Journal of Travel Medicine

International Society of Travel Medicine
Established 1991
Promoting healthy travel worldwide

Journal of Travel Medicine, 2021, 1–5
https://doi.org/10.1093/jtm/taaa238
Advance Access Publication Date: 4 January 2021
Original Article

Original Article

Acute schistosomiasis in paediatric travellers and comparison with their companion adults

Dr. Shira Rabinowicz[1,2,*], Prof Eyal Leshem[2,3] and Prof Eli Schwartz[2,3]

[1]Paediatric Neurology Unit, Edmond and Lily Safra Children's Hospital, Sheba Medical Center, Ramat Gan, Israel, [2]Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel and [3]The Center for Travel Medicine and Tropical Diseases, Sheba Medical Center, Ramat Gan, Israel

*To whom correspondence should be addressed. Tel: +972-546334272/+972-3-5302687, Fax: +972-3-5305031. Email: shirarabi@gmail.com

The findings were presented in the Asia Pacific Travel Health Conference in Thailand, 2018.

Submitted 1 November 2020; Revised 18 December 2020; Accepted 21 December 2020

Abstract

Background: Schistosomiasis in non-immune travellers can cause acute schistosomiasis, a multi-systemic hypersensitivity reaction. Little is known regarding acute schistosomiasis in children. We describe acute schistosomiasis in paediatric travellers and compare them with adult travellers.
Methods: A retrospective study of paediatric travellers (0–18 years old) diagnosed with schistosomiasis at Sheba Medical Center. Patients' findings are compared with those of adult travellers from the same travel groups.
Results: in total, 18 children and 24 adults from five different trips to Tanzania, Uganda, Nigeria and Laos were infected (90% of the exposed travellers). The median bathing time of the infected children was 30 min (interquartile range (IQR) 15–30 min). The most common presentations were respiratory symptoms in 13 (72%), eosinophilia in 13 (72%) and fever in 11 (61%). Acute illness included a median of 2.5 symptoms. Three children required hospitalization and three were asymptomatic. Fatigue was significantly less common in children compared with similarly exposed adults (33% vs 71%, $P = 0.03$). Rates of hospitalization and steroid treatment were similar. The median eosinophil count in children was 1045 cells/μl (IQR 625–2575), lower than adults [2900 cells/μl (IQR 1170–4584)], $P = 0.02$.
Conclusions: Children may develop acute schistosomiasis following short exposure to contaminated freshwater, demonstrating a high infection rate. Severity seems to be similar to adults, although children report fatigue less commonly and show lower eosinophil counts. The disease should be suspected in children with multi-systemic illness and in asymptomatic children with relevant travel history.

Key words: Acute schistosomiasis, katayama syndrome, children, travel, tropical disease

Introduction

Schistosoma is a common infectious parasite in low-income countries in the tropics, especially in Africa.[1] Humans, the trematode's' definitive hosts, acquire the disease by contact with freshwater contaminated with cercaria excreted by infected snails that serve as an intermediate host.[2] In endemic countries, the population is repeatedly exposed to the parasite from early childhood[3–5] or in-utero,[2,6] leading to chronic infections.[2,7] Chronic schistosomiasis may lead to various complications,[8] including irreversible damage to the gastrointestinal and urinary tract and eventually malignancy.[9,10]

In contrast to the local population in endemic regions, schistosomiasis in non- immune travellers presents more commonly as 'acute schistosomaisis', also known as 'katayama syndrome', including fever, urticarial rash, cough, abdominal pain, fatigue, myalgia and headache. These symptoms typically begin 2–12 weeks post-exposure, due to hypersensitivity inflammatory (serum sickness-like) reaction to antigens released during cercarial and schistosomule (the young form) migration.[7,11]

This is unique to a primary exposure to the parasite and, therefore, is seen only in travellers from non-endemic countries. This was illustrated in a large cohort of Israeli travellers diagnosed with schistosomiasis, where about ~70% presented with acute schistosomiasis.[7,12–14]

Although acute schistosomiasis has been extensively described in adult travellers, data on acute schistosomiasis in children

Table 1. Demographic and exposure data of adults and children exposed to schistosomiasis (*N* adults = 33, N children = 20)

	Total	Children	Adults	
Infected, *N* (%)	48 (91%)	18 (90%)	30 (91%)	
Included in the analysis[a]	*N* = 42	*N* = 18	*N*=24[a]	
Tanzania (group 1)	3	2	1	
Tanzania (group 2)	23	9	14	
Laos	4	2	2	
Nigeria	4	1	3	
Uganda	8	4	4	
Exposure duration in minutes (median, IQR)		30 (15–30)[b]	30 (30–60)[c]	
Gender F/M	19/23	9/9	10/14	
Age in years (median, range)		13 (6–19)	47 (23–69)	
Diagnosis	Confirmed	31	12	19
	Probable	11	6	5

[a]Further clinical data of six infected adult travellers were missing, hence they were not included in the additional analysis.
[b]Data available for 14/18 patients.
[c]Data available for 15/24 patients.

are scarce,[15,16] as most reports from western countries focus on immigrants, including paediatric population with chronic disease.[17–20]

In recent years, paediatric travellers have also become a potential target population due to an increase in family trips to developing countries.[21,22] Herein, we describe a cohort of 18 children diagnosed with acute schistosomiasis and compare their presentation to the accompanying adults with the same exposures.

Methods

This is an observational retrospective study. Medical records of all children (age 0–18 years) who consulted the Institute of Travel Medicine and Tropical Disease at Sheba Medical Center, Israel, from 2005 onwards were searched for the diagnosis of schistosomiasis.

All the children diagnosed with schistosomiasis were part of five travel groups that included children and accompanying adults. Each group was investigated following the identification of an index case.

Diagnosis of schistosoma infection was made in patients who had an at-risk exposure. The diagnosis was classified as confirmed if serology was positive and highly probable if the patient had symptoms consistent with acute schistosomiasis (fever, rash, cough) or eosinophilia (absolute eosinophil count ≥500 cells/microl).

The serologic tests in patients who returned from Africa were performed at the Israel Ministry of Health laboratory. The test is based on soluble egg antigen ELISA and it is not species-specific.[23] A convenient samples were sent to the Centers for Disease Control (CDC) laboratory for species-specific diagnosis.

In any identified case, data were collected using a structured questionnaire and review of the medical record, including demographics, exposure details, clinical data and laboratory tests.

Asymptomatic patients who were found through cluster investigation (by positive serology or eosinophilia) were included as well. Screened patients whose serology tests were negative for schistosomiasis and patients whose medical records were missing were excluded.

Disease characteristics of the children were compared to those of adults who took part in the same trips (family and group members). Continuous variables were compared between children and adults with Mann–Whitney test. Categorical variables were reported by their absolute and relative frequencies and compared between children and adults by Fischer's exact test.

Results

The five screened travel groups had returned from various countries in Africa and Laos. All were tourists except for a family of Israeli expatriates in Nigeria for whom it was also the first freshwater exposure in Africa. The groups included 20 children and 33 adults with a history of freshwater contact in the destination. Five patients were excluded due to negative serology and six were excluded due to missing medical records. Hence, 18 children and 24 adults were included (Table 1). The median duration of exposure was similar in adults and children, but the interquartile range (IQR) of the adults' exposure time was longer (Table 1).

Disease Characteristics in Children

The diagnosis was made based on positive serology results in 12 children (Table 1). The serologic tests for patients returning from Africa were not species-specific. However, serum samples of eight travellers returning from Tanzania (group 2) were additionally sent to the CDC laboratory for species analysis, yielding positive results for *S. mansoni* in all patients and *S. haematobium* coinfection in three.

Serologic tests of the patients from Laos were positive for *S. japonicum*, probably *S. Mekongi* due to the area of exposure. Other diagnostic tests are detailed in Table 2.

The main symptoms seen in children were respiratory (cough, wheezes), fever and gastrointestinal (abdominal pain/diarrhea), as shown in Table 3. In two cases, prolonged respiratory symptoms were eventually attributed to asthma, one of them required steroid treatment. Three patients were asymptomatic.

The median incubation period from exposure to symptom onset was 35.5 days [*n* = 14, IQR 21–50 days]. The shortest

Table 2. Demographic and laboratory details of infected children

	Age	Sex	Country of exposure	Symptoms	Serologic tests	Stool microscopy	Urinalysis	Absolute eosinophil Count (cells/microl)	Timing of tests (days)
Patient 1	12	F	Tanzania (Group 1)	+	+	−	Normal	80	109
Patient 2	14	F	Tanzania (Group 1)	−	+	−	Normal	380	109
Patient 3	12	F	Tanzania (Group 2)	−	Not performed	−	Not performed	500	54
Patient 4	12	F	Tanzania (Group 2)	+	+	Not performed	Normal	1130[a]	43
Patient 5	13	M	Tanzania (Group 2)	+	+	Not performed	Erythrocytes	1430[b]	62
Patient 6	13	M	Tanzania (Group 2)	+	Not performed	Not performed	Normal	650	54
Patient 7	15	M	Tanzania (Group 2)	+	Not performed	−	Normal	2150	54
Patient 8	8	M	Tanzania (Group 2)	+	Not performed	−	Normal	1090	55
Patient 9	17	M	Tanzania (Group 2)	+	Not performed	Not performed	Normal	690	56
Patient 10	6	F	Tanzania (Group 2)	+	Not performed	−	Normal	320	54
Patient 11	15	M	Tanzania (Group 2)	−	+	Not performed	Not performed	NA	NA
Patient 12	9	F	Laos	+	+	+	Not performed	4300	68
Patient 13	6	M	Laos	+	+	Not performed	Not performed	3000	68
Patient 14	10	F	Nigeria	+	+	Not performed	Normal	3000	71
Patient 15	18	M	Uganda	+	+	−	Not performed	9700	60
Patient 16	18	F	Uganda	+	+	Not performed	Not performed	600	53
Patient 17	16	F	Uganda	+	+	Not performed	Not performed	1000	53
Patient 18	13	M	Uganda	+	+	Not performed	Not performed	920[c]	85

[a]Eosinophil counts at repeated tests: day 76–980 eosinophils/microl, day 110–580 eosinophils/microl.
[b]Eosinophil counts at repeated tests: day 54–960 eosinophils/microl.
[c]Eosinophil counts at repeated tests: day 56–430.

was in patients with headache as the presenting symptom ($n = 2$, median 18 days), and longest for patients with cough as the presenting symptom ($n = 3$, median 68 days).

Hospitalization was required for three children: a 12-year-old girl with prolonged fever and abdominal pain, a 9-year-old girl with recurrent fevers and urticaria and a 13-year-old boy with severe fatigue.

All children with a confirmed or probable diagnosis were prescribed praziquantel 60 mg/kg for 1 day at least 10 weeks post-exposure.[24] Three children (17%) were additionally treated with systemic steroids prior to or concomitantly with praziquantel for the following indications: fever and severe abdominal pain, recurrent fever and urticaria and severe multi-systemic symptoms (headache, musculoskeletal pain, fever and abdominal pain). Doses of prednisone ranged between patients from 0.3 to 1 mg/kg/day for several days. When steroids were prescribed together with praziquantel, another dose of anti-parasitic treatment was administered three months post-exposure.

Comparison Between Children and Adults

We compared the rate of symptoms between children and adults (Table 3). The prevalence of fatigue was significantly higher in adults compared with children. Respiratory symptoms were more common in children, although this finding was not significant. The median number of symptoms was 2.5 in children, compared with three symptoms in adults ($P = 0.7$).

Adults had more prominent findings in blood tests, and significantly higher absolute eosinophil counts (Table 3). More adults than children were treated with systemic steroids, but

Table 3. Disease presentation and laboratory results in children compared with adults

	Adults ($N = 24$)	Children ($N = 18$)	P value
Incubation time in days (median, range)[a]	26 (13–165)	35.5 (7–85)	0.27
Asymptomatic (*N*, %)	4 (17%)	3 (17%)	1
Respiratory (*N*, %)	11 (46%)	13 (72%)	0.12
Fever (*N*, %)	18 (75%)	11 (71%)	0.5
Gastrointestinal (*N*, %)	8 (33%)	8 (44%)	0.53
Fatigue (*N*, %)	17 (71%)	6 (33%)	**0.03**[c]
Skin rash/itch (*N*, %)	8 (33%)	5 (28%)	0.75
Myalgia (*N*, %)	10 (42%)	4 (22%)	0.32
Headache (*N*, %)	6 (25%)	3 (17%)	0.7
Hospitalizations (*N*, %)	3 (21%)	3 (17%)	1
Steroid treatment (*N*, %)	7 (29%)	3 (17%)	0.47
Eosinophilia (>500 cells/µl), (*N*, %)[b]	19 (79.2%)	13 (72.2%)	0.72
Moderate eosinophilia (>1500 cells/µl), (*N*, %)	14 (58.3%)	5 (27.8%)	0.06
Absolute eosinophil count (cells/µl), (median, IQR)	2900 (1170–4584)	1045 (625–2575)	**0.02**[c]
Elevated liver enzymes (above upper limit of range for age)	10 (41.7%)	3 (17%)	0.1

[a]Data available for 14 children and 16 adults.
[b]Data available for 17 children and 20 adults. If a few blood tests were taken, the highest values of eosinophils and liver enzymes were included in the analysis.
[c]Bold font indicates statistical significance.

this was not significant. Rates of hospitalization were similar (Table 3).

Discussion

Very few data are available on acute schistosomiasis in the paediatric population. As family trips to endemic areas become more popular,[18,21,22] the delineation of the symptomatology in children is becoming increasingly important,

The attack rate in children was 90%, as previously reported in adults.[25–27] In children, very scarce information exists.[15,16] A recent report by Cnops *et al*.[28] showed a high infection rate also with a distinct species of *S. Haematobium* together with a bovine species *S. Mattheei*.

The main symptoms in returning paediatric travellers diagnosed with schistosomiasis were cough, fever and gastrointestinal discomfort/diarrhea. In addition, most children had eosinophilia.

Our results suggest that disease characteristics are fairly similar to previously reported data in adults.[11,12,14,29] This is also consistent with the recent report by Cnops *et al*.[28]

However, fatigue was significantly more prominent in adults, possibly because it is not a typical complaint in the paediatric population. Respiratory symptoms were more common in children, although not significantly, and were prolonged, as was previously described in adults.[30] A possible explanation may be the increased susceptibility of children to airway hyperreactiveness,[31] since acute schistosomiasis is a hypersensitivity reaction.[30] The rates of severe disease requiring hospitalization or steroid treatment were similar.

Abnormal laboratory results, including eosinophilia and elevated liver enzymes, were more prominent in adults. However, children also showed a high rate of eosinophilia, although absolute values were lower than those of adults. A possible explanation is that children underwent less repeated blood tests that could prove abnormalities. Values of the three children that were tested multiple times indicate that the eosinophil count may fluctuate over time (Table 2). The fluctuation in eosinophil counts was also shown in the recent report by Cnops *et al* on a 'non-classic' hybrid schistosoma species, reaching maximal values at weeks 7–8 post exposure.[28]

The diagnosis of acute schistosomiasis may often be challenging and thus delayed.[32] The most common symptoms of acute schistosomiasis, fever and gastrointestinal complaints, are the most common reported symptoms in paediatric returning travellers in general.[21,22,33–35] However, our results underline a few points that distinguish patients with acute schistosomiasis. First, the vast majority came back from Sub- Saharan Africa and were exposed to freshwater, emphasizing the importance of travel history. Second, the rate of respiratory symptoms in patients with acute schistosomiasis was exceptionally high (72%) compared with other returning paediatric travellers.[21,35] Two more characteristic features of acute schistosomiasis are the prolonged incubation time, and the multi-systemic presentation.[7]

This study has a few limitations. First, the data are retrospective and were collected for clinical purposes. Hence, symptoms details might be missing and laboratory follow-up in children was less adherent. Second, some of the patients were diagnosed on a clinical basis only and were treated empirically. In addition, the sample size is relatively small and therefore we may have missed some significant differences between paediatric and adult patients. However, the advantage of this study is the comparison between children and adults who experienced similar exposures.

In summary, schistosomiasis is highly infectious in endemic areas, and young travellers may exhibit the same syndrome as adults, with a multi-systemic presentation. It is required to inform travellers to endemic areas about the risk of freshwater exposure. Post-travel, it is important to closely review travel history and be aware of multi-systemic illness and eosinophilia among those returning from endemic areas, including children.

Conflict of interest

None declared.

Author contribution

S.R.—acquisition of data, analysis and interpretation of data and drafting the manuscript. E.L.—acquisition of data, analysis and interpretation of data, revision the manuscript. E.S.—study conception and design, analysis and interpretation of data, revision of manuscript.

References

1. Chitsulo L, Engels D, Montresor A, Savioli L. The global status of schistosomiasis and its control. *Acta Trop* 2000; **77**:41–51.
2. Colley DG, Bustinduy AL, Secor WE, King CH. Human schistosomiasis. *The Lancet* 2014; **383**:2253–64.
3. Bustinduy AL, Parraga IM, Thomas CL *et al.* Impact of polyparasitic infections on anemia and undernutrition among Kenyan children living in a Schistosoma haematobium-endemic area. *Am J Trop Med Hyg* 2013; **88**:433–40.
4. Touré S, Zhang Y, Bosqué-Oliva E *et al.* Two-year impact of single praziquantel treatment on infection in the national control programme on schistosomiasis in Burkina Faso. *Bull World Health Organ* 2008; **86**:780–7.
5. Kinung'hi SM, Magnussen P, Kaatano GM *et al.* Malaria and helminth co-infections in school and preschool children: a cross-sectional study in Magu district, north-western Tanzania. *PLoS One* 2014; **9**:e86510.
6. Wamachi J, Kioko JH, Ouma JW *et al.* Develops in utero in humans B cell sensitization to helminthic infection B cell sensitization to helminthic infection develops in utero in humans. *J Immunol Ref* 1998; **160**:3578–84.
7. Ross AG, Vickers D, Olds GR *et al.* Katayama syndrome. *Lancet Infect Dis* 2007; **7**:218–24.
8. Slobbe L, Demeyere TBJ, van Genderen PJJ *et al.* Ectopic cutaneous Schistosoma haematobium in the inguinal region. *J Travel Med* 2007; **26**:1–2.
9. Ross AGP, Bartley PB, Sleigh AC *et al.* Schistosomiasis. *N Engl J Med* 2002; **346**:1212–20.
10. Tamarozzi F, Gobbi F. Urinary bladder lesions in a migrant from Africa. *J Travel Med* 2019; **26**.
11. Bottieau E, Clerinx J, de Vega MR *et al.* Imported Katayama fever: clinical and biological features at presentation and during treatment. *J Infect* 2006; **52**:339–45.
12. Meltzer E, Artom G, Marva E *et al.* Schistosomiasis among Travelers : new aspects of an old disease. *Emerg Infect Dis* 2006; **12**:1696–700.
13. Leshem E, Maor Y, Meltzer E *et al.* Acute schistosomiasis outbreak: clinical features and economic impact. *Clin Infect Dis* 2008; **47**:1499–506.
14. Logan S, Armstrong M, Moore E *et al.* Short report: acute schistosomiasis in travelers: 14 years' experience at the hospital for tropical diseases, London. *Am J Trop Med Hyg* 2013; **Jun;88**: 1032–4.
15. Chunge CN, Chunge RN, Masinde MS, Atinga JN. An outbreak of acute schistosomiasis following a church retreat to Mwanza, Tanzania, 2008. *J Travel Med* 2011; **18**:408–10.
16. Clerinx J, Bottieau E, Wichmann D *et al.* Acute schistosomiasis in a cluster of travelers from Rwanda: diagnostic contribution of schistosome DNA detection in serum compared to parasitology and serology. *J Travel Med* 2011; **18**:367–72.
17. Gautret P, Mockenhaupt FP, Von Sonnenburg F *et al.* Local and international implications of schistosomiasis acquired in Corsica, France. *Emerg Infect Dis* 2015; **21**:1865–8.
18. Mendoza-Palomar N, Sulleiro E, Perez-Garcia I *et al.* Schistosomiasis in children: review of 51 imported cases in Spain. *J Travel Med* 2020; **27**:1–3.
19. Zammarchi L, Gobbi F, Angheben A *et al.* Schistosomiasis, strongyloidiasis and Chagas disease: the leading imported neglected tropical diseases in Italy. *J Travel Med* 2020; **27**.
20. Comelli A, Riccardi N, Canetti D *et al.* Delay in schistosomiasis diagnosis and treatment: a multicenter cohort study in Italy. *J Travel Med* 2020; **27**.
21. Hagmann S, Neugebauer R, Schwartz E *et al.* Illness in children after international travel: analysis from the GeoSentinel surveillance network. *Pediatrics* 2010; **125**:e1072–80.
22. Rabinowicz S, Schwartz E. Morbidity among Israeli paediatric travellers. *J Travel Med* 2017; **1**:24.
23. Casacuberta-Partal M, Janse JJ, van Schuijlenburg R *et al.* Antigen-based diagnosis of Schistosoma infection in travellers: a prospective study. *J Travel Med* 2020; **27**.
24. Cucchetto G, Buonfrate D, Marchese V *et al.* High-dose or multi-day praziquantel for imported schistosomiasis? A systematic review. *J Travel Med* 2019; **26**.
25. Soentjens P, Cnops L, Huyse T *et al.* Diagnosis and clinical Management of *Schistosoma haematobium – Schistosoma bovis* hybrid infection in a cluster of Travelers returning from Mali. *Clin Infect Dis* 2016; **63**:1626–9.
26. Visser LG, Polderman AM, Stuiver PC. Outbreak of schistosomiasis among Travelers returning from Mali, West Africa. *Clin Infect Dis* 1995; **20**:280–5.
27. Schwartz E, Kozarsky P, Wilson M, Cetron M. Schistosome infection among river rafters on Omo River, Ethiopia. *J Travel Med* 2005; **12**:3–8.
28. Cnops L, Huyse T, Maniewski U *et al.* Acute schistosomiasis with a S. Mattheei x S. Haematobium hybrid species in a cluster of 34 Travelers infected in South Africa. *Clin Infect Dis* 2020. https://pubmed.ncbi.nlm.nih.gov/32215659/ 12 December 2020, date last accessed.
29. Nicolls DJ, Kozarsky PE, Weld LH *et al.* Characteristics of schistosomiasis in travelers reported to the GeoSentinel surveillance network 1997-2008. *Am J Trop Med Hyg* 2008; **79**:729–34.
30. Schwartz E, Rozenman J, Perelman M. Pulmonary manifestations of early schistosome infection among nonimmune travelers. *Am J Med* 2000; **109**:718–22.
31. Martinez FD, Wright AL, Taussig LM *et al.* Asthma and wheezing in the first six years of life. The group health medical associates. *N Engl J Med* 1995 Jan 19; **332**:133–8.
32. Jauréguiberry S, Paris L, Caumes E *et al.* Acute schistosomiasis, a diagnostic and therapeutic challenge. *Clin Microbiol Infect* 2010; **16**:225–31.
33. Newman-Klee C, D'Acremont V, Newman CJ *et al.* Incidence and types of illness when traveling to the tropics: a prospective controlled study of children and their parents. *Am J Trop Med Hyg* 2007; **77**:764–9.
34. Herbinger K, Drerup L, Alberer M. Spectrum of imported infectious diseases among children and adolescents returning from the tropics and subtropics. *J Travel Med* 2012; **19**:150–7.
35. Hunziker T, Berger C, Staubli G *et al.* Profile of travel-associated illness in children, Zurich, Switzerland. *J Travel Med* 2012; **19**:158–62.