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Outbreak of *Schistosomiasis mansoni* in a Spanish dance and percussion ensemble acquired in the Republic of Guinea



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ABSTRACT

Introduction: Schistosomiasis is a neglected tropical disease endemic in 78 countries worldwide. The acute phase, commonly referred to as Katayama fever, is more frequently observed in travelers than in migrants. Despite significant progress in understanding its pathology, many aspects of this disease remain unclear, posing challenges to timely diagnosis and management.

Methods: This observational retrospective study was conducted at the National Referral Unit for Imported Tropical Diseases, located at Hospital La Paz-Carlos III in Madrid, Spain. The study included a total of 14 members of a dance and percussion ensemble that traveled to the Republic of Guinea from March 3 to March 18, 2023. Patients with confirmed or probable schistosomiasis were included in the analysis.

Results: Twelve patients had suspected acute schistosomiasis. Of these, 78.5% were female. The predominant clinical manifestations included fever (91.6%), eosinophilia (100%), acute diarrhea (91.6%), and abdominal pain (83.3%). All patients reported a history of freshwater exposure in Guinea. *Schistosoma* serology was positive in all cases, and stool samples from five patients revealed the presence of *Schistosoma mansoni* eggs. Acute symptoms were managed with corticosteroids, leading to clinical improvement in all cases. Thereafter, all patients were treated with praziquantel at a dose of 40 mg/kg/day, administered in two separate doses four weeks apart.

Conclusion: Freshwater exposure in tropical regions is the primary risk factor for acquiring schistosomiasis. Early diagnosis and treatment during the acute phase are crucial to prevent complications and long-term sequelae.

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Brote de esquistosomiasis aguda en un grupo de danza y percusión en la República de Guinea

RESUMEN

Introducción: La esquistosomiasis es una enfermedad tropical desatendida, distribuida en 78 países diferentes. La fase aguda se conoce como fiebre de Katayama y es más común en los viajeros que en los migrantes. A pesar de los años transcurridos desde su descubrimiento, aún se desconocen muchos aspectos de la enfermedad.

Palabras clave:

Esquistosomiasis

Fiebre de Katayama

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Métodos: Se realizó un estudio observacional retrospectivo en la unidad de referencia nacional de enfermedades tropicales importadas del Hospital La Paz-Carlos III de Madrid, España. Se incluyeron a los 14 viajeros de un grupo de danza y percusión que habían viajado a la República de Guinea del 3 al 18 de marzo de 2023. Se analizaron los datos de los pacientes con diagnóstico confirmado o probable de esquistosomiasis.

Resultados: Se incluyeron 12 pacientes con sospecha de esquistosomiasis aguda. El 78,5% eran mujeres. El 91,6% presentó fiebre, el 100% eosinofilia, el 91,6% diarrea aguda y el 83,3% dolor abdominal. Todos ellos tenían antecedentes de baños de agua dulce durante el viaje. La serología para esquistosoma fue positiva en el 100% de los casos y en 5 pacientes se detectaron huevos de *S. mansoni* en las heces. Los síntomas agudos fueron tratados con corticosteroides con mejoría clínica. Todos recibieron tratamiento con praziquantel (40 mg/kg/día) en 2 dosis diferentes separadas por 4 semanas.

Conclusión: El baño en agua dulce en zonas tropicales es la principal vía de infección para esquistosomiasis. Es importante diagnosticar la esquistosomiasis durante la fase aguda para tratarla lo antes posible y evitar futuras complicaciones.

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Introduction

Schistosomiasis is, together with strongyloides, the most prevalent neglected tropical disease worldwide affecting more than 230 million people.¹ Transmission occurs when cercariae, the larval form of the parasite, penetrate human skin during contact with contaminated freshwaters.² These larvae are released by specific freshwater snails, which serve as intermediate hosts.³ *Schistosoma* is a trematode and there are seven species that infect humans: *S. mansoni*, *S. haematobium*, *S. intercalatum*, *S. mekongi*, *S. japonicum*, *S. guineensis*, and *S. malayensis*. There have been reports of hybrid species infections (*S. mansoni*–*S. haematobium*, *S. haematobium*–*S. mattheei* and *S. haematobium*–*S. bovis*).⁴

The clinical manifestations of schistosomiasis differ between the acute and chronic phases and depend on the infecting *Schistosoma* species. In the chronic phase, the infection can present as hepatosplenic, intestinal, urogenital, pulmonary, or neurological disease—depending on the species involved. Katayama fever or acute schistosomiasis may present with a broad spectrum of symptoms three to eight weeks after the infection, related to migrating schistosomula and deposition of eggs.⁵ Most common symptoms are fever, cough, abdominal pain, headache, diarrhea, asthenia or skin lesions.⁶ An elevated eosinophil count (>450/μL) is often observed shortly after symptom onset.⁷ Symptoms can resolve spontaneously over a period of days to weeks.

Katayama fever is considered a systemic hypersensitivity reaction to circulating immune complexes and schistosome antigens. Initial treatment involves corticosteroids; however, there is no established guideline regarding the optimal corticosteroid dosage. Some guidelines and articles recommend to administer the first dose of praziquantel (40 mg/kg once) alongside prednisolone (1 mg/kg per day for 1–3 days) 8–12 weeks after freshwater exposure. A subsequent praziquantel regimen (40 mg/kg once) without corticosteroids is indicated 4–6 weeks after the first doses.^{13,5}

Diagnosing schistosomiasis during the acute phase can be challenging, as serological tests may yield negative.⁸ Microscopic examination for schistosome eggs in urine, feces, or tissue biopsies is a common diagnostic method, but it is only effective 30–50 days post-infection, once the parasites have matured and started oviposition.⁹ Molecular techniques, such as polymerase chain reaction (PCR), have a better sensitivity and specificity, although these are usually not available at most centers.¹⁰ Circulating cathodic antigen (CCA) and circulating anodic antigen (CAA) in urine or serum can aid in diagnosis.¹¹ The point-of-care CCA test is also utilized to monitor patients post-treatment to assess cure.¹²

Currently, there is no effective vaccine against schistosomiasis. Preventive measures primarily focus on avoiding contact with con-

taminated freshwater sources. Public health strategies, including mass drug administration, snail control, and health education, are essential components in the control and eventual elimination of schistosomiasis.¹⁴

Bearing in mind the gaps in diagnosis and management of acute schistosomiasis, here we detail a cluster of cases in a group of travelers that presented with Katayama fever to our clinic.

Methods

Retrospective observational study in the national referral unit of imported Tropical diseases in Hospital La Paz-Cantoblanco-Carlos III and Internal Medicine Department of Hospital de Villalba both located in Madrid, Spain. The study included all travelers from a dance and percussion ensemble that participated in a course in the Republic of Guinea between March 3 and March 18, 2023. Inclusion criteria required participants to have traveled with the group during these dates and to have tested positive for schistosomiasis. Individuals with negative serological or microscopic findings for *Schistosoma* were excluded.

Informed consent was obtained from all participants before data collection. Demographic and clinical data, including age, sex, medical history, prior travel to tropical regions, freshwater exposure history, total number of freshwater contact events, the date of the last exposure, symptom onset and type, laboratory parameters, imaging results, microbiological findings, treatments, and co-infections, were systematically recorded.

Microbiological diagnostics performed at Hospital La Paz-Cantoblanco-Carlos III included serological analysis using the *S. mansoni* IgG enzyme immunoassay (EIA) (Master-Labor, S.L., Madrid, Spain). Urine samples were examined microscopically using polycarbonate filters for eggs, while stool samples were analyzed microscopically after concentration with Parasep[®] tubes (Apacor, Berkshire, England, UK) and fixed with Alcorfix[®] (alcohol-based fixative). Screening for protozoa, including *Blastocystis* spp., *Cryptosporidium* spp., *Cyclospora cayentanensis*, *Dientamoeba fragilis*, *Entamoeba histolytica*, and *Giardia intestinalis*, was performed using the Allplex[™] GI-Parasite Assay (Seegene Inc., Seoul, Korea). For patients presenting with acute or subacute diarrhea, bacterial pathogens such as *Aeromonas* spp., *Campylobacter* spp., *Clostridium difficile* toxin B, *Salmonella* spp., *Shigella* spp., *Enteroinvasive Escherichia coli* (EIEC), *Vibrio* spp., and *Yersinia enterocolitica* were identified using the Allplex[™] GI-Bacteria (I) panel. Positive bacterial PCR results were further confirmed by direct culture of stool samples for identification and antibiogram preparation.

Molecular diagnosis was performed at Instituto de Salud Carlos III (ISCIII) by qPCR on stool samples from all 12 patients.

Between 1 and 6 stool samples perpatient were analyzed. DNA was extracted from 250 mg of stool using the QIAamp® PowerFecal® Pro DNA Kit in a QIAcube instrument following manufacturer's instructions. Extracted and purified DNA samples were eluted in 100 µL of PCR-grade water and kept at 4 °C until further molecular analysis. Primers and probes were designed to amplify the 121 bp tandem repeat sequence Sm1-7 (GenBank accession number M61098) as described previously.¹⁵ Reactions were performed in duplicate and using extraction blanks and qPCR blanks as control for cutoff calculation. 20 µL reactions contained 5 µL of DNA, 10 µL of Quantimix easy kit (Biotools), 1 µL of PrimeTime® standard qPCR Assay that included 500 nM of primers Fwd (CCACGCTCTCGCAAATAATCT and Rv (CAACCGTTCTATGAAAATCGTTGT) each and 300 nM of probe (FAM-TCCGAAACCACTGGACGGATTTTATGAT-TAMRA). Thermocycler settings consisted of an initial step of 2 min at 95 °C followed by 45 cycles of 15 s at 95 °C and 60 s at 60 °C. This analysis was also performed in a single sample of urine 7 (out of the total 12) patients, where DNA was extracted as described below.

Molecular diagnostics were conducted at the Instituto de Salud Carlos III (ISCIII) via quantitative PCR (qPCR) on stool samples collected from all 12 patients, with between one and six samples analyzed per individual. DNA was extracted from 250 mg of stool using the QIAamp® PowerFecal® Pro DNA Kit on a QIAcube instrument, following the manufacturer's protocol. Purified DNA was eluted in 100 µL of PCR-grade water and stored at 4 °C until further analysis. Primers and probes targeting the 121-bp tandem repeat sequence Sm1-7 (GenBank accession number M61098) were used for qPCR analysis as described previously. Each 20 µL reaction contained 5 µL of extracted DNA, 10 µL of Quantimix Easy Kit (Biotools), and 1 µL of PrimeTime® standard qPCR assay, comprising 500 nM forward (CCACGCTCTCGCAAATAATCT) and reverse (CAACCGTTCTATGAAAATCGTTGT) primers and 300 nM of FAM-labeled probe (TCCGAAACCACTGGACGGATTTTATGAT-TAMRA). Thermocycling conditions included an initial denaturation step at 95 °C for 2 min, followed by 45 cycles of 15 s at 95 °C and 60 s at 60 °C. This methodology was also applied to urine samples collected from seven patients, with one sample analyzed per patient. DNA from urine was extracted using the Quick-DNA Urine Kit, and qPCR targeting the Dra1 repetitive motif of *S. haematobium* was performed to rule out co-infections.⁷

Data analysis was conducted using SPSS® software. Ethical approval for the study was obtained from the Research Ethics Committee of Hospital La Paz (PI-5829).

Results

Between March 3 and 18, 2023, fourteen patients traveled together to the Republic of Guinea to participate in a dance and drumming course. Of these, two travelers were excluded from the study due to the absence of a schistosomiasis diagnosis. One of these patients presented with periorbital edema and acute diarrhea, symptoms she had experienced previously. Corticosteroid treatment led to symptom improvement. Diagnostic evaluations, including serology and blood PCR, ruled out schistosomiasis and *Loa loa* infections; no schistosoma eggs were detected in fecal or urine samples. A repeat serological test three months later remained negative. Despite compatible epidemiology and clinical manifestations, the patient did not receive praziquantel treatment, as she did not seroconvert on schistosoma serology.

Of the 12 cases, 10 were women (71.4%) with a median age of 45.8 years (SD 33–54). All participants were Spanish nationals residing in the province of Madrid. They were healthy except one of them who had a medical history of ulcerative colitis (not receiving immunosuppressive treatment). Seven patients reported prior traveling history to other countries such as Peru, Venezuela, Mex-



Fig. 1. Dubréka waterfalls.

Table 1
Presented symptoms during schistosomiasis acute phase.

Symptom (N = 12)	Presented (%)	No presented (%)
Fever (%)	11 (91.6%)	1 (8.4%)
Acute/subacute diarrhea (%)	11 (91.6%)	1 (8.4%)
Abdominal pain (%)	10 (83.3%)	2 (16.6%)
Myalgias (%)	8 (66.6%)	4 (33.3%)
Headache (%)	7 (58.3%)	5 (41.6%)
Chills (%)	6 (50%)	6 (50%)
Swimmer's itch (%)	4 (33.3%)	8 (66.6%)
Cough (%)	3 (25%)	9 (75%)
Skin lesions (%)	1 (8.4%)	11 (91.6%)
Swimmer's dermatitis (%)	0	12 (100%)
Haematuria (%)	0	12 (100%)

ico, Nepal, Cape Verde, Senegal and Republic of Guinea in 2019. Three had never traveled abroad, and data were missing for the remaining two. Notably, two individuals reported prior freshwater exposure: one in the Republic of Guinea and another in Cape Verde. Most travelers had attended a pre-travel consultation to receive international vaccines and antimalarial prophylaxis. However, none of the patients reported previous swimming or bathing in freshwater during their travels. Ten patients had taken anti-malarial prophylaxis during travel; however, two discontinued the medication due to possible side effects, while two others did not use prophylaxis.

During the travel, the median number of freshwater exposures in Dubréka waterfalls was three (SD 1–5). All participants swam at the beginning of the trip (between March 3 and 10), and six bathed again between March 14 and 17. Symptom onset occurred between April 1 and 26 (Fig. 1).

Four of them presented diarrhea and general malaise during the travel or in the immediate return. Presenting symptoms and blood parameters are summarized in Tables 1 and 2.

One patient developed skin lesions in the arms (Fig. 2).

Eosinophilia (>450 cells/µL) was observed in 100% of the patients. The highest recorded eosinophil count was 7800 cells/µL, with a median value of 2680 cells/µL (SD 7800–850 cells/µL).

An anteroposterior chest X-ray was performed on three patients who presented with respiratory symptoms (cough). No abnormalities were detected in two patients, while nonspecific alterations were noted in the other. Abdominal ultrasound examinations were conducted on eight patients, all of which yielded normal results (Fig. 3).

Serological and microbiological findings are summarized in Table 3.

Table 2
Alterations of blood parameters during schistosomiasis acute phase.

Parameter (normal values) (%)	High	Normal
Eosinophils (%)	12 (100%)	0
AST (0–40) (%)	8 (66.6%)	4 (33.3%)
ALT (0–35) (%)	10 (83.3%)	2 (16.6%)
GGT (0–38) (%)	7 (58.3%)	5 (41.6%)
LDH (100–190) (%)	9 (75%)	0 ^a
PCR (0–5) (%)	11 (91.6%)	1 (8.4%)

AST: aspartate aminotransferase, ALT: alanine transaminase, GGT: gamma-glutamyl transferase, LDH: lactate dehydrogenase, PCR: C-reactive protein.

^a In 3 cases the values are not available.



Fig. 2. Skin lesions during acute schistosomiasis.

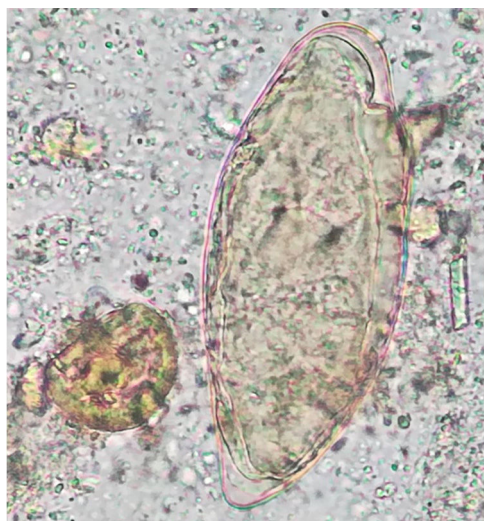


Fig. 3. Microscopy of *Schistosoma mansoni* egg.

Table 3
Diagnosis test used.

Test	Positive	Negative	Not performed
Serology (IgG, EIA)	12 (100%)	0	0
Feces <i>Schistosoma</i> eggs	5 (41.6%)	7 (58.3%)	0
Urine <i>Schistosoma</i> eggs	0	12 (100%)	0
Feces <i>Schistosoma</i> qPCR	11 ^a	1 (after Praziquantel)	0
Blood <i>Schistosoma</i> qPCR	4 ^a	5	3
Urine <i>Schistosoma</i> qPCR	1 (8.6%)	6	5

EIA: enzyme immunoassay.

^a One patient had undetermined result.

Prednisone (1 mg/kg) was prescribed upon the onset of symptoms for a duration of 5–12 days. The treatment duration was individualized based on the persistence of symptoms, cases generally received oral steroids until two days after symptoms resolved. In three patients who initially received corticosteroids for 5, 8, and 9 days, treatment was resumed for an additional five days due to symptom recurrence. After completing the course of treatment, all patients remained asymptomatic. One patient who was asymptomatic did not receive corticosteroid treatment.

All twelve patients received praziquantel (40 mg/kg in a single dose) alongside prednisone (1 mg/kg daily for three days) between May 12 and 26, except for one patient who had been treated earlier. A second dose of praziquantel (40 mg/kg, single dose) was administered without prednisone between June 12 and 27.

Co-infection with *Blastocystis hominis* was identified in five patients. Additionally, *Shigella* spp./EIEC was detected in fecal samples via PCR, and *Dientamoeba fragilis* was confirmed in one case using PCR.

Eosinophilia resolved in eleven patients one month after completing prednisone therapy. The patient with the highest eosinophil count (7800 cells/ μ L) demonstrated a reduction to 1200 cells/ μ L five months after the initial dose of prednisone. This patient was subsequently lost to follow-up, and no further evaluations were conducted. The remaining eleven patients were followed up for six months after treatment, during which they remained asymptomatic, had negative stool parasite tests, and exhibited normal eosinophil counts.

Discussion

Acute schistosomiasis is more commonly observed in travelers than in migrants, likely due to the latter’s chronic exposure leading to acquired immunity.¹⁶

We report a cohort of travelers who contracted schistosomiasis during the same trip. The probable transmission route was bathing in freshwater in sub-Saharan regions. Of the fourteen travelers, twelve contracted the disease, resulting in an infection rate of 85.7%, which is notably high. Previous studies have reported infection rates ranging from 69% to 97%.^{16,17}

The group spent several days at the beginning and end of their trip in Dubréka, a town immediately north of Conakry, and the intervening days on Roume Island. As of 2007, 38 districts in Guinea were endemic for schistosomiasis, with *S. mansoni* prevalence rates between 30% and 47%. The World Health Organization (WHO) has implemented prophylaxis and treatment campaigns using praziquantel; however, coverage did not reach 50% in 2018.¹⁸

Despite all fourteen individuals bathing in the same waterfalls, two did not become infected. Literature indicates that a single exposure can be sufficient to acquire schistosomiasis.¹⁹ All participants were travelers, not migrants, consistent with published data.^{16,20}

The interval between exposure and symptom onset ranged from 28 to 49 days, aligning with other reports.⁵

Fever and eosinophilia were the most common presentation of Katayama fever in our cohort. Although cough is typically a fre-

quent symptom of acute schistosomiasis, we only observed it in three patients, none of whom exhibited lung infiltrates on chest X-ray.⁷ Thoracic CT scans were not performed due to the self-limiting nature of the cough.

All patients had a positive serology for *Schistosoma*, however, in only five cases there were *S. mansoni* eggs detected in stools. The precise latency period between contamination and egg production remains uncertain. Detection of eggs in stool depends on the presence of worms in the venous plexus of the intestinal mucosa. It is estimated that mating occurs after 28–35 days, with egg excretion commencing after 40–50 days.²² In early-stage infections, such as Katayama fever, egg excretion is often limited or absent, therefore serology is the preferred diagnostic method for non-immune travelers.²¹

PCR-based detection of *Schistosoma* DNA in stool or urine is more sensitive than parasitological methods,²³ particularly in patients from non-endemic countries where the parasite burden may be lower.²⁴ In this patient cohort, stool PCR exhibited high sensitivity, with only one patient having negative results by both PCR and microscopy. Possible explanations for this negative result include single-sex infection or prior praziquantel treatment. Conversely, the sensitivity of PCR conducted on blood samples was relatively low, detecting *Schistosoma* DNA in only 5 out of 9 patients. A prospective multicenter European study using blood samples revealed PCR detection of acute *S. mansoni* infections in 35 out of 38 patients at initial presentation, showing a sensitivity of 92%.²⁵

Although *S. mansoni* eggs are occasionally found in urine, the identification of cell-free nucleic acids circulating in the blood and partially excreted into urine has introduced novel approaches to microbiological diagnosis, proving effective in *S. mansoni* detection.²⁶ However, in the reported group of travelers, only one out of 11 patients tested positive for *S. mansoni*-DNA in urine. DNA fragments from death cells that appearing in urine present relatively low molecular size fragments (100–200 bp) which should be considered when deciding on methods of DNA extraction and PCR designs. The amplification of small-sized amplicons or repetitive genomic sequences significantly enhances sensitivity.²⁶

In this series, treatment was based on the consensus statement for schistosomiasis of the Spanish society of infectious diseases and Clinical Microbiology (SEIMC) and Spanish Society of Tropical Medicine and International Health (SEM-TSI),²⁷ as well as the guidelines from the Centers for Disease Control and Prevention (CDC).²⁸ Notably, the 5-day prednisone regimen was insufficient for symptom control, as three patients required resumption of corticosteroid therapy after discontinuation. The longest treatment duration with prednisone was 14 days at a dosage of 1 mg/kg.

The praziquantel treatment regimen remains undefined and controversial. Some authors recommend weight-adjusted doses administered on a single day, while others advocate for two doses on consecutive days or 15 days apart. The recommended dosage for each *Schistosoma* species varies between studies.^{5,29,30}

Long-term follow-up of patients treated for schistosomiasis is essential to ensure infection resolution and prevent complications. While this cohort was monitored for six months, future studies should emphasize the need for extended follow-up protocols, particularly in different clinical or epidemiological contexts. Regular evaluations of eosinophilia, parasitological tests, and molecular diagnostics like PCR could help detect residual infections and improve treatment outcomes, contributing to better management strategies and disease control efforts.

This article underscores a critical public health concern regarding the emergence and spread of infectious diseases. Given that autochthonous schistosomiasis cases have been reported in Europe, specifically in Corsica, France,³¹ and in Almeria (Spain)³² physicians should maintain a high index of suspicion for this parasitic

disease to prevent individual disease progression, chronicity, and further transmission.

Pre-travel consultations are a valuable opportunity not only for vaccine administration but also for advising travelers on other risks associated with their destinations.²⁰

Conclusion

Katayama syndrome, an acute manifestation of schistosomiasis, predominantly affects non-immune individuals experiencing their initial infection. In our cohort of twelve patients, all presented with eosinophilia accompanied by nonspecific symptoms. Administration of prednisone proved highly effective in alleviating acute phase symptoms; however, some patients required more than the standard 10-day course to achieve complete symptom resolution. Treatment with praziquantel was well tolerated across the cohort. It is imperative that pre-travel consultations emphasize the importance of avoiding freshwater exposure in endemic regions to prevent schistosomiasis infection.

Author statements

Any author has any financial interests or connections.

Author contribution

All authors contributed equally to the writing and research of this article.

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Conflict of interest

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