (17.8)	37 (16.5)	0.1
1–2	28 (38.4)	115 (51.3)	
None	32 (43.8)	72 (32.1)	
Household latrine			
Pit	70 (95.9)	207 (92.8)	0.4
Flush	3 (4.1)	16 (7.2)	
Source of drinking water			
Well, rain, or other	5 (6.8)	14 (6.2)	0.5
Communal tap	51 (69.9)	170 (75.9)	
Home tap	17 (23.3)	40 (17.9)	
Hygiene¶			
Four of 6 unhygienic practices	50 (68.5)	133 (59.4)	0.2
Five of 6 unhygienic practices	15 (20.6)	40 (17.9)	0.6

* Data are no. (%) of participants unless otherwise indicated. *P* values were calculated by Fisher's exact test for categorical variables and Wilcoxon rank sum test for continuous variables.
 † Participants without formal education or with postsecondary education were recorded as completing 0 or 13 years of school, respectively.
 ‡ One US Dollar = 4,499 Zambian Kwacha (September 25, 2003).
 § Excludes bathrooms and passages.
 ¶ Unhygienic practices include rarely washing hands before meals, rarely washing hands after toilet use, rarely wearing shoes outside, rarely wearing shoes when using the toilet, and failure to boil or chlorinate drinking water. Rarely is defined performing the activity less than two of three times.

parameters that were predictive of helminth infection at $P = 0.05$ (Table 3). Study participants who had recently visited a rural area were more than twice as likely (OR = 2.2, 95% CI = 1.0–4.6) to be infected with intestinal helminths ($P = 0.04$). Individuals with a history of prior helminth infection were half as likely to be infected with geohelminths as participants without such a history (OR = 0.5, 95% CI = 0.3–1.0). Persons who reported recent history of food shortage were also less likely (OR = 0.5, 95% CI = 0.3–0.8) to be infected with geohelminths than persons who had not run out of food in the previous month ($P = 0.01$). Concurrent residence with one or two children 6–14 years old (OR = 0.6, 95% CI = 0.3–1.0) and illiteracy (OR = 0.5, 95% CI = 0.3–1.0) were also associated with a lower risk of helminth infection. The associations between either recent food shortage or illiteracy and current helminth status were not modified by prior history of helminth infection.

DISCUSSION

The prevalence of intestinal helminthiasis within an adult HIV-infected population in Lusaka, Zambia was considerably higher (24.9%) in this study than in previous reports from other urban sub-Saharan African settings. Of those individuals infected with helminths, the majority had either *A. lumbricoides* or hookworm, two of the most common parasites in sub-Saharan Africa and other developing regions. Parasite loads were of relatively low intensity and risk factors for and protective factors from infection were limited to a parsimonious set of sociodemographic parameters.

The aggregate prevalence from four previous parasitology

surveys among HIV-infected persons in Lusaka, Zambia was 15%.^{10,11} Estimates from other surveys in developing settings have been somewhat varied. In Ethiopia, more than 70% of adults had intestinal helminth infections regardless of HIV serostatus.⁷ In contrast, fewer than 5% of HIV-infected persons in a rural Tanzanian cohort were infected with intestinal helminths.¹⁹ Among 120 HIV-infected adults in northern India, the prevalence of helminth infection was 1%.²⁰ In contrast, approximately half of an urban Honduran HIV-seropositive cohort of similar size had at least one type of geohelminth infection.²¹ Results from other urban HIV-infected communities in Latin America yielded helminth frequencies of 2–20%.^{6,22} The reason for this variability is most likely multifactorial. Although these studies used formol-ether concentration methods they were still limited by small sample size and reliance on examination of only one stool specimen per participant. Behavioral and ecologic patterns may also contribute to the differences in parasite distributions.^{23,24}

The repertoire of intestinal nematodes that we detected was similar to the findings of other African surveys except for *Trichuris trichiura*, which was not detected in any of the participants in our study. This finding is consistent with results of previous Zambian studies,¹⁰ but contrasts with *T. trichiura* rates of up to 20% in other sub-Saharan African locations.^{24,25} We expected a low frequency of schistosomiasis (2.4%) because there is little opportunity for autochthonous transmission. Although we found a high prevalence of hookworm, we may still have underestimated the intensity of infection, since hookworm ova, if not preserved, are best detected within hours of collection. We limited a detection bias by examining preserved as well as fresh specimens, but cannot rule out the possibility that some ova were missed by Kato-Katz quantification methods on fresh specimens. It is difficult to interpret the prevalence estimate of *S. stercoralis* because larval diagnosis by microscopy, although definitive, is much less sensitive than serologic techniques.²⁶ The importance of identifying *S. stercoralis* infections was originally underscored by the belief that *S. stercoralis* hyperinfection might be more common among patients with acquired immunodeficiency syndrome,²⁷ as is the case with human T cell lymphotropic virus type-1.²⁸ It has since been shown that systemic strongyloidiasis is of comparable prevalence and severity in HIV-infected and HIV-uninfected persons, although there remains debate.²⁹

The majority of helminth-infected participants in this cohort presented with light infections, most likely because we used the most sensitive stool examination techniques available to assess the true burden of parasitic disease among HIV-infected persons in Lusaka, Zambia. Obtaining fecal specimens from three separate days instead of from one day and by using Kato-Katz and formol-ether concentration techniques in addition to direct wet preparation can theoretically increase the sensitivity of ova detection by microscopy from 40–58% to 90–95%, depending on the parasite of investigation.^{30,31}

None of the variables that measured personal hygiene, either in composite or separately, were associated with geohelminth or schistosome infection. Neither were indicators of socioeconomic status such as income, employment, or housing conditions predictive of helminth status. As has been reported in Argentina and Brazil, however, we found that per-

TABLE 3

Multivariable adjusted likelihood of geohelminth infection in association with sociodemographic characteristics, previous infection, and residential information among 74 Zambian adults coinfecting with human immunodeficiency virus type 1 (HIV-1) and geohelminths and 223 Zambian adults infected with only HIV-1*

Variable	Adjusted OR (95% CI)	P
Sociodemographic characteristics		
Age	1.0 (0.9–1.0)	0.2
Illiterate	0.5 (0.3–1.0)	0.06
Employment		
Unemployed	0.6 (0.3–1.3)	0.2
Self	0.6 (0.3–1.2)	0.2
Formal	Reference	
In past 30 days, ≥ 1 day without food	0.5 (0.3–0.8)	0.01
History of helminth infection	0.6 (0.3–1.0)	0.05
History of housemate's helminth infection	0.7 (0.4–1.2)	0.2
Residential information		
Duration at current residence, median years (range)	1.0 (0.9–1.0)	0.4
Recent visit to rural village	2.2 (1.0–4.6)	0.04
No. of children age 6–14 years in household		
3–6	1.3 (0.5–3.1)	0.6
1–2	0.6 (0.3–1.0)	0.06
None	Reference	
Household latrine		
Pit	1.9 (0.5–7.0)	0.3
Flush	Reference	

* OR = odds ratio; CI = confidence interval. Variables with univariate P values ≤ 0.2 were included in the multivariable logistic regression model. ORs, 95% CIs, and P values were calculated before removal from the backward elimination model.

sons who had spent time in a rural area were at increased risk of having helminths in their stool.^{32,33} Participants who reported a history of helminth infection in themselves or among family members had a diminished likelihood of infection in the current study, suggesting that persons who were infected previously were treated for their infection before enrollment in the study. We did not collect information regarding recent treatment with anthelmintics because we initially excluded individuals who had receive anthelmintic therapy within one month prior to study initiation. Reports of diminished food supply and illiteracy were protective for helminth infection. This finding contradicts other studies that report an inverse correlation between measures of socioeconomic status and risk of helminth acquisition.^{34,35} It is possible that individuals of lower socioeconomic status were more likely to be subjected to routine mass deworming campaigns than were more affluent and educated participants. However, when examining the interaction between these measures and prior helminth infection, a surrogate for recent treatment, we found no association.

Although we did not include an HIV-seronegative comparison group, we know from other Zambian studies that our prevalence estimate is higher than previously reported in either HIV-infected or HIV-uninfected cohorts from the same urban population. The lack of an adequate internal comparison group prevents us from drawing comparative inferences about the prevalence of or risk factors for helminth infections across populations of differing HIV serostatus. Neither can we make any direct comparisons with local rural populations because this study was conducted entirely in an urban environment. The cross-sectional study design also limits our ability to comment on the incidence of helminth acquisition and association. We found few associations of hygienic practice, socioeconomic status, and living conditions with helminth status, indicating, perhaps, that risk factors for helminth infection may be neither specific nor easily identified in urban African settings, where the standard of living is often uniformly poor across the population.

Geohelminth infections are generally benign in immunocompetent persons, but may be of particular detriment to the natural history of HIV disease. Work from Ethiopia and Israel has shown that helminth-infected persons exhibit a number of immunologic abnormalities that may increase their susceptibility to HIV infection or may increase the rate of disease progression if these persons are already infected with the virus.^{36,37} The same group of investigators showed that treatment and successful elimination of enteric helminths in individuals coinfecting with HIV and helminths significantly decreased plasma HIV RNA levels.³⁸ Although subsequent studies have yielded conflicting results,^{39,40} it is clear that helminths have a disruptive influence on host immunity. The potential for adverse interactions between helminth infections and HIV, coupled with a high helminth prevalence of 25% in this urban, HIV-infected cohort, suggests that diagnosis and treatment of intestinal helminths should be a routine part of HIV care in parasite-endemic developing countries. Where this approach is logistically infeasible, mass deworming strategies may provide an appropriate alternative given the low cost and low toxicity of anthelmintics and the high prevalence rates of intestinal helminth infection expected.

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