The Relative Influence of Polyparasitism, Environment, and Host Factors on Schistosome Infection

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Abstract. Where prevalence of geohelminths and schistosomes is high, co-infections with multiple parasite species are common. Previous studies have shown that the presence of geohelminths either promotes or is a marker for greater prevalence and intensity of *Schistosoma mansoni* infections. Some of this apparent synergy may simply represent shared conditions for exposure, such as poor sanitation, and may not suggest a direct biologic interaction. We explored this question in a study of 13,279 school children in Jequié, Bahia, Brazil, with a survey of demographic characteristics and stool examinations. Cross-sectional analysis revealed a statistically significant increase in the prevalence and intensity of *S. mansoni* infection with increasing numbers of geohelminth species (OR 2.5, 95% CI 1.38–3.64). Less than 20% of the strength of this association was contributed by socioeconomic status or environmental conditions. Thus, polyparasitism itself, as well as intrinsic host factors, appears to produce greater susceptibility to additional helminth infections.

INTRODUCTION

Among helminth infections, schistosomiasis is considered one of the most important health problems, not only for its high prevalence but also for its potential to develop into severe clinical forms precisely at a time of greatest human productivity.[1] More than 200 million people are infected with schistosomes according to the World Health Organization, and 500–600 million are at risk because of inadequately protected water supplies and precarious sanitary conditions.[2]

In most areas, schistosomiasis is not the only chronic parasitic infection found. It is estimated that 26–68% of the individuals with schistosomiasis are carriers of an additional helminthic infection, such as hookworms, *Ascaris lumbricoides*, or *Trichuris trichiura*.[3] These parasites can aggravate the morbidity due to schistosome infection, especially in young children.[4]

Various authors have demonstrated a synergism between simultaneous infection with geohelminths and the burden of schistosomiasis,[5–8] but whether this effect was the result of shared environments, host factors, intrinsic parasite biology, or a combination of these factors is usually not explored. This study will address the relative contribution of these different factors by evaluating correlations between prevalence and intensity of *Schistosoma mansoni* infection and co-infection with hookworms, *A. lumbricoides*, and *T. trichiura*. We further evaluated the influence of socioeconomic status and environmental conditions.

MATERIALS AND METHODS

Population and study area. The study was located in the city of Jequié, a district center in the southern region of the state of Bahia, Brazil. The total population of the municipal district was 120,396 in 1991. This city is situated in one of the most prosperous districts in the State, and it constitutes an economic pole of regional attraction for surrounding cities and rural areas. The Contas River flows through the district. This river is highly polluted with raw sewage from homes and businesses present along its banks. It is fed by equally polluted streams flowing from the rest of the city.

In the course of 2 months, some 13,279 individuals 7–17 years of age were examined for intestinal helminths. This corresponds to 40% of individuals in this age range who were resident in the city.

Informed consent. Informed consent was obtained for all study subjects before clinical and parasitologic studies. This study was approved by the Human Investigation Committees of University Hospitals of Cleveland and of the Oswaldo Cruz Foundation, Salvador, Bahia, Brazil. Individuals infected with intestinal helminths were treated with albendazole, and individuals infected with *S. mansoni* were treated with oxamniquine at WHO-recommended doses.

Stool examination. The collection of stool samples was carried out by house-to-house distribution of lidded plastic containers that were collected on the following day. The Kato–Katz quantitative stool exam,[9] carried out by laboratory staff trained by the National Health Foundation (FNS), was used to determine parasite species and intensity of infection. Identification of hookworm eggs was performed 2 hours after preparing the slides. Quality control for the stool examinations was carried out by a technician hired independently for this job who re-examined 10% of all slides.

Index of socioeconomic and environmental conditions. An indicator of the environmental and household conditions was constructed from demographic information obtained by interviews with childcare providers. A questionnaire was administered for a sample of 1,766 schoolchildren infected with a low or moderate intensity of at least 1 species of helminth. The sample was obtained in areas of the city with the highest prevalence of *S. mansoni* infections. Variables describing household conditions and sanitation were dichotomized as favorable (0) or unfavorable (1) and tested for statistically significant associations with the presence or absence of anemia in a logistic regression model. Those that remained significant (*P* < 0.05) were included in the index (Table 1). Thirteen variables were found to be significant, and the sum of

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TABLE 1
Prevalence and intensity of *S. mansoni* infection by number of geohelminth species observed in schoolchildren

| No. of geohelminth species | Infection by *S. mansoni* | | | | | Total no. examined |
| | Positive fecal exam | | | Negative | | |
	N	%*	Average (epg)†	N	%	
0	785	11.9	97.5	5,815	88.1	6,600
1	816	22.1	109.8	2,872	77.9	3,688
2	740	30.0	120.5	1,727	70.0	2,467
3	174	33.2	122.0	350	66.8	524
Total	2,515	18.9	109.5	10,764	81.1	13,279

* χ^2 test for trend in prevalence, $P < 0.001$.
† Test for linearity, $P < 0.001$.

TABLE 2
Prevalence of infection by *S. mansoni* by species of infecting geohelminth

| Geohelminth species | Infection by *S. mansoni* | | | | Individuals examined |
| | Positive | | Negative | | |
	N	%	N	%	N
None	785	11.9	5,815	88.1	6,600
*A. lumbricoides**	311	20.0	1,243	80.0	1,554
T. trichiura	462	24.1	1,458	75.9	1,920
Hookworm	43	20.1	171	79.9	214
Hookworm + *T. trichiura*	596	29.2	1,447	70.8	2,043
Hookworm + *A. lumbricoides*	44	36.7	76	63.3	120
T. trichiura + *A. lumbricoides*	100	32.9	204	67.1	304
T. trichiura + *A. lumbricoides* + hookworm	174	33.2	350	66.8	524

* Only comparing the prevalence of *A. lumbricoides* with *T. trichiura*, $P = 0.004$.

values for each of these variables was used as the index of socioeconomic status, environmental, and living conditions.[10] The 50th percentile of the index for this community was used to define those with better (score 0–6) or worse (score 7–13) living conditions.

Statistical analysis. The prevalence and intensity of infection with *S. mansoni* were compared with the number of infecting intestinal helminth species by χ^2 and t tests, respectively. Multivariable logistic regression was used to evaluate the effect of multiple intestinal helminth infections on the prevalence of *S. mansoni*, where the infection with *S. mansoni* was the dependent variable coded as not infected (0) or infected (1). The independent variable was the number of infecting geohelminth species consisting of a dummy variable (1 geohelminth) with two levels (2 and 3 geohelminths). This model was adjusted for sex, age, socioeconomic index, and environmental conditions. The magnitude of association was estimated by calculating the odds ratio using the 95% CI as a measure of precision, and all statistical analyses were two-tailed. All data were analyzed with the computer program SPSS/PC+, v. 10.0 (SPSS, Inc., Chicago, IL).

RESULTS

Among the 7- to 17-year-old students in the study, prevalence of *S. mansoni* was 18.9%, of *A. lumbricoides* 31.8%, of
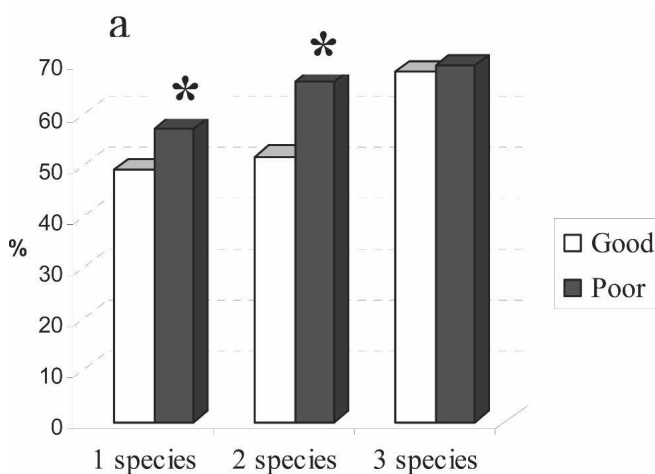
T. trichiura 35.8%, and of hookworms 8.6%. The data reveal a statistically significant trend of an increase in prevalence ($P < 0.001$) and intensity ($P < 0.001$) of infection by *S. mansoni* as the number of associated intestinal parasites increased. In the absence of infection by these intestinal parasites, prevalence of infection by *S. mansoni* was 11.9%. This value is not statistically different from that in the presence of one species of intestinal helminth (22.1%), but in the presence of 2 (30.0%) or 3 species (33.2%), the prevalence is nearly triple that where *S. mansoni* alone was found. The parasite burden of *S. mansoni* infection varied from 97.5 eggs/g of feces (epg) when taken as isolated infection, increasing, respectively, to 109.8, 120.5, and 122.0 epg when associated with 1, 2, or 3 species ($P < 0.001$). This effect was independent of the combination of the additional infecting species (Table 2).

Because these infections have been linked to poverty and poor sanitation, the effects of economic and environmental conditions were studied on a sample of 1,766 children. The prevalence of schistosome infection increased with increasing numbers of infecting geohelminths (Figure 1a). When stratified for socioeconomic conditions, those with poor socioeconomic and environmental conditions had significantly higher
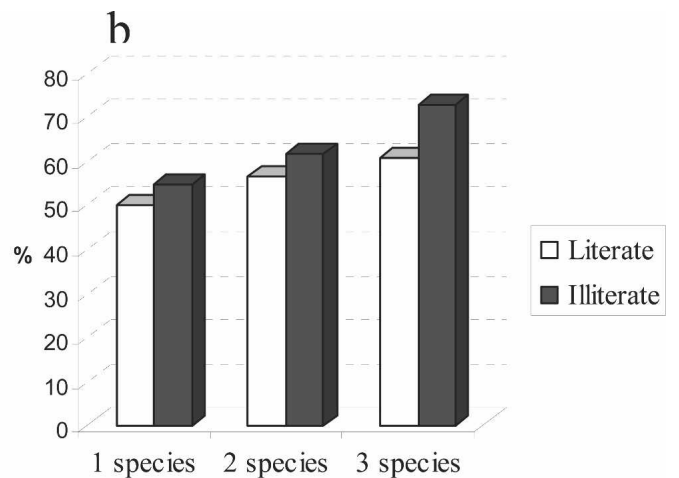

FIGURE 1. Prevalence of *S. mansoni* by socioeconomic status and environmental conditions. (a) Percent (%) of children within each category of good or poor socioeconomic status and environmental conditions who were infected with *S. mansoni*. *Differences between groups are significant, $P = 0.02$ and $P < 0.01$, respectively. (b) Percent (%) of children living with a head of household, who is illiterate or literate, who were infected with *S. mansoni*. There were no significant differences.

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TABLE 3

Contribution of sex, age, socioeconomic, and environmental conditions to the association of geohelminth infection with *S. mansoni* prevalence

No. of infecting helminths	OR unadjusted (95% CI)	OR adjusted* (95% CI)	% Change after adjustment
1 species	1 (reference)	1 (reference)	–
2 species	1.32 (1.08–1.60)	1.33 (1.07–1.63)	−0.8%
3 species	2.05 (1.38–3.64)	1.71 (1.12–2.61)	16.6%

* Adjusted for sex, age and socio-economic level, environmental conditions.

prevalence of schistosome infection (1 species, $P = 0.024$; 2 species, $P < 0.001$), except those with 3 infecting species ($P = 0.875$). The educational level of the head of household was not significantly different for any category of infection (Figure 1b).

To estimate the relative contribution of the host factors of socioeconomic conditions, age, and sex, we carried out logistic regression analysis adjusting for these factors (Table 3). Only 16% of the unadjusted odds ratio could be attributed to these variables, indicating that the majority of this effect was due to some aspect of the intrinsic host biology or that polyparasitism itself is responsible for the apparent increased susceptibility to *S. mansoni.*

DISCUSSION

These studies reveal an increase in the prevalence and intensity of infection by *S. mansoni* associated with an increase in the number of species of intestinal parasites hosted. The biologic basis for this phenomenon is of course a result of factors both extrinsic and intrinsic to the host. The relative weights of the individual's socioeconomic status and environmental conditions, however, in this study were minor compared with other factors associated with the host–parasite interaction. Studies of host genetics measuring variance of worm burden have likewise demonstrated a low degree of contribution from environmental factors to this variance.[11]

On the host side, it is possible to speculate that genetic factors and/or certain behaviors result in a higher susceptibility to co-infection in certain population groups. This, too, has been supported by recent genetic studies of parasite infection, where up to 66% of the variation in *S. mansoni* worm burden was attributed to a single or a few host genes.[12] What has been less widely discussed, perhaps, is the contribution of multiple infecting species (polyparasitism) itself and its affects on susceptibility.

From our results, polyparasitism is not merely a marker for poor sanitation and economic conditions; the data presented may also suggest that multiple infections in themselves may increase susceptibility. There is evidence that the risk of an individual presenting with greater morbidity from parasitic infection could result from a combination of the number of infecting helminth species as well as the intensity of each infection.[6] Clinical and epidemiologic studies from various parts of the world have indicated a positive association between the intensity of several infection and morbidity by *S. mansoni.*[4] Other studies have shown that there are progressively more negative effects of *S. mansoni* infection on hemoglobin levels[10] and cognitive functions[13,14] when associated with increasing numbers of infecting geohelminth species.

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