

Schistosomiasis among Young Children in Usoma, Kenya

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Abstract. Although schistosomiasis burden is greatest among school-age children (SAC) (6–15 years of age), infection among preschool-age children (PSAC) (1–5 years), may be underestimated in endemic areas. We conducted a cross-sectional study evaluating *Schistosoma mansoni* infection among children 1–15 years of age in a highly endemic community in Kenya. Diagnostic tests included stool exam (Kato/Katz technique), serum testing for schistosome-specific antibodies, and urine testing for circulating cathodic antigen (CCA). Overall, 268 SAC and 216 PSAC were enrolled; prevalence increased with age, with 14% of 1 year olds and more than 90% of children > 10 years of age infected. Stool exam was more sensitive among SAC than PSAC, but performance was similar after adjusting for infection intensity (based on CCA). Schistosomiasis poses a threat to PSAC in endemic areas, and stool exam may underestimate the prevalence of infection. Control programs in such areas should consider PSAC in addition to SAC.

INTRODUCTION

Chronic schistosomiasis affects more than 200 million people worldwide.^{1,2} Standard age prevalence curves for *Schistosoma mansoni*, which are based on egg excretion, show that both prevalence and intensity of infection peak between 10 and 15 years of age, after which prevalence declines gradually over years and infection intensity decreases more rapidly.³ The age distribution of infection rates and intensity is generally attributed to high levels of contact with cercariae-contaminated water among school-aged children and adolescents followed by less water contact and the development of an acquired protective immunity against infection in older adolescents and adults.^{4–6} Because of their importance in terms of the prevalence, morbidity, and transmission of schistosomiasis, along with the logistical ease of distributing praziquantel in educational settings, mass treatment of school-aged children is a cornerstone of schistosomiasis control activities.^{7,8}

In contrast, younger children are often thought to be not infected with schistosomes or to have such low intensity infections that they do not suffer morbidity. Most mass treatment programs have not been designed to include them and younger children are often not even screened for the possibility of infection.⁹ However, in areas endemic for schistosomiasis, very young children are also in regular contact with water in locations where infected snails are present and infants are bathed in water where transmission is occurring.^{10–13} Infections in young children may be missed because they are not usually examined or the testing method most commonly used for epidemiologic research (examination of a single stool specimen by Kato–Katz thick smears) may not be sufficiently sensitive, particularly in detecting light infections.^{14,15} Indeed, when more sensitive techniques such as multiple stool samples or serologic assays have been used to survey young children, sizeable proportions have been found to be infected.^{11,13,16}

Immunity may also influence the ability to detect schistosome infections in young children. Previous studies on human infection with *S. mansoni* suggest a role for the immune response in efficient egg excretion.¹⁷ It is possible that younger children have not developed the appropriate immune responses

to excrete eggs, leading to false negative results when stool examinations are used for diagnosis. We carried out a cross-sectional observational study of the prevalence of *S. mansoni* among children in a highly endemic area using both serologic assays and stool exams to detect infections. We tested the sensitivity of single and multiple stool exams compared with serologic diagnosis across age groups.

MATERIALS AND METHODS

Study setting and population. The study location was Usoma, a small community on the shores of Lake Victoria near Kisumu in Western Kenya. High rates of *S. mansoni* infection have been documented among men from the community who are self employed as sand harvesters; such work involves extensive contact with lake water. No mass drug administration with praziquantel had been carried out in Usoma before the study. We attempted to enroll all children 12 months to 15 years of age from the community in the study. On the basis of a census completed earlier in the year, we anticipated that there would be ~680 children in Usoma in this age range. Children < 12 months of age were excluded because of potential persistence of maternal antibody that could lead to false positive serologic test results. The study protocol was approved by the Scientific Steering Committee of the Kenya Medical Research Institute (KEMRI), the Ethical Review Committee of Kenya, and the Institutional Review Board of the Centers for Disease Control and Prevention.

Data collection. After obtaining informed consent from parents (and assent from child participants > 7 years of age), a questionnaire was administered to the parents of enrolled children to gather demographic and epidemiologic information, such as age, gender, duration of residency in the community, and variables related to *S. mansoni* exposure. Heights and weights were measured using standard procedures and Z-scores were calculated for height-for-age and body mass index (BMI)-for-age based on World Health Organization (WHO) growth standards.^{18,19}

Quantitative determination of *S. mansoni* and soil-transmitted helminths was performed through evaluation of stool by the Kato/Katz fecal thick smear technique. The children were asked to provide fresh stool samples, one per day produced on three consecutive days, which were then used to prepare duplicate slides that were examined for the presence of eggs.

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Each slide was read by at least two well-trained technologists, yielding a total of 12 egg counts per child from six fecal smears. Arithmetic means of the 12 egg counts were calculated and expressed as eggs per gram (epg) of stool, and classified as light- (1–99 epg), moderate- (100–399 epg), or heavy-intensity (≥ 400 epg) *S. mansoni* infections.² A finger-stick blood sample was tested using the schistosome adult worm protein (SWAP)-specific enzyme-linked immunosorbent assay (ELISA).²⁰ A child with one or more positive stool slides or with positive SWAP ELISA results was considered infected with *S. mansoni*. Because Usoma has not been targeted by any preventive chemotherapy, positive serologic results were likely to represent true infections. A fresh urine sample was also requested and was tested with a commercially available circulating cathodic antigen (CCA) assay (Rapid Medical Diagnostics, Pretoria, South Africa), which includes a standard curve that allows for a gross estimate of infection intensity.^{20,21} Urine CCA was detected by carbon-conjugated antibody and measured as either negative or as 1-, 2-, or 3-plus. Among those children who tested positive for *S. mansoni* by stool and/or SWAP ELISA, infections were classified as low intensity (CCA negative or 1-plus), or high intensity (CCA 2- or 3-plus).

Blood samples were also used to test for malaria and anemia. Thick blood smears were stained with Giemsa and examined for the number of malaria parasites per 300 leukocytes. Infection status was defined by the presence of a single parasite. Hemoglobin levels were determined using a portable, battery-operated hemoglobinometer (HemoCue, Angelholm, Sweden). Anemia was defined according to Kenyan clinical guidelines: < 10.0 g/dL for children < 5 years of age, < 11.0 g/dL for children 5 to 8 years of age, and < 12.0 g/dL for children ≥ 9 years of age; anemia was classified as mild if hemoglobin was > 8.0 g/dL, moderate if 5.0–8.0 g/dL, and severe if < 5.0 g/dL.²²

Treatment with praziquantel, albendazole, and Coartem (artemether-lumefantrine) was provided for schistosomiasis, other helminths, and malaria infections, respectively, as needed. Praziquantel was dosed based on weight (single dose of 40 mg/kg). The treatment of children < 4 years of age was overseen by a local pediatrician, because safety data are limited for this age group.²³ For children too young to swallow pills, praziquantel pills were crushed and administered mixed with water.

Data handling and analysis. Questionnaire data were collected on handheld computers that were programmed using Visual CE (Syware, Inc., Cambridge, MA). Laboratory results were entered using Microsoft Excel (Microsoft Corporation, Redmond, WA). Data were analyzed using SAS Enterprise Guide version 4 (SAS Institute Inc., Cary, NC). Proportions were calculated with 95% confidence intervals (CI). The sensitivities of diagnostic tests were evaluated; a child with a positive test for *S. mansoni* by stool and/or SWAP ELISA was considered a true positive. Comparisons across groups were done using Fisher's exact test and *P* values < 0.05 were considered significant.

RESULTS

A total of 484 children were enrolled, with ages ranging from 1 to 15 years. The mean age was 6.8 and the median was 7 years. Study subjects were divided into two age groups: preschool-age children (PSAC) aged 1–5 years, of which there were 216; and school-age children (SAC) aged 6–15 years, of

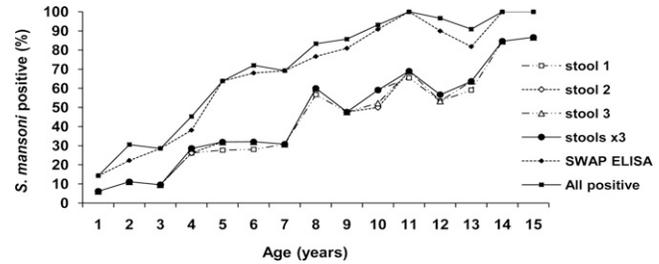


FIGURE 1. *Schistosoma mansoni* infection prevalence by stool and/or schistosome adult worm protein (SWAP) enzyme-linked immunosorbent assay (ELISA) by age.

which there were 268. The overall prevalence of schistosomiasis for the study population was 39% (95% CI = 34–43) by stool examination, 62% (95% CI = 57–66) by SWAP ELISA, and 65% (95% CI = 61–69) by stool and/or SWAP ELISA.

Figure 1 depicts the proportion of children with *S. mansoni* by stool and/or SWAP ELISA by age. The prevalence rate was 14% among 1 year olds and increased steadily with age. More than 90% of children over age 10 were infected. Each of three single stool exams achieved similar results, and the use of multiple stool exams did not increase the sensitivity of the test.

Schistosoma mansoni infection by age group (SAC versus PSAC) is presented in Table 1. By all testing modalities, a greater proportion of SAC were infected with *S. mansoni* compared with PSAC. Overall, 37% of PSAC and 88% of SAC were considered to have true infections ($P < 0.0001$). Among all infected children, a significantly greater proportion of SAC compared with PSAC had intense infections, as indicated by a urine CCA result of 2- or 3-plus. Intensity as measured by epg was also higher among SAC than PSAC. Among PSAC children with positive stool samples for *S. mansoni*, 24 (63%) had low-intensity infections, 9 (24%) had moderate-intensity, and 5 (13%) had heavy-intensity infections. Among SAC, the numbers (and proportions) with low-, moderate-, and heavy-intensity infections were 60 (40%), 62 (42%), and 27 (18%), respectively ($P = 0.044$).

Several well-recognized risk factors for schistosomiasis were more common among SAC than among PSAC (Table 1). All but one of the parents of SAC reported that the child ever visited the lake, compared with 71% of parents of PSAC

TABLE 1
Schistosoma mansoni infection, lake water exposure, and anti-parasitic treatments by age group*

	PSAC N = 216		SAC N = 268		P value
	n	%	n	%	
Stool-positive	38	17.6	149	55.6	< 0.0001
Serology-positive	73	33.8	226	84.3	< 0.0001
Stool- and/or serology-positive	79	36.6	235	87.7	< 0.0001
Urine CCA ++/+++†	19	27.1	106	48.2	0.002
Ever visit lake	154	71.3	267	99.6	< 0.0001
Swim in lake	73	47.4	197	73.8	< 0.0001
Wash clothes in lake	0	0	56	21.0	< 0.0001
Bathe in lake	151	98.0	257	96.2	0.390
Visit lake ≥ 4 ×/week	40	26.0	87	32.6	0.186
Bathe in lake water	197	91.2	253	94.4	0.211
Ever treated for schistosomiasis	0	0	0	0	–
Ever treated for malaria	216	100	268	100	–
Treated in past 3 months	96	44.6	90	33.8	0.018

* PSAC = preschool-age children; SAC = school-age children.

† Compared with circulating cathodic antigen (CCA) negative or “+”; denominator includes stool- or serology-positive with CCA results, $N = 290$.

TABLE 2
Schistosomiasis-associated morbidities by age group and infection status

	PSAC				P value	SAC				P value
	<i>S. mansoni</i> positive* N = 79		<i>S. mansoni</i> negative N = 137			<i>S. mansoni</i> positive* N = 235		<i>S. mansoni</i> negative N = 33		
	n	%	n	%		n	%	n	%	
Anemia†	33	41.8	65	47.4	0.479	97	41.3	7	21.2	0.035
Mild (> 8.0 g/dL)	22	27.8	48	35.0	0.295	82	34.9	4	12.1	0.009
Moderate (5.0–8.0 g/dL)	11	13.9	16	11.7	0.672	14	6.0	3	9.1	0.449
Severe (< 5.0 g/dL)	0	0	1	0.7	1.000	1	0.4	0	0	1.000
Height-for-age Z-score‡ < -2	24	30.4	42	30.7	0.883	53	22.6	5	15.2	0.821
BMI-for-age Z-score‡ < -2	4	5.2	11	8.4	0.299	2	3.8	0	0	0.708

* Positive by stool exam and/or schistosome adult worm protein (SWAP) enzyme-linked immunosorbent assay (ELISA).

† < 10.0 g/dL for children < 5 years, < 11.0 g/dL for children aged 5–8 years, and < 12.0 g/dL for children aged ≥ 9 years.

‡ Excludes biologically implausible values.

PSAC = preschool-age children; SAC = school-age children; BMI = body mass index.

($P < 0.0001$). Swimming and washing clothes in the lake were also significantly more common among SAC compared with PSAC. However, among those children who ever visited the lake, more than 95% of both PSAC and SAC bathed in the lake, and the frequency of visiting the lake was similar across age groups. No parent reported a child having ever been treated for schistosomiasis. In contrast, all children from both age groups had received treatment of malaria; PSAC were significantly more likely to have received antimalarials within the past 3 months. No parents were able to specify whether the antimalarial received had been Coartem (which also has antischistosomal activity²⁴).

Among PSAC (Table 2) there was no association between *S. mansoni* infection and related morbidities such as anemia, stunting (as indicated by the height-for-age Z-score), or wasting (as indicated by the BMI-for-age Z-score). Among SAC, *S. mansoni* infection was significantly associated with anemia, particularly mild anemia. Schistosomiasis did not appear to have any impact on stunting or wasting in the older age group.

Table 3 summarizes the sensitivities by age group of stool and the SWAP ELISA for detecting *S. mansoni* infections. All stool exams—whether single or a composite of three exams—were significantly less sensitive for detecting infection in PSAC compared with SAC. In contrast, the SWAP ELISA detected similar levels of infection across both age groups. After controlling for infection intensity by stratifying the *S. mansoni*-positive children into those with a CCA that was negative or +, and those with ++ or +++ (Table 4), the sensitivities of single and multiple stool exams were also similar across age groups.

The prevalences of *S. mansoni*, malaria, *Trichuris trichiura*, hookworm, and *Ascaris lumbricoides* infections among the

study population by age are presented in Figure 2. *Schistosoma mansoni* was the most common parasitic infection identified across all ages. Table 5 compares the prevalence of other parasitic infections among those children infected and uninfected with *S. mansoni*. *Trichuris trichiura* and malaria infections were significantly associated with *S. mansoni* infection.

DISCUSSION

In this cross-sectional, community-wide study of children in an area that is highly-endemic for schistosomiasis where mass chemotherapy has not been used, we found high rates of infection among children of all ages. As expected, rates of infection were highest among SAC, with nearly 90% of children in this age group infected. All 14 and 15 year olds tested were positive for *S. mansoni*. We also found surprisingly high prevalence rates among young children, with 14% of 1 year olds infected and a prevalence that increased steadily with age. Among PSAC, more than a third of the children were infected with a disease that is not generally considered a public health problem in this age group. Our data suggest that, similar to older children, young children may be exposed to *S. mansoni* through bathing in lake water—whether they go to the lake to bathe or bathe at home with water carried from the lake. Other studies have reported high rates of *S. mansoni*^{7,11,13,16} and *Schistosoma haematobium*^{10,25,26} among young children in endemic areas. Our study findings support other authors' conclusions that schistosome infections can be common in children younger than school age in endemic areas.^{9,13}

TABLE 3

Sensitivities of single stool exams, multiple stool exams, and SWAP ELISA by age group*

	<i>S. mansoni</i> positive PSAC N = 79		<i>S. mansoni</i> positive SAC N = 235		P value
	n	%	n	%	
Stool 1	35	44.3	144	61.3	0.012
Stool 2	37	46.8	145	61.7	0.025
Stool 3	38	48.1	145	61.7	0.036
Stool ×3	38	48.1	149	63.4	0.018
SWAP ELISA	73	92.4	226	96.2	0.220

* Positive by stool and/or schistosome adult worm protein (SWAP) enzyme-linked immunosorbent assay (ELISA) considered true positive.

PSAC = preschool-age children; SAC = school-age children.

TABLE 4

Sensitivities of single and multiple stool exams, controlling for infection intensity*

	<i>S. mansoni</i> positive PSAC, N = 50		<i>S. mansoni</i> positive SAC, N = 113		P value
	n	%	n	%	
Urine CCA neg/+					
Stool 1	15	30.0	43	38.0	0.377
Stool ×3	17	52.2	47	50.1	0.389
	<i>S. mansoni</i> positive PSAC, N = 19		<i>S. mansoni</i> positive SAC, N = 106		P value
	n	%	n	%	
Urine CCA ++/+++					
Stool 1	15	79.0	91	85.8	0.488
Stool ×3	15	79.0	92	86.8	0.475

* Positive by stool and/or schistosome adult worm protein (SWAP) enzyme-linked immunosorbent assay (ELISA) considered true positive.

PSAC = preschool-age children; SAC = school-age children; CCA = circulating cathodic antigen.

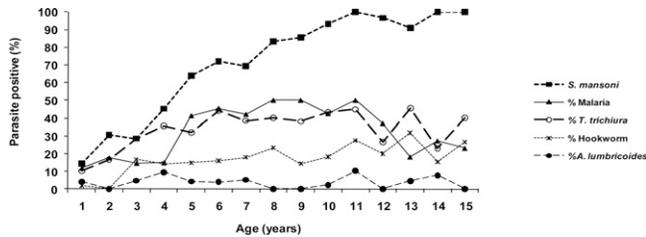


FIGURE 2. Prevalence of *Schistosoma mansoni*, malaria, *Trichuris trichiura*, hookworm, and *Ascaris lumbricoides* infections by age.

Despite the substantial prevalence of infection among PSAC, schistosomiasis-related morbidities were not associated with infection in this age group. *Schistosoma mansoni* was associated with anemia in older children—a finding consistent with numerous other studies. The association remained significant after adjusting for infection with malaria and soil-transmitted helminths (data not shown). The lack of schistosomiasis-associated morbidities in the young children in this study may reflect lower intensity infections that perhaps do not lead to measurable sequelae. Yet there is growing recognition that even low intensity infections can have important long-term consequences for the health of affected individuals,²⁷ and it is possible that consequences of infection at a young age may take years to manifest and may not become apparent in the short term despite ongoing harm to the infected child.

The significantly higher prevalence of malaria and *T. trichiura* infections observed among *S. mansoni*-infected children suggests that children with schistosomiasis may also be at increased risk for additional parasitic infections. This association may be particularly important among PSAC, because young children suffer the greatest burden of malaria morbidity and mortality.²⁸ However, this observation requires further investigation before firm conclusions can be drawn.

With respect to the sensitivity of stool exams for *S. mansoni*, in our study three stools performed no better than a single stool exam across all ages. Although other studies have found single stool exam to be less sensitive than multiple stool exams, it is possible that the relatively high intensity of infection observed in our study population may have improved the yield of a single stool exam. Nonetheless, stool exams were overall less sensitive than serology, and had particularly poor sensitivity among PSAC. However, after controlling for infection intensity using CCA as a crude marker of worm burden, the sensitivity of stool was similar across age groups.

The study had several limitations. The lack of a gold standard for diagnosing schistosomiasis based on serology meant that our results may have been affected by misclassification

bias. We also had limited quality assurance of stool sample collection—containers for the second and third stool samples were left at the house and picked up the following day. Thus, it was not possible to verify that stool samples were actually produced by the child that submitted the specimen. Usoma is a single community that is highly endemic for *S. mansoni*. The results are therefore not directly applicable to areas with lower levels of transmission. Finally, urine CCA is a crude proxy for infection intensity and may not fully explain the difference in stool sensitivity observed between PSAC and SAC.

In conclusion, our findings show that young children are indeed at risk for schistosomiasis infection. And although PSAC are currently not targeted by schistosomiasis control activities, it may be worthwhile for programs to consider including them in preventive chemotherapy campaigns, especially where the prevalence is high among SAC.^{9,13} The use of praziquantel among young children has been hindered by a lack of safety data among children < 4 years of age,^{9,23} and no widely available liquid formulation; however, recent studies in which young children have been treated with praziquantel have reported no major adverse effects.^{10,11,13} We found that the sensitivity of stool exams for *S. mansoni* was limited, especially among PSAC; the observed difference in its performance across age groups is likely a function of infection intensity. Further investigation of the long-term effects of infection in young children is necessary to better understand how schistosomiasis impacts community health. In areas with a high prevalence of infection, the contribution of young children to transmission in the community should be considered when designing and implementing strategies to control this disease.

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TABLE 5

Prevalence of other parasitic infections by *Schistosoma mansoni* infection status

	<i>S. mansoni</i> positive* N = 294†		<i>S. mansoni</i> negative N = 160†		P value
	n	%	n	%	
<i>Trichuris trichiura</i>	114	36.3	44	25.9	0.012
Hookworm	56	17.8	23	13.5	0.248
<i>Ascaris lumbricoides</i>	12	3.8	7	4.1	1.000
Malaria‡	111	37.8	33	20.1	0.002

* Positive by stool exam and/or schistosome adult worm protein (SWAP) enzyme-linked immunosorbent assay (ELISA).

† Denominators vary because of missing values for other parasitic infections.

‡ Malaria results unavailable for 30 children, N = 454.

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