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THE EFFECT OF MEDICATION ON QUESTIONNAIRE ANALYSIS OF CHILDREN WITH *SCHISTOSOMA MANSONI* INFECTION IN TANZANIA

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Abstract: The effect of mass treatment on questionnaire results in the diagnosis of schistosomiasis mansoni was examined in 267 school children in an endemic area of Tanzania by Kato-Katz analysis of fecal specimens. The questionnaire asked for information about self-diagnosis, abdominal symptoms, blood in stools, history of wild water contact, stool examination and medication for schistosomiasis, and knowledge of the disease. A logistic regression analysis disclosed a significant association between schistosomiasis and "diarrhea" ($p = 0.007$; odds ratio, 32.0; confidence interval, 2.5 - 403.3) and "abdominal enlargement" ($p = 0.003$; odds ratio, 15.2; confidence interval, 2.6 - 90.1) among 61 children who had no history of medication for schistosomiasis. The sensitivity and specificity of the model were 86% and 64%, respectively. In contrast, no significant correlation was observed either for the 116 treated children, or for all the 267 children after the mass treatment. We conclude, therefore, that for children who had no history of medication for schistosomiasis, the questionnaire for abdominal manifestations provides reliable information on *S. mansoni* infection. However, once a child takes medication, the questionnaire becomes unreliable. This observation suggests that immunomodulation by anti-schistosomiasis drugs that kill adult worms exerts an effect on the appearance of abdominal manifestations and might explain the ambiguity of clinical symptoms in chronically infested patients, except in terminal cases. Further studies are required to develop a simple, rapid and cost-effective diagnostic method for monitoring *S. mansoni* infection after medication in local areas without resort to laboratory-based identification of schistosomiasis.
Key words: *Schistosoma mansoni*, self-diagnosis, selective mass treatment, Tanzania

INTRODUCTION

Schistosomiasis is one of the widespread parasitic diseases with important public health implications in sub-Saharan countries. Disease control depends mostly on medication treatment, because praziquantel, the drug of choice, is safe and relatively inexpensive [1]. Several approaches for community-based treatment have been developed, including mass treatment, selective population treatment and selective group treatment [2]. The main target population is school-age children between 5 and 15 years old, because they show the highest prevalence and intensity in the entire population [2, 3, 4] and because they are the main source of the transmission of infection. Following WHO recommendations, school-based mass treatment with praziquantel has been conducted in many high prevalence areas [5].

The strategy emphasizing school-based mass treatment, however, is not cost-effective in low prevalence areas. The prevalence usually declines to a low level after a series of mass treatments in high prevalence areas. Subsequently, the school-based mass treatment approach should be replaced

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with selective treatment. The most reliable diagnostic method for *Schistosoma mansoni* (*S. mansoni*) infection is detection of eggs in feces, with a rapid and simple Kato-Katz thick smear stool examination being applied to this end. However, well-trained health personnel and microscopes are required for this laboratory diagnosis, and it is laborious, time-consuming, and expensive. Therefore, a similarly rapid and simple yet cost-effective individual diagnostic method is required. This kind of simple method has been developed for the screening of *Schistosoma haematobium* infection based on self-reported haematuria and self-diagnosis [6, 7, 8, 9]. Regarding *S. mansoni* infection, several morbidity studies have been carried out since the early 1970s, before the discovery of an effective medication (praziquantel). These studies found that *S. mansoni* frequently causes abdominal pain, blood in stool, bloody diarrhea, diarrhea in general, hepatomegaly, and splenomegaly [3, 10, 11, 12, 13, 14, 15, 16]. Based on theses studies, the diagnosis by questionnaire approach has been conducted for *S. mansoni* infection since 1985, initially focusing on subjective symptoms and the observation of stool appearance. But since studies reported low to moderate sensitivities and specificities [17, 18, 19], the questionnaires have been extended to include anamnestic information such as water-contact behavior [20, 21, 22, 23]. This approach, which was undertaken in several endemic areas, disclosed the potential of questionnaires for the identification of *S. mansoni* infection on the individual level [17, 18, 20, 22, 23, 24]. Supportive evidence for the application of a questionnaire for identification of *S. mansoni*, however, is still scarce, especially in the wake of mass treatment with praziquantel.

The purpose of this study was to evaluate the efficacy of questionnaires in the assessment of *S. mansoni* in one endemic area, with reference to the history of praziquantel medication in school-age children. An analysis was conducted to evaluate the potential of a questionnaire applied separately to children with and without a history of praziquantel medication.

MATERIALS AND METHODS

Cross sectional surveys on *S. mansoni* infection were conducted among Tanzanian children three times before and after mass treatment. The first questionnaire survey with stool examination was carried out in January and February 2001, and mass treatment was administered immediately after the survey. One month later, an additional stool examination for evaluation of efficacy of treatment was conducted. The second questionnaire survey with stool examination was carried out in February and March 2002, about one year after the treatment.

Area studied: The study area was Lower Moshi located in the southern part of the suburbs of Moshi Town in Kilimanjaro Region, Tanzania. The annual climate is divided into four periods: the long rainy season from March to June, cool dry season from July to October, short rainy season in November, and hot dry season from December to February. The main economic activity is wet-rice cultivation. The land is well developed for paddy cultivation with irrigation canals where water flows throughout the year. People usually cultivate crops three times a year. An agricultural development project supported by Japan International Cooperation Agency (JICA) has been conducted in this area since the 1970s.

Study population: The study was conducted in four primary schools; Mabogini, Rau River, Oria and Chekereni. There were 1,033 children registered in grades three and four in 2001.

Stool examination: A stool sample container was distributed to each child for collection of stool on the next day or the day after. Double 20 mg Kato-Katz thick smears [25] were processed and examined for the ova of *S. mansoni*, *Ascaris lumbricoides*, *Trichuris trichiura*, and hookworms by trained technicians and the authors. The number of eggs found in the samples was expressed as eggs per 1 gram (EPG) to reveal the intensity of infection. The presence of eggs was assessed for prevalence of infection. Geometric mean was calculated for expressing intensity of groups.

Questionnaire survey: The questionnaire consisted of five parts containing a total of 35 questions (see Tables 3 and 4 for the questionnaire contents). The first part focused on self-diagnosis, with the question “Do you think you have bilharzia (*Kichocho* in local Swahili language)?” The second part dealt with 18 self-reported clinical manifestations self-recognized during the last two weeks prior to the survey, including abdominal pain, diarrhea, constipation, abdominal enlargement, and blood in stool. The third part dealt with the history of contact with irrigation and river water including swimming, bathing, fishing (mainly net-fishing), washing clothes, fetching water, and other purposes. The fourth part dealt with anamnestic information: blood in stool in the past, experience of stool examination, and history of anti-schistosomiasis medication. The last part dealt with recognition and knowledge of schistosomiasis. The questionnaire was written in Swahili, the local language. Under the supervision of a Tanzanian doctor, a field assistant read out the questions to the children in groups of 20, and the children completed the forms individually. Children recorded their answers as ‘yes’, ‘no’ or ‘don’t

know'. We combined 'no' and 'don't know', and used the percentage of 'yes' replies to determine prevalence.

Treatment: Mass treatment with praziquantel was carried out in the schools under the supervision of a medical nurse in February 2001. Each child received 40 mg/kg of praziquantel. At the end of the study, the infected children were treated again. For the treatment of intestinal parasitic infection, we used mebendazole at a dose of 600 mg per person as a mass treatment in February 2001 and as a selective treatment in March 2002.

Analysis: The results of the study were analyzed using the SPSS® (version 11.5) software package. First, the prevalence of infestation by age and sex and by all the 35 variables in the questionnaire was calculated. Then the odds ratios (ORs) of infection were calculated and tested by Chi-square analysis. By using the variables correlated at less than the 0.10 level in univariate analyses, logistic regression analysis was conducted to assess the associations with infection after correcting for age and sex. The sensitivities and specificities of logistic regression models were calculated to assess the effectiveness of the questionnaire as a tool for individual diagnosis of infection. The analysis was conducted separately for those who had received treatment before the mass treatment and for those who had never received the treatment.

Ethical guidelines: This study was part of an epidemiological survey permitted by the National Institute of Medical Research, Ministry of Health, United Republic of Tanzania. We started the program by explaining the outline of the study to local authorities. Then we explained orally the purpose and methods of the study to the school children, their parents and teachers at school assemblies. At mass treatment, we treated all children who desired treatment irrespective of enrollment in the study. We treated infected children again for *S. mansoni* and other helminthes at the end of the study in March 2002. Informed consent was not obtained in written form.

RESULTS

Number of subjects for analysis: Out of 1,033 children registered in grades 3 and 4 in the 4 schools, demographic data such as sex and age were obtained from 830 children (417 males and 413 females, aged 7 to 17). Out of these 830 children, 267 (32.2%) had undergone three stool examinations, mass treatment after the first survey, and two questionnaires. The present analysis is restricted to these 267 children. The number of children by age and sex is shown in Table 1 with prevalence of *S. mansoni* infection. No significant difference in age or sex were observed between the 267 children and the rest of the 830 children.

Prevalence and the intensity of *S. mansoni* infestation: Among the 267 children, the prevalence of schistosomiasis was 67.4% and the mean intensity of schistosoma eggs in feces was 29.9/g at the first stool examination prior to mass treatment (Figure 1). The prevalence and intensity were not significantly different either by sex or by age. The prevalence decreased to 6.4% (McNemar test, $p < 0.001$) and the mean intensity to 0.3/g (t-test, $p < 0.001$) one month after the mass treatment (2nd fecal analysis). However, the prevalence increased to 27.0% (McNemar test, $p < 0.001$) with a slight increase in the mean intensity to 2.5/g (t-test, $p < 0.001$) one year after the treatment (3rd fecal analysis), although this prevalence and intensity were still significantly lower than those prior to mass treatment (McNemar test $p < 0.001$, t-test $p < 0.001$, respectively). The mean EPG calculated from only positive samples decreased from 160.8/g ($n = 180$) to 74.8/g ($n = 17$) by mass treatment and then increased to 105.2/g ($n = 72$) one year after the treatment. The prevalence of heavy infection (more than 400 EPG) de-

Table 1 The number of children and prevalence of *S. mansoni* infection before mass-treatment by age and sex

	Boys			Girls		
Age	Examined	Infected	Prevalence (%)	Examined	Infected	Prevalence (%)
7-9	9	7	(77.8)	17	11	(64.7)
10	30	20	(66.7)	29	21	(72.4)
11	41	29	(70.7)	50	31	(62.0)
12	32	23	(71.9)	19	9	(47.4)
13	15	10	(66.7)	10	7	(70.0)
14-17	11	9	(81.8)	4	3	(75.0)
Sub-total	138	98	(71.0)	129	82	(63.6)

In total, 267 children were examined and 180 (67.4%) were egg-positive.
No significant difference was found between sex or age.

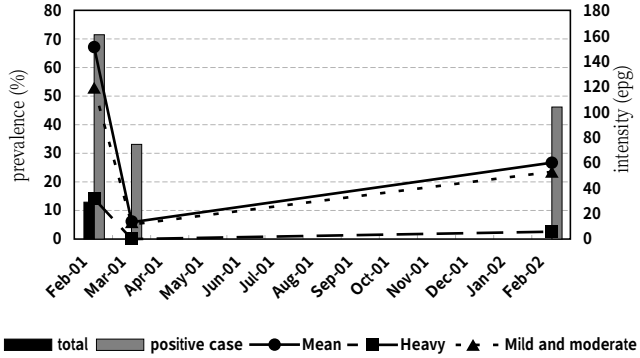

Figure 1 Prevalence and intensity of *S. mansoni* infection before, one month after, and one year after mass treatment. Solid line with circles: mean prevalence of infection; Dotted line with triangles: prevalence of mild and moderate infection (100 EPG or more); Dashed line with square: prevalence of heavy infection (400 EPG or more); Black bars: mean intensity (geometric mean EPG for the 267 children); Gray bars: mean intensity of positive cases (geometric mean EPG of 180, 17, 72 children, respectively).

creased from 14.2% to 0.4% by treatment, then increased to 3.0% after one year.

Experience of treatment: Of the 267 children, 61 had no history of medication for schistosomiasis before the mass treatment, while 116 children had a medication history. The remaining 90 children were not sure either way. The prevalence and intensity of infection did not differ significantly between non-treated and treated children (59.0% and 17.6/g for the former and 62.9% and 21.4/g for the latter) in the first stool examination.

Prevalence of water contact activities: About 90% of children reported having contact with irrigation/river water for the purpose of swimming/playing, bathing, crossing water and washing clothes, and fetching water in the first survey. About 40% of children had contacted water for the purpose of fishing in the first survey. The percentage of children contacting irrigation/river water in the second survey decreased slightly from the first survey in all activities.

Results of questionnaire survey in relation to egg detection before mass treatment for the 267 children: Before mass treatment, the most common symptom was “abdominal pain” (60%) followed by “headache” (52%) and “abdominal discomfort” (40%). But, no manifestation showed a significant increase with the level of intensity (Table 2). “Constipation” and “net-fishing” showed a significant correlation with infection (both $p < 0.05$) and “diarrhea” and “history of blood in stool” showed borderline significance (both, $p < 0.10$, by Chi-square test, Tables 3 and 4). For a

Table 2 Prevalence of signs and symptoms by the level of intensity of *S. mansoni* infection before mass-treatment

Manifestations	Percentage of “yes” answers in the questionnaire					Somers’ d	p
	Total	Level of intensity §					
		Negative	Mild	Moderate	Heavy		
		0 epg	1 - 99 epg	100 - 399epg	400 epg<		
	(n=267)	(n=87)	(n=51)	(n=91)	(n=38)		
abdominal pain	59.6	52.9	62.7	61.5	65.8	0.149	0.459
headache	52.4	46.0	51.0	58.2	55.3	0.130	0.415
abdominal discomfort	40.4	33.3	43.1	42.9	47.4	0.109	0.398
easy to be tired	28.8	25.3	31.4	29.7	31.6	0.451	0.834
fever	24.3	20.7	31.4	28.6	13.2	0.863	0.141
loss of appetite	20.6	20.7	27.5	16.5	21.1	0.609	0.491
cough	19.9	19.5	23.5	22.0	10.5	0.475	0.428
nausea/vomiting	18.4	16.1	21.6	20.9	13.2	0.943	0.632
constipation	17.2	10.3	27.5	19.8	13.2	0.371	0.058
diarrhea	16.5	10.3	19.6	18.7	21.1	0.085	0.303
fatigue	14.2	10.3	21.6	14.3	13.2	0.646	0.339
abdominal enlargement	14.2	9.2	19.6	17.6	10.5	0.391	0.233
dizziness/lassitude	12.4	10.3	13.7	12.1	15.8	0.482	0.845
skin rash	10.1	10.3	11.8	9.9	7.9	0.686	0.945
blood in stool	5.2	3.4	5.9	5.5	7.9	0.335	0.330
itching skin	4.5	3.4	3.9	4.4	7.9	0.383	0.348
weight loss	4.1	2.3	5.9	6.6	0.0	0.753	0.840
asthma	3.7	3.4	5.9	4.4	0.0	0.477	0.549

§ Intensity is categorized according to the definitions of WHO

Table 3 Prevalence of self-diagnosis and 2-week-recognition of symptoms before and after treatment, and for non-treated and treated and the odds ratio between infected and non-infected

Self-diagnosis and recognition of symptoms within two weeks	Percentage of "yes" answers in the questionnaire (%)				Odds ratio and its 95% confidence interval			
	Before treatment			After treatment	Before treatment			After treatment
	all (n=267)	never treated (n=61)	treated (n=116)	all (n=267)	all (n=267)	never treated (n=61)	treated (n=116)	all (n=267)
self-diagnosis	7.7	6.7	9.0	25.8	0.90 0.314-2.586	2.09 0.204-21.382	0.53 0.144-1.957	1.15 0.623-2.107
loss of appetite	20.6	44.3	19.8	43.8	0.99 0.527-1.867	2.38 0.819-6.890	1.13 0.435-2.941	1.12 0.649-1.925
nausea/vomiting	18.4	27.9	25.0	61.4	1.26 0.637-2.486	0.99 0.317-3.085	3.72* 1.299-10.665	1.06 0.610-1.858
abdominal enlargement	14.2	29.5	5.2	7.1	1.98 0.865-4.512	9.20* 1.881-44.998	0.57 0.110-2.966	2.09 0.805-5.429
abdominal discomfort	40.4	62.3	29.3	71.5	1.56 0.917-2.669	2.82 § 0.965-8.222	1.97 0.817-4.741	0.80 0.442-1.431
abdominal pain	59.6	72.1	43.1	85.4	1.50 0.895-2.524	1.97 0.634-6.115	1.26 0.587-2.713	1.82 0.766-4.338
diarrhea	16.5	19.7	25.9	49.4	2.09 § 0.957-4.575	10.56* 1.265-88.184	1.89 0.755-4.719	1.91* 1.101-3.316
constipation	17.2	36.1	10.3	38.2	2.24* 1.029-4.887	5.25* 1.500-18.380	1.88 0.479-7.342	0.96 0.550-1.677
blood in stool	5.2	8.2	6.0	30.5	1.82 0.495-6.708	3.00 0.315-28.586	3.76 0.437-32.349	1.31 0.737-2.332
easy to be tired	28.8	57.4	25.9	41.2	1.30 0.729-2.318	2.55 § 0.890-7.279	1.89 0.755-4.719	0.88 0.505-1.524
fatigue	14.2	24.6	17.2	63.7	1.66 0.751-3.690	2.31 0.640-8.333	2.74 § 0.850-8.808	1.30 0.734-2.312
fever	24.3	45.9	26.7	58.1	1.35 0.731-2.509	1.50 0.534-4.214	2.52 § 0.979-6.484	1.29 0.740-2.243
cough	19.9	37.7	19.8	58.6	1.03 0.541-1.959	1.52 0.521-4.426	1.44 0.541-3.851	1.59 0.904-2.805
asthma	3.7	9.7	3.4	16.1	1.13 0.286-4.492	1.44 0.242-8.524	1.80 0.181-17.869	1.21 0.593-2.479
weight loss	4.1	4.9	4.3	32.2	2.24 0.473-10.582	1.41 0.121-16.470	2.43 0.263-22.522	0.75 0.415-1.363
dizziness/lassitude	12.4	23.0	14.7	50.2	1.33 0.591-3.006	1.33 0.387-4.592	3.16 § 0.854-11.725	1.07 0.622-1.834
skin rash	10.1	18.0	12.1	30.3	0.96 0.414-2.241	0.80 0.215-2.979	2.37 0.621-9.008	1.85* 1.051-3.273
headache	52.4	68.9	38.8	83.5	1.47 0.878-2.456	0.78 0.255-2.371	2.54* 1.111-5.788	1.13 0.537-2.375
itching skin	4.5	3.3	8.6	43.8	1.47 0.389-5.586	0.69 0.041-11.505	2.52 0.510-12.472	1.12 0.649-1.925

*: significant at 0.05 level
§ : borderline significant at 0.1 level

binary logistic regression analysis using "constipation", "net fishing", "history of blood in stool", "diarrhea", age, and sex as independent variables, only "constipation" (odds ratio, OR = 2.27, confidence interval, CI = 1.04 - 4.96) was positively associated with infection (Table 5a). The prediction of the model, however, was not significant.

Results of questionnaire survey in relation to egg detection at one year after mass treatment for the 267 children: Results: "Abdominal pain", "headache" and "abdominal discomfort" remained common at one year after the treatment. The prevalence of all signs and symptoms except "abdominal enlargement" increased from the first questionnaire (Table 3). The prevalence of "abdominal enlargement" decreased from 14% before treatment to 7% at one year after treatment. The prevalence of self-diagnosis of *S. mansoni* infection was 8% before the treatment and increased to 26% one year after the treatment.

"Diarrhea" and "skin rash" were significantly associated with schistosomiasis (both $p < 0.05$), and "bathing" showed a borderline significant association with prevalence ($p=0.09$). For a binary logistic regression analysis using "diarrhea", "skin rash", "bathing", age, and sex as independent variables, only "diarrhea" (OR = 1.96, CI = 1.13 -

Table 4 Questionnaire of history of wild water contact, knowledge and recognition, experience of fecal examination, fecal blood hisotry and treatment before and after treatment, and for non-treated and treated and the odds ratio between infected and non-infected

	Proportion of answering "yes" (%)				Odds ratio and its 95% confidence interval			
	Before treatment			After treatment	Before treatment			After treatment
	all (n=267)	never treated (n=61)	treated (n=116)	all (n=267)	all (n=267)	never treated (n=61)	treated (n=116)	all (n=267)
Water contact activities								
any purpose	91.0	96.7	87.1	83.7	0.39 0.128-1.165	1.46 0.087-24.468	0.23* 0.048-1.051	1.63 0.716-3.733
swimming/playing	90.5	88.1	87.5	53.6	0.80 0.317-2.004	1.11 0.224-5.463	0.62 0.178-2.162	1.12 0.649-1.922
bathing	91.7	91.5	89.4	49.8	0.77 0.289-2.074	2.36 0.363-15.309	0.52 0.129-2.083	1.60 § 0.926-2.764
fishing	38.7	22.0	10.6	17.6	1.84* 1.056-3.220	0.75 0.217-2.594	0.79 0.225-2.788	1.34 0.677-2.655
crossing the water	92.9	94.9	85.6	36.7	0.99 0.357-2.729	0.72 0.061-8.387	0.70 0.222-2.227	1.44 0.832-2.509
washing clothes	94.1	96.6	87.5	59.2	0.70 0.218-2.283	1.48 0.088-24.847	0.40 0.103-1.551	1.55 0.878-2.722
fetching water	88.5	84.7	89.4	54.3	0.88 0.381-2.018	1.20 0.287-5.021	0.83 0.226-3.023	1.25 0.724-2.160
for agricultural purpose	87.7	84.7	84.6	55.8	1.10 0.501-2.416	1.20 0.287-5.021	0.44 0.131-1.467	1.07 0.618-1.838
for animal husbandry	78.3	67.8	75.0	29.2	0.77 0.400-1.471	0.26* 0.075-0.945	0.58 0.223-1.480	0.83 0.451-1.516
Anamnestic information								
Have you ever had blood in stool?	23.0	23.0	28.7	no data	2.08 § 0.985-4.392	5.75* 1.158-28.551	1.94 0.769-4.883	no data
Have you ever taken medication for schistosomiasis?	60.7	0	100.0	72.2	1.07 0.588-1.947	(-) (-)	1.00 (-)	1.30 0.697-2.438
Have you ever taken fecal examination?	83.9	50.8	No data	95.5	1.22 0.556-2.656	0.92 0.333-2.562	(-) (-)	1.11 0.293-4.231
Recognition and knowledge on the disease								
Have you ever heard of disease of bilharzia?	83.1	50.8	87.8	79.6	1.50 0.774-2.906	2.79 § 0.971-8.034	0.11* 0.014-0.894	1.20 0.598-2.391
Do you know what bilharzia is?	68.4	23.0	78.3	47.9	1.07 0.617-1.860	2.02 0.553-7.367	0.18* 0.050-0.639	1.17 0.676-2.014
Contacting with river water causes bilharzia?	34.7	16.9	43.9	16.1	1.22 0.702-2.116	(-) (-)	0.84 0.393-1.803	0.79 0.368-1.703
Drinking river water causes bilharzia?	22.4	15.3	36.8	62.2	1.11 0.592-2.084	(-) (-)	0.98 0.445-2.137	1.11 0.631-1.937

*: significant at 0.05 level

§ : borderline significant at 0.1 level

3.43) was positively associated with infection (Table 5d). The prediction of the model, however, was not significant. The level of intensity of infection was also related with "diarrhea", increasing from 45% of negative children, to 52% of lightly infected children, to 66% of moderately infected children and to 75% of heavily infected children (Somers'd test, $p < 0.05$, data not shown).

Results of questionnaire survey in relation to egg detection before mass treatment for the 61 non-treated and 116 treated children: Next, we compared the 61 non-treated and 116 treated children. In children without a history of medication for schistosomiasis, "diarrhea", "constipation", "abdominal enlargement", and "recognition of blood in stool" were significantly associated with schistosomiasis by univariate analyses. "Abdominal discomfort", "easy to be tired", and "recognition of the disease (yes to the question "Have you ever heard of bilharzia?")" were associated with borderline significance in these children (Tables 3 and 4). Recognition of blood in stool over the past two weeks was not significant, but a history of this recognition was significant in the non-treated children.

Among the 116 children with a medication history, meanwhile, "nausea/vomiting", "headache", recognition of the disease, and knowledge of the disease (yes to the question "Do you know what bilharzia is?") were significant,

Table 5 Logistic regression of *S. mansoni* infection with questionnaire's items

a. Before mass-chemotherapy (all children, n = 267)

Variable	Parameter estimate	Standard error	p	Odds ratio	95.0% C.I † †	
					Lower	Upper
Constipation	0.820	0.399	0.040	2.271	1.039	4.961
Constant	0.822	1.106	0.458	2.274		

Sensitivity = 100%, Specificity = 0%

b. Before mass-chemotherapy, (never-treated children, n = 61)

Variable	Parameter estimate	Standard error	p	Odds ratio	95.0% C.I. † †	
					Lower	Upper
Diarrhea	3.466	1.293	0.007	31.993	2.538	403.342
Abdominal enlargement	2.719	0.909	0.003	15.166	2.553	90.080
Constant	-7.923	3.582	0.027	0.000		

Sensitivity = 86.1%, Specificity = 64%

c. Before mass-chemotherapy, (ever-treated children, n = 116)

	Parameter estimate	Standard error	P	Odds ratio	95.0% C.I. † †	
					Lower	Upper
Recognition of the disease	-1.671	0.655	0.011	0.188	0.052	0.679
Constant	2.862	2.001	0.153	17.488		

Sensitivity = 100%, Specificity = 2.4%

d. After mass-chemotherapy, (all children, n = 267)

	Parameter estimate	Standard error	p	Odds ratio	95.0% C.I. † †	
					Lower	Upper
Diarrhea	0.675	0.284	0.017	1.964	1.126	3.425
Constant	-2.232	1.193	0.061	0.107		

Sensitivity = 0%, Specificity = 100%

but abdominal manifestation was not significant (Tables 3 and 4). "Fever", "dizziness", "fatigue" and "contact with river water for any purpose" showed borderline significance.

We examined the effect of treatment on selected manifestations using binary logistic regressions explaining *S. mansoni* infection for the 61 non-treated children (Table 5b) and for the 116 treated children (Table 5c). In the non-treated children, "diarrhea" (p = 0.007, OR = 32.0, CI = 2.54 - 403.3) and "abdominal enlargement" (p = 0.003, OR = 15.2, CI = 2.55 - 90.1) were significantly associated with infection, and the model prediction was significant (Chi-square = 26.98, p < 0.001). The sensitivity and the specificity of the logistic predictive model were 86.1% and 64.0%, respectively.

In the treated children, only knowledge of the disease was significantly and negatively associated with prevalence, and the prediction was significant (the model Chi-square = 10.085, p = 0.018) (Table 5c). But, the specificity of the model prediction was very low (2.4%), while the sensitivity was 100%.

Other parasitic infections: The prevalence of eggs of *A. lumbricoides*, *T. trichiura a*nd hookworm was 6.7%, 10.9%, and 9.0% respectively in the first examination. It declined to 5.3%, 4.9% and 4.1% respectively one year after mass treatment. At the first survey, *A. lumbricoides* infection was correlated with *S. mansoni* infection (Chi-square = 9.329, p = 0.002), but it was not significantly associated with any sign or symptom of *S. mansoni* infection. Hookworm infection was correlated with "constipation". However, it did not correlate with *S. mansoni* infection. *T. trichiura* infection showed no correlation with *S. mansoni* infection or with any sign or symptom.

DISCUSSION

The present study was conducted in a high endemic area according to the WHO definition [4], the prevalence of schistosomiasis being 67.4% among school children aged from 7 to 17 years old. The results indicated that subjective abdominal symptoms are related with infection of *S. mansoni* and that questionnaire on the subjective abdominal symptoms can be used for the screening of *S. mansoni* infection in children who have never undergone treatment for *S. mansoni* infection. "Diarrhea" and "abdominal enlargement" correlated well with infection when the children had

no history of treatment. These correlations were not seen in children who had undergone treatment in the past, although the prevalence and intensity of infection did not differ from those of the non-treated children. At one year after mass treatment, no suitable model for the prediction of *S. mansoni* infection was obtained by using self-diagnosis, subjective symptoms, water contact behavior, anamnestic information, or recognition and knowledge of the disease.

S. mansoni causes a chronic disease with various stages and many symptoms and signs at each stage, adult worms being present in the mesenteric veins and eggs in various organs including the liver, lungs and gastrointestinal tract. Deposition of eggs in the alimentary tract causes mucosal lesions frequently associated with hemorrhage resulting in blood in the stool. The abdominal symptoms might be influenced by adult worms in the mesenteric veins and egg embolism scattered from the adult female worms. The human body responds to schistosomula during acute infection or when eggs are retained in tissue [26]. Regarding adult worms, no response has been observed around the live worms. Colley advocated the hypothesis that praziquantel treatment alters host-parasite relationships, leading to multiple immunologic changes through the killing of adult worms. The antigens released from dead adult worms cause many immune responses and produce some resistance to reinfection [27]. This hypothesis is supported by an animal experiment using immuno-compenent and deficient mice [28]. B cell deficient mice showed a delayed response after praziquantel treatment, suggesting that the immunological responses are required for the killing of adult worms during treatment. Taken together, this evidence and our results suggest that the abdominal manifestations become obvious in the host who has recently been infected and not treated by medication.

The association between intensity of infection and morbidity was frequently reported. It was shown that complaints of “abdominal pain” and “blood in stool” correlated significantly with *S. mansoni* egg counts in a high prevalence village [11]. Heavily infected individuals frequently complained of “abdominal pain” [14]. Our study, however, did not confirm any correlation between intensity of infection and the prevalence of abdominal symptoms. The reason for this is not clear. “Abdominal discomfort”, “diarrhea”, “constipation”, “easy to be tired” and “abdominal enlargement” were associated with the level of intensity of infection (Somers’d test, $p = 0.021$, 0.003, 0.004, 0.038 and < 0.001, respectively) in the non-treated children. Almost all of these children had abdominal manifestations. On the other hand, “dizziness/lassitude”, “nausea/ vomiting” and “headache” were associated with the level of intensity of infection (Somers’d test, $p = 0.030$, 0.014 and 0.018, respectively) in the treated children.

One of the limitations of the present study is that it examined only the ova of helminthes in fecal specimens and did not determine other causes of “diarrhea” and “abdominal enlargement” such as protozoan or bacterial intestinal infection. Since abdominal manifestations are non-specific, it is impossible to overrule other causes. In fact our results show that the infection of hookworm causes “constipation” as an abdominal symptom, although the prevalence was not high. The intestinal parasitic infestation did not contribute significantly to the abdominal manifestations in our study because of its low prevalence, although the hookworm infection was significant as a cause of “constipation”. From this viewpoint, the abdominal manifestation should be applied while ruling out other intestinal infections and infestations.

“Blood in stool” is well documented as the most notable subjective sign of *S. mansoni* infection. Sukuwa (1985) and Proietti (1989) reported that “blood in stool” had the highest specificity (94.9%) [17] and the highest positive predictive value (38.9%) [18] among the symptoms. In the present study, however, “recognition of blood in stool” did not prove to be a specific sign of infection. With regard to the individual perception of clinical manifestations, the only reliable variables identified were “diarrhea” and “abdominal enlargement”. The reason may be that our study population was limited to school children while the previous studies included adults.

In the variables of risk factors such as self-diagnosis, water contact history, anamnestic information, and recognition and knowledge of the disease, we did not identify any significant variable that could be used for individual diagnosis. The use of risk factors has been reported to be limited in its potential to identify the infection of *S. mansoni*. Utzinger (2000) argued that recalled water-contact patterns collected by questionnaire might be useful for self-diagnosis of schistosomiasis, showing sensitivity and specificity of “crossing the river” to be 61-70% and 47-52%, respectively, and those of “swimming/bathing” to be 77-81% and 37-68% respectively [23]. According to Brooker (2001), the reported “swimming” had 80% sensitivity and 83% specificity [21]. However, Lima e Costa (1998) pointed out that sociodemographic variables and water contact activities associated with *S. mansoni* infection differed among the study areas, thus their validity for diagnosis of infection similarly differed among the areas [22]. Unlike previous studies, water contact behavior was not correlated with infection in our study. The reason might be that we did not define the period of the behaviors in the questionnaire and therefore that many children reported having contact with the irrigation/river water.

After a series of mass treatments in high prevalence areas, prevalence will decrease considerably. Subsequently, the school-based mass treatment approach might be replaced by selective treatment, and children can be monitored for re-infection individually. But as the present study showed, diagnosis by questionnaire becomes inapplicable once children take medication. Although stool examination is the most reliable method for individual identification of *S. mansoni* infection in an area of low intensity infection, other simple, rapid and cost-effective individual diagnostic methods are still required in areas where laboratory examination has not been established. Moreover, it is imperative that old-fashioned questionnaire analysis be analyzed for usefulness for schistosomiasis using praziquantel-resistant clone [29].

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